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Conference Report

2024 Biomedtracker Datamonitor Healthcare Post-ASCO Report

June 2024

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Summary

The 2024 Annual Meeting of the American Society of Clinical Oncology (ASCO) was held in Chicago from May 31 - June 4, 2024. This post-meeting report features commentary from our analysts on key presentations at the conference as well as a compilation of all data events added to Biomedtracker in conjunction with the meeting.

As a reminder, our ASCO coverage will continue throughout the conference and beyond. Our coverage will include:

- **June 11 – Post-ASCO Webinar**
- **June 12 – Post-ASCO Podcast**

About the Author

Biomedtracker is an independent research service that offers proprietary clinical assessments and patient-based revenue forecasts of developmental drugs within a comprehensive and intuitive drug information database. Clients from the pharmaceutical, biotech, and investment industries rely on Biomedtracker for its insight on the likelihood of approval, commercial potential, and future data and regulatory catalysts for drugs within the competitive landscape of every important disease and indication. Over the last several years, Biomedtracker has become the leader in providing objective information alongside evidence based clinical assessments and investment research on pipeline drugs worldwide. For more information on getting direct access to Biomedtracker, please email clientservices@citeline.com.

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Onureg for Acute Myelogenous Leukemia (AML)

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - QUAZAR (Maintenance)
Market Group:	Oncology
Lead Company:	Bristol Myers Squibb Company (BMY)
Partner Companies:	N/A
Former Companies:	Celgene
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

An abstract entitled "A post-hoc analysis of outcomes of patients with acute myeloid leukemia with myelodysplasia-related changes (AML-MRC) who received oral azacitidine (Oral-AZA) maintenance therapy in the QUAZAR AML-001 study" was presented at the American Society of Clinical Oncology Annual Meeting on June 3, 2024.

Data in this event has been created solely from the abstract program.

Background

AML-MRC represents 25%–34% of all AML cases, and patients with this AML subtype generally have poor outcomes. In this subanalysis of the QUAZAR AML-001study, we report outcomes of patients with AML-MRC who received Oral-AZA vs placebo (PBO).

Methods

QUAZAR AML-001 was a phase 3 study of Oral-AZA maintenance therapy in patients with AML in first remission after intensive chemotherapy who were not eligible for hematopoietic stem cell transplantation (HSCT). Patients ≥ 55 years of age with AML and intermediate- or poor-risk cytogenetics received Oral-AZA 300 mg or PBO QD for 14 d per 28-d cycles. In this analysis, WHO 2008 criteria were used to identify patients with secondary AML and/or patients with AML-MRC (both groups are referred to as AML-MRC in this analysis). Data on mutational profiles at diagnosis were not available. Overall survival (OS) from time of randomization to time of death from any cause after censoring for HSCT, and relapse-free survival (RFS) from time of randomization, were calculated using the Kaplan–Meier method. Duration of measurable residual disease (MRD) negativity achieved on treatment was calculated from the first MRD-negative assessment.

Results

Overall, 101/472 patients had AML-MRC; 56/238 (23.5%) patients in the Oral-AZA arm and 45/234 (19.2%) patients in the PBO arm. Karyotype/cytogenetics data at diagnosis were available for 87/101 (86.1%) patients with AML-MRC and 331/371 (89.2%) patients with non-AML-MRC. A greater proportion of AML-MRC than non-AML-MRC patients had poor-risk cytogenetics (20/101 [19.8%] vs 46/371 [12.4%]), del(5q) (10/87 [11.5%] vs 9/331 [2.7%]), and monosomy 7/del(7q) (9/87 [10.3%] vs 14/331 [4.2%]). Median OS did not significantly differ in patients with AML-MRC vs non-AML-MRC in either treatment arm (Oral-AZA: 19.9 mo vs 25.1 mo, P = 0.2694; PBO: 14.8 mo vs 14.9 mo, P = 0.2099). In both treatment arms, the median RFS was inferior for patients with AML-MRC vs non-AML-MRC (Oral-AZA 7.5 mo vs 10.5 mo, P = 0.0430; PBO: 3.7 mo vs 4.9 mo, P = 0.0109). Oral-AZA significantly prolonged median OS and RFS, and the duration of MRD negativity for patients with AML-MRC compared with PBO (Table).

Conclusions

Oral-AZA significantly improved OS and RFS compared with PBO for patients with AML-MRC indicating that Oral-AZA maintenance is an effective treatment option for these patients with particularly poor prognosis.

Comment

AML-MRC is a common AML subtype, accounting for ~20-25% of AML cases and associated with low remission rates. Although there is no established standard of care for patients with this specific AML subtype, typical treatments include intensive chemotherapy and HSCT (for patients able to proceed to transplantation). Onureg, an oral formulation of azacitidine, remains the choice maintenance treatment across all AML subtypes, following its FDA approval in September 2020, based on results from the Phase III QUAZAR AML-001 trial for patients with AML in remission who are ineligible to receive HSCT. Onureg was the first maintenance treatment to show clinical benefits in AML.

Data from QUAZAR looking at a cohort of patients with the poorly prognostic AML-MRC subtype were presented at ASCO 2024 and highlight the benefits of maintenance Onureg in this subgroup of patients. Onureg's comparative benefit was emphasized by a prolonged median OS (19.9 months versus 14.8 months), as well as a prolonged RFS (7.5 months versus 3.7 months) in patients treated with Onureg versus the placebo group. The duration of MRD negativity among patients who were negative during the study or at baseline was also significantly longer for patients on Onureg (8.1 months) compared to placebo (0 months). As expected, however, non-AML-MRC patients had significantly better survival outcomes, but do not overshadow the benefits Onureg affords to patients with AML-MRC, for whom outcomes are typically poor.

While Onureg is still being investigated in combination with Venclexta in the Phase III VIALE-M trial for all-comers irrespective of HSCT suitability, these results highlight the importance of the clinical benefit offered so far by maintenance Onureg, supporting its continued uptake even in patients who generally have worse survival outcomes based on their disease subtype.

Source:

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 6522)
Citeline Analysis

Zanidatamab for Biliary Tract Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase IIb - HERIZON-BTC-01
Market Group:	Oncology
Lead Company:	Jazz Pharmaceuticals plc (JAZZ)
Partner Companies:	BeiGene (BGNE) Zymeworks (ZYME)
Former Companies:	N/A
Change to Likelihood of Approval:	1%
Likelihood of Approval:	96% (4% Above Avg.)
Average Approval:	92%

Jazz Pharmaceuticals announced long-term follow-up results from the Phase IIb HERIZON-BTC-01 clinical trial of zanidatamab in previously treated, unresectable, locally advanced, or metastatic HER2-positive biliary tract cancer (BTC). An abstract entitled "Zanidatamab in previously-treated HER2-positive (HER2+) biliary tract cancer (BTC): Overall survival (OS) and longer follow-up from the phase 2b HERIZON-BTC-01 study" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data from the study were last seen in January 2024.

Design

The trial evaluated zanidatamab (20 mg/kg IV once every 2 weeks) in patients with HER2-positive, locally advanced unresectable, or metastatic BTC who had received prior gemcitabine-containing therapy. Patients with prior HER2-targeted therapy use were excluded from the trial. All patients were required to have centrally confirmed HER2-amplified tumors (assessed by *in situ* hybridization). Patients (n=87) were assigned into two cohorts based on tumor IHC status: Cohort 1 (n=80) included patients who were IHC 2+/3+ (HER2-positive) and Cohort 2 (n=7) included patients who were IHC 0/1+. The median duration of follow-up was 21.9 (16-34) months. Tumors were assessed every 8 weeks per RECIST v1.1. Updated efficacy analyses include only Cohort 1, while safety analyses include Cohorts 1 and 2.

Endpoints

Per the abstract, the primary endpoint was cORR. Select secondary endpoints included duration of response (DoR), OS, and frequency and severity of adverse events (AEs). Updated efficacy analyses include only Cohort 1; safety analyses include Cohorts 1 and 2.

Results

As of July 28, 2023, data from HER2-positive BTC patients enrolled in Cohort 1 (n=80) demonstrated:

- With longer follow-up, the cORR was maintained from the initial analysis (n=33; 41.3%) (95% CI: 30.4, 52.8), with one additional complete response (n=2; 2.5%).
    - Although the trial was not designed to detect treatment effects by HER2 status, as previously reported, in a pre-planned subgroup analysis of cORR by HER2 expression, responses were observed in patients with IHC 3+ tumors (cORR: 51.6% [95% CI: 38.6%-64.5%]) and IHC 2+ tumors (cORR: 5.6% [95% CI: 0.1-27.3%]).
- A two-month increase in the median DoR to 14.9 months (95% CI: 7.4, not reached).
    - In patients with IHC3+ tumors, the median DoR was 14.9 months (95% CI: 7.4, not reached).
    - The DOR in the 1 responder with IHC 2+ tumors was 7.5 months.
- A median OS (95% CI) of 15.5 months (95% CI: 10.4, 18.5).
    - The median OS in patients with IHC 3+ was 18.1 months (95% CI: 12.2, 23.2).
    - The median OS in patients with IHC 2+ was 5.2 months (95% CI: 3.1, 10.2).
- Median progression-free survival (PFS) was maintained (5.5 months [95% CI: 3.6, 7.3]) compared with the initial analysis, which had a

data cutoff of October 10, 2022.

- In patients with IHC 3+ tumors, the median PFS was 7.2 months (95% CI: 5.4, 9.4) months.
- In patients with IHC 2+ tumors, the median PFS was 1.7 months (95% CI: 1.0, 3.3) months.

Most Common Adverse Events

As previously reported for Cohorts 1 and 2, zanidatamab demonstrated a manageable and tolerable safety profile, with no new safety signals identified and no deaths that were treatment related. TRAEs leading to dose reductions remained infrequent. Serious TRAEs occurred in eight (9.2%) patients. One patient experienced serious TRAEs since the initial analysis (alanine aminotransferase increased and aspartate aminotransferase increased).Treatment discontinuation rate was 2.3% and no additional patients discontinued treatment due to TRAEs since the initial analysis.

Conclusions

Results from this long-term analysis of the Phase IIb HERIZON-BTC-01 trial indicate that zanidatamab monotherapy demonstrated sustained and durable antitumor responses in previously treated patients with HER2-positive unresectable, locally advanced, or metastatic BTC and support the clinically meaningful benefit of continued treatment with zanidatamab. The safety profile in all enrolled patients remained manageable with favorable tolerability compared with the initial analysis. Two (2.3%) patients discontinued treatment due to treatment-related adverse events (TRAEs).

Comment

These updated results for Cohort 1 of the pivotal HERIZON-BTC-01 trial evaluating zanidatamab for second-line or later, unresectable, locally advanced, or metastatic *HER2*-amplified biliary tract cancer (BTC) continue to impress. Zanidatamab is a HER2-targeted bispecific antibody that binds to two distinct domains on HER2. Cohort 1 was the main cohort of the trial and enrolled patients with a HER2 status of IHC 3+ (n=62) or IHC2+ (n=18). Cohort 2 was an exploratory cohort that enrolled IHC 1+ (n=3) or IHC 0 (n=4) patients. Cohort 1 of the HERIZON-BTC-01 trial previously reported a confirmed ORR (cORR) of 41.3% and a median duration of response (mDOR) of 12.9 months in 80 patients. With longer follow-up, the cORR remains at 41.3% with one additional response deepening such that the CR rate increased from 1.25% to 2.5%. With longer follow-up (approximately two years), the mDOR increased from 12.9 months to 14.9 months and the median PFS was maintained at 5.5 months. Zanidatamab lead to a median OS of 15.5 months (18.1 months in patients with IHC 3+ tumors, 5.2 months in patients with IHC 2+ tumors).

In the press release, a physician associated with the company noted that historically the median OS for second-line patients treated with standard-of-care chemotherapy is 6-9 months so the OS of 18.1 months for patients with IHC 3+ tumors is very encouraging. The 5.2 months OS for patients with IHC 2+ tumors is less encouraging. Also lower for the IHC 2+ patients was the ORR (5.6% vs 51.6%) and the mDOR (1.7 vs 7.2 months) suggesting that if approved, zanidatamab may be reserved for IHC 3+ patients.

In April 2024, Enhertu received a tumor agnostic approval from the FDA supported by three Phase II trials from the DESTINY clinical development program including DESTINY-PanTumor02. The accelerated approval was for the treatment of patients with unresectable or metastatic HER2 positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options. At ASCO, results were presented from a 41-patient BTC cancer cohort of DESTINY-PanTumor02. The cohort included 16 IHC 3+ patients, 14 IHC 2+ patients, 3 IHC 1+ patients, and 7 IHC 0 patients. The ORR for the cohort was 22.0% with all of the responses in IHC3 + patients who reported an ORR of 56.3%. The IHC3+ patients also reported a mDOR of 8.6 months, a median PFS of 7.4 months, and a median OS of 12.4 months. Supported by the HERIZON-BTC-01 trial, zanidatamab is currently under priority review by the FDA for second-line HER2+ BTC with a PDUFA date of November 2024. If approved, zanidatamab will be the first HER2-targeted therapy specifically approved for BTC and will be favored over Enhertu due to its larger trial but also due to its more favorable safety profile. As we await the FDA decision, we are increasing the LOA by an additional 1%.

A confirmatory Phase III trial is enrolling first-line HER2+ BTC patients and is evaluating zanidatamab combined with CisGem chemotherapy with or without a PD-1/L1 inhibitor (either Keytruda or Imfinizi). Another Phase III trial, HERIZON-GEA-01, is expected to read-out in late 2024 and is evaluating zanidatamab in combination with chemotherapy with or without Beigene's PD-1 inhibitor Tevimbra for first-line, unresectable, locally advanced/metastatic gastroesophageal adenocarcinoma. Finally, a Phase III trial (EMPOWHER) has been announced for zanidatamab for HER2+ breast cancer patients who have progressed on Enhertu.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 4091)
PR Newswire 06/01/2024 (JAZZ)
Citeline Analysis

CG0070 for Bladder Cancer

Event Date:	06/02/2024
Event Type:	Trial Data - Final Results (Clinical Analysis)
Trial Name:	Phase II - CORE1 (w/Keytruda)
Market Group:	Oncology
Lead Company:	CG Oncology, Inc. (CGON)
Partner Companies:	ANI Pharmaceuticals (ANIP) Kissei Pharmaceutical (4547) Lepu Biopharma (2157) Novartis (NVS)
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	54% (10% Above Avg.)
Average Approval:	44%

CG Oncology announced final results from the Phase II CORE-001 clinical trial of its oncolytic immunotherapy candidate, cretostimogene, in combination with pembrolizumab for the treatment of BCG-Unresponsive, High-Risk Non-Muscle Invasive Bladder Cancer (HR-NMIBC) with Carcinoma in Situ (CIS) will be presented at the American Society of Clinical Oncology (ASCO) 2024 Annual Meeting. An abstract entitled "Final results of CORE-001: A phase-2, single arm study of cretostimogene grenadenorepvec in combination with pembrolizumab in patients with BCG-unresponsive, non-muscle invasive bladder cancer with carcinoma in situ" was presented at the meeting on June 2, 2024.

Data from this study were last seen in April 2023.

Context

The Phase II CORE-001 trial was conducted in collaboration with Merck Sharp & Dohme. The combination of cretostimogene and pembrolizumab received FDA Breakthrough Therapy Designation. Results to be presented are an update from previously reported data in the abstract.

Design

Per the abstract, 35 pts were treated with cretostimogene ($1x10^{12}$ viral particles) in combination with pembrolizumab at a dose of 400 mg IV q6 weeks. Cretostimogene induction was given as 6 weekly intravesical instillations followed by 3 weekly maintenance doses at months 3, 6, 9, 12, and 18. Pts with persistent CIS or high-grade Ta tumors at the 3mo assessment were eligible for re-induction. Pembrolizumab was administered for up to 24mo. Response assessments included cystoscopy, urine cytology, cross-sectional imaging, and mandatory bladder mapping biopsies at 12mo.

Endpoints

Per the abstract, the primary endpoint was CR at 12mo. Secondary endpoints included CR at any time, duration of response (DOR), CR at 24mo, cystectomy-free survival, and safety. Exploratory endpoints included analyses of baseline viral receptor expression, free E2F levels, PD-L1 status, urinary cytokine panels and measures of viral replication.

Results

- As of the data cutoff on February 5, 2024, the CR rate in the intention-to-treat (ITT) population at 12-months and any time, was 57% (20/35) [95% confidence interval (CI), 40-73%] and 83% (29/35) (95% CI, 70-95%), respectively. As of May 17, 2024, the CR rate in the ITT population at 24 months was 54% (19/35) (95% CI, 37-71%).
- Of the patients in a CR at 12 months, 95% of patients (19/20) maintained a CR for another 12 months.
- Median DoR has not been reached but exceeds 21 months.
- Additionally, the Kaplan-Meier estimates for CR rate at 12 and 24 months were 77.3% (95% CI, 58.1-88.5%) and 69.6% (95% CI,

49.4-83.0%), respectively.

- Progression-free survival (PFS) at 24 months is 100% with no patients progressing to muscle invasive cancer or metastatic disease; Cystectomy-free survival (CFS) at 24 months was 80%; for patients in CR, CFS at 24 months was 100%.

Most Common Adverse Events

- Treatment-related adverse events (TRAEs) were consistent with the individual agents and demonstrate no synergistic toxicity.

Conclusion

Per the abstract, the efficacy and safety of cretostimogene plus pembrolizumab for treatment of BCG-UR, HR NMIBC with CIS demonstrates best-in-class CR and DOR compared to current FDA-approved therapies, with an acceptable AE profile. Further investigation of this combination therapy is warranted.

Comment

These positive data for CG Oncology's cretostimogene grenadenorepvec from the Phase II CORE-001 study in combination with Keytruda represent a positive step forward as the oncolytic adenovirus seeks approval in high-risk NMIBC. Keytruda remains the current FDA-approved standard of care for high-risk unresponsive NMIBC, offering an opportunity to cretostimogene as a combination therapy to increase physician familiarity should it be approved for this indication.

In the proof-of-concept Phase II trial, an impressive CR of 82.9% at any time was observed for the cretostimogene-Keytruda combination, which compares favorably to Keytruda alone, which showed a 41% CR at any time in the single-arm Phase II KEYNOTE-057 trial. In addition, compared to a median duration of response of 16.2 months for Keytruda in KEYNOTE-057, the median DOR was not reached, but exceeded 21 months, and no progression to MIBC or metastatic disease was observed in CORE-001, which bodes well for cretostimogene's chances of approval and outlines the combination as a strong challenger to Keytruda alone in this setting, as well as more recently approved newcomers to the setting Adstiladrin and Anktiva. In addition, the BOND-003 pivotal Phase III trial is assessing cretostimogene monotherapy in BCG-refractory NIMBC patients. The promising efficacy demonstrated in preliminary studies such as CORE-001, however, prime the drug to corner a significant proportion of the market through leveraging the established familiarity of Keytruda, its novelty as a bladder-sparing option for treatment, and its favorable safety profile. We are therefore increasing the drug's LOA by 5%.

Source:

Globe Newswire 05/24/2024 (CGON)
American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract 4601)
Citeline Analysis

INB-200 for Brain Cancer (Malignant Glioma; AA and glioblastoma (GBM))

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase I - Newly Diagnosed GBM (University of Alabama at Birmingham)
Market Group:	Oncology
Lead Company:	IN8bio, Inc. (INAB)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	5% (Same As Avg.)
Average Approval:	5%

IN8bio presented preliminary clinical data of INB-200 at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago. An abstract entitled "INB-200: Fully enrolled phase 1 study of gene-modified autologous gamma-delta (γδ) T cells in patients with newly diagnosed glioblastoma multiforme (GBM) receiving maintenance temozolomide (TMZ)" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data in this event has been created solely from the abstract program.

Methods

The Phase I study assessed the safety and preliminary efficacy of the addition of DeltEx DRI gamma-delta T cells to maintenance therapy with TMZ. The trial assessed the administration of $1x10^7$ cells per dose across three different dosing regimens increasing from a single dose delivered on cycle 1 day 1 during maintenance in Cohort 1, to three doses delivered on day 1 of cycles 1-3 in Cohort 2, to six doses delivered on day 1 of cycles 1-6 in Cohort 3. Thirteen patients have been enrolled and treated with INB-200, including three patients in Cohort 1 (1 dose), four patients in Cohort 2 (3 doses) and six patients in Cohort 3 (6 doses).

Per the abstract, pohorts (C) 1, 2 and 3 received 1, 3 or 6 doses (1 x 107 DRI cells/dose) into the resection cavity with 150 mg/m2 of IV TMZ on Day (D) 1 of each Stupp maintenance cycle. The primary endpoint is safety and secondary endpoints include survival; immunologic correlative analyses are included. Dose limiting toxicities (DLTs) are defined as treatment related ≥ grade (G) 3 cardiopulmonary or hepatic toxicity, G4 toxicity exceeding 72 hours or neurologic deterioration that exceeds 2 weeks.

Results

The preliminary data demonstrated that 92% of evaluable patients treated with INB-200 exceeded a median PFS of 7 months (median follow-up: 11.7 months) with concomitant temozolomide (TMZ), as of a data cutoff date of May 30, 2024. The survival data along with radiographic improvements are indicative of positive treatment effects, which highlight the potential of IN8bio's genetically modified, chemotherapy-resistant gamma-delta T cells as a potential first-in-class therapy for patients with newly diagnosed glioblastoma (GBM).

- All patients who completed all protocol mandated doses surpassed a median standard-of-care PFS of 7 months, with a majority also exceeding the expected PFS based on their age and MGMT status of their tumors.
- 92% of evaluable patients treated with INB-200 for GBM exceeded a median PFS of 7 months achieved with the standard-of-care regimen (Stupp regimen).
- One patient with an IDH-mutant glioma remains alive and progression free at 34.9+ months; IDH-mutant patients in a recently published clinical trial of an IDH inhibitor demonstrated a median PFS of 11.1 months in the control arm and 28.5 months in the experimental arm.
- Preserved gamma-delta T cells were found in relapsed tumor 148 days after initial DRI infusion in one patient with paired biopsies, pointing to durability of DRI gamma-delta T cells.
- Radiographic evaluation pre- and post-treatment included resolution of midline shift in one patient with evidence of changes in enhancement attributed to treatment effect in multiple patients. One subject was found to have a 36% decrease in a lesion attributed to positivpe treatment effect.

Per the abstract, 23 patients were enrolled, with 11 dosed and 2 awaiting dosing (61% male; median age 68 (range: 21-74); 92% IDH-WT, 54% MGMT unmethylated). No DLTs, cytokine release syndrome (CRS) or neurotoxicity (ICANS) are reported. Most common adverse events were decreased WBC/platelet count, asthenia, fatigue, hydrocephalus, headache, decreased appetite, urinary tract infection, thrombosis and balance disorder. Conclusions:γδ T cells successfully infused with peripheral TMZ-based lymphodepletion evidenced with near or below normal range T, B, and NK subsets for up to 1 year. The majority of dosed patients who received DRI exceeded the expected median PFS of 7 months (5.8-8.2 months) with Stupp alone and had manageable toxicity with a continued trend in PFS. Long-term follow-up for durability of PFS and OS continue.

Most Common Adverse Events

- No treatment-related serious adverse events, dose-limiting toxicities, cytokine release syndrome, infusion reactions, or immune effector cell-associated neurotoxicity syndrome have been reported in any cohort.
- The most common treatment emergent adverse events were Grade 1-2 toxicities consisting of white blood cell and platelet count decreases related to standard-of-care TMZ.

Comment

With over 100,000 worldwide incident cases of glioblastoma (GBM) in 2023, this highly aggressive type of primary brain neoplasm remains very challenging to treat. The 5-year relative survival rates for GBM vary by age group and range from 5.6% in adults aged over 40 years, to 26% in adolescents and young adults, and while surgery, radiotherapy and chemotherapy can help in disease management, approximately 70% of GBM patients experience disease progression within one year.

IN8bio's INB-200 is a genetically modified autologous gamma-delta T cell product in development for newly diagnosed GBM. Gamma-delta T cells are a subset of immune cells with properties of both the innate and the adaptive immune system, hypothesized to be able to distinguish between healthy and cancer cells and kill the latter, as well as recruit and activate additional immune effector cells to the site of the tumor. They target NKG2D ligands, which are upregulated on tumor cells post-alkylating chemotherapy exposure. INB-200's gamma-delta T cells express MGMT, which is involved in resistance to alkylating drugs like temozolomide. The level of MGMT protein expression in glioma cells has been correlated to the alkylating agents' efficacy, and the methylation of the MGMT by temozolomide is the main contributor to the drug's cytotoxic effect.

Although coming from a small patient sample, the Phase I data presented at ASCO 2024 show the potential INB-200 (administered in the resection cavity at the same time as temozolomide maintenance) has in treating newly-diagnosed GBM patients, with most of the dosed patients achieving a median PFS of 7 months (although some exceeded this value). This, however, is the same as the median PFS currently achieved with radiotherapy and temozolomide, the standard of care in this setting, so for this novel therapy to pass any future regulatory hurdles and gain traction with prescribing physicians, it would need to better this outcome, especially as temozolomide is genericized.

While we await long-term follow-ups from this trial, the LOA for INB-200 remains unchanged.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 2042)
Globe Newswire 06/03/2024 (INAB)

Datopotamab Deruxtecan for Breast Cancer

Event Date:	05/31/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - I-SPY2.2
Market Group:	Oncology
Lead Company:	Daiichi Sankyo Co., Ltd. (4568)
Partner Companies:	AstraZeneca (AZN)
Former Companies:	N/A
Change to Likelihood of Approval:	-2%
Likelihood of Approval:	9% (2% Below Avg.)
Average Approval:	11%

	None	None	None	None	None	None
Treatment Description	HR+HER2-Immune-DRD- (RPS S1)	HR-HER2-Immune-DRD- (RPS S2)	HER2-Immune+ (RPS S3)	HER2-Immune-DRD+ (RPS S4)	HR+HER2-	HR-HER
Number of Patients	36	11	46	9	53	50
Number of Evaluable Patients	N/A	N/A	N/A	N/A	N/A	N/A
Estimated pCR Rate After Dato-DXd Alone *(Endpoint=Primary)*	0.02 ± 0.02 (P=0.00)	0.14 ± 0.06 (P=0.37)	0.34 ± 0.09 (P=0.24)	0.31 ± 0.12 (P=0.21)	0.09 ± 0.04 (P=0.10)	0.29 ± 0.07 (P=0.06

An abstract entitled, "Rates of pathologic complete response (pCR) after neoadjuvant datopotamab deruxtecan (Dato): Results from the I-SPY2.2 trial," was presented at the American Society of Clinical Oncology (ASCO) Annual Meeting on May 31, 2024.

Data summarized in this event are solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

I-SPY2.2 is a multicenter Phase II platform sequential multiple assignment randomized trial (SMART) evaluating novel experimental regimens in the neoadjuvant breast cancer setting. The novel therapy is given as first in a sequence (Block A), followed by standard chemo/targeted therapies (Block B/C) if indicated. The goal is to identify agents that lead to pCR after novel targeted agents alone, or in sequence with optimal therapy assigned based on the tumor response predictive subtype (RPS). RPS incorporates expression-based immune, DNA repair deficiency (DRD), and luminal signatures with hormone receptor (HR) and HER2 status to classify patients by subtype: S1: HR+HER2-Immune-DRD-; S2: HR-HER2-Immune-DRD-; S3: HER2-Immune+; S4: HER2-Immune-DRD+; S5: HER2+/non-Luminal; S6: HER2+/Luminal.

RPS S1, S2, S3 and S4 were eligible for assignment to datopotamab deruxtecan (Dato) in Block A. Patients (pts) were followed by MRI during treatment (at 3, 6 and 12 weeks after start of Blocks A and B). Predicted responders by MRI and biopsy at the end of Block A or B have the option of going to surgery early, otherwise they proceed to next treatment Block (B +/- C). Randomization to Block B includes a taxane-based regimen specific to the RPS, and options include S1: paclitaxel; S2 and S3: paclitaxel + carboplatin + pembrolizumab; S4: paclitaxel + carboplatin vs. paclitaxel + carboplatin + pembrolizumab. Patients who did not go to surgery after Block B proceeded to Block C (AC or AC + Pembrolizumab if HR-HER2-).

Endpoints

The primary endpoint is pCR. Efficacy is evaluated within each RPS and HR+HER2- and HR-HER2- signatures. To estimate the arm's efficacy as a standalone therapy, investigators use a Bayesian covariate-adjusted model to estimate the pCR rate and compare the posterior distribution to a subtype-specific fixed threshold. This model uses pCR data when available and MRI data when pCR is not. To estimate pCR rate in the context of a multi-decision treatment regimen, investigators use a Bayesian model based on if and when a pCR occurred in the trial. The posterior is compared to a subtype-specific dynamic control generated from historical I-SPY data.

Results

103 pts were randomly assigned to the Dato arm between August 2022 and August 2023. All patients have proceeded beyond Block A; 33 went to surgery after Dato alone.

Conclusion

Dato monotherapy was active, particularly in the HR-HER2- signature, but did not meet the prespecified threshold for graduation in I-SPY 2.2.

Comment

AstraZeneca and Daiichi Sankyo's potent TROP2-directed antibody-drug conjugate datopotamab deruxtecan (Dato-DXd) selectively delivers a potent topoisomerase I inhibitor payload directly into tumor cells. The drug has shown prior efficacy in the Phase I TROPION-PanTumor01 trial and the Phase III TROPION-Breast01 trial, which investigated use in the metastatic pretreated breast cancer space. In a bid to explore Dato-DXd's potential earlier in the treatment algorithm – and at tapping into an even more lucrative setting – the drug is now being investigated in the Phase II I-SPY2.2 trial in the neoadjuvant setting for women with high-risk clinical Stage II/III breast cancer. I-SPY2.2 is assessing the efficacy of Dato-DXd in sequence with standard chemotherapy to identify treatment strategies for subsets of breast cancer based on the molecular characteristics of the tumor. The primary endpoint is pathologic complete response (pCR), defined as elimination of invasive cancer in the breast and lymph nodes at the time of surgery .

Currently, neoadjuvant chemotherapy is frequently used in early-stage breast cancer, but similarly treated patients have highly varied tumor relapse rates, clinical outcomes, and survival. It was hoped that Dato-DXd as an addition to chemotherapy could increase patient outcomes in this setting, and help inform the treatment pathway based on the results of the different predictive molecular biomarkers. Unfortunately, the results of this trial show that Dato-DXd is not as efficacious as hypothesized. While 32% of patients who received the drug were able to skip traditional chemotherapy and progress straight to surgery, no subtype met the prespecified pCR thresholds, which would have allowed for progression to a Phase III trial. Dato-DXd was most active in patients with the immune-positive subtype (observed pCR rate of 0.31) and triple-negative breast cancer (TNBC) patients (observed pCR rate of 0.35), with the threshold set at 0.4 in these subtypes. In terms of safety, there were no new safety signals compared to those of TROPION-Breast01, and importantly no discontinuations due to toxicity.

The results of this study could provide some insight into the potential outcomes of the pivotal Phase III TROPION-Breast04 trial, which is investigating Dato-DXd in combination with Imfinzi in the neoadjuvant setting in TNBC and HER2-low breast cancer patients. Topline data are expected in 2028 on the dual primary endpoints of pCR and event-free survival, as well as on the secondary endpoints of OS and disease-free survival (DFS). The disappointing results from I-SPY2.2 do not necessarily indicate failure of the TROPION-Breast04 trial. For example, despite Imfinzi's nonsignificant increase in pCR rate in the Phase II GeparNUEVO trial, the addition of Imfinzi to neoadjuvant chemotherapy was associated with significant improvement in OS and DFS, which are the secondary endpoints of TROPION-Breast04.

While further late-phase data for Dato-DXd are awaited, AstraZeneca and Daiichi Sankyo will likely turn their focus back to the highly anticipated Phase III DESTINY-Breast11 trial, investigating Enhertu as a neoadjuvant therapy in patients with high-risk HER2-positive early-stage breast cancer, with data expected later in 2024. These data will likely set a benchmark for TROPION-Breast04. Given these disappointing results and the delayed Phase III data as compared to DESTINY-Breast11, we are decreasing Dato-DXd's LOA by 2%.

Source:

American Society of Clinical Oncology (ASCO) 05/31/2024 (Abstract LBA509)
Citeline Analysis

Scemblix for Chronic Myelogenous Leukemia (CML)

Event Date:	05/31/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - ASC4FIRST
Market Group:	Oncology
Lead Company:	Novartis AG (NVS)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

Novartis presented results from the pivotal Phase III ASC4FIRST trial as a late-breaking abstract at the 2024 American Society of Clinical Oncology (ASCO) meeting. An abstract entitled "ASC4FIRST, a pivotal phase 3 study of asciminib (ASC) vs investigator-selected tyrosine kinase inhibitors (IS TKIs) in newly diagnosed patients (pts) with chronic myeloid leukemia (CML): Primary results" was presented on May 31, 2024.

Data from this study were last seen in January 2024.

Context

The trial remains ongoing, with the next scheduled analysis at week 96 to evaluate the key secondary endpoint (MMR at week 96) and additional secondary endpoints. These results have been submitted to the US Food and Drug Administration (FDA) via the Oncology Center of Excellence Real-Time Oncology Review (RTOR) program and Scemblix has been granted Breakthrough Therapy Designation. They will also be presented as a plenary at the European Hematology Association (EHA) 2024 Congress in June. Results were also presented at an ASCO investor event on June 2, 2024.

Design

ASC4FIRST is a Phase III, head-to-head, multicenter, open-label, randomized study of oral Scemblix 80 mg QD vs. investigator-selected first- or second-generation TKIs (imatinib, nilotinib, dasatinib or bosutinib) in 405 adult patients with newly diagnosed Ph+ CML-CP.

Endpoints

The two primary endpoints of the study are to compare efficacy of asciminib vs. investigator-selected SoC TKIs and to compare efficacy vs. that of TKIs within the stratum of participants with imatinib as pre-randomization selected TKI, based on proportion of patients that achieve MMR at week 48. The study remains ongoing with key secondary endpoints of proportion of patients that achieve MMR at week 96 and a safety endpoint of discontinuation of study treatment due to an AE (TTDAE) by week 96. The study also assesses additional secondary safety and efficacy endpoints, including MMR, MR4, MR4.5, complete hematological response (CHR) and BCR::ABL1 ≤1% at and by all scheduled data collection time points; duration of and time to first MMR, MR4 and MR4.5; time to treatment failure; event-free survival, failure-free survival, progression-free survival and overall survival.

Results

Scemblix (asciminib) demonstrated superior major molecular response (MMR) rates at week 48 compared to investigator-selected standard-of-care (SoC) tyrosine kinase inhibitors (TKIs) imatinib, nilotinib, dasatinib and bosutinib, and compared to imatinib alone in patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP). Scemblix also showed a numerical improvement in MMR at week 48 vs. second-generation (2G) TKIs (nilotinib, dasatinib and bosutinib).

The median follow-up was 16.3 and 15.7 months for Scemblix and investigator-selected SoC TKIs, respectively. Nearly 20% more patients treated with Scemblix achieved MMR at week 48 vs. investigator-selected SoC TKIs, and nearly 30% more patients achieved MMR at week 48 vs. imatinib alone. Patients treated with Scemblix also achieved deeper rates of molecular responses (MR4 and MR4.5) compared with

investigator-selected SoC TKIs and imatinib alone.

Most Common Adverse Events

Additionally, Scemblix demonstrated a favorable safety and tolerability profile, with fewer adverse events (AEs) and treatment discontinuations vs. both imatinib and 2G TKIs. In newly diagnosed patients, the safety profile was consistent with previous registration studies with no new safety concerns observed. Fewer grade ≥3 AEs, dose adjustments to manage AEs, and half the rate of AEs leading to treatment discontinuation were reported for Scemblix vs. both imatinib and 2G TKIs.

Conclusion

Per the abstract, ASC is the only agent to show statistically significant superior efficacy and safety and tolerability vs all current standard-of-care front-line Tx, with potential to be the therapy of choice for CML.

Comment

Novartis will undoubtedly be rejoicing at the demonstration of Scemblix's superiority as a first-line agent compared to all other tyrosine kinase inhibitors (TKIs) on the market, including blockbuster Dasynoc. These primary analysis results from the Phase III ASC4FIRST trial demonstrate treatment with Scemblix to improve the 48-week major molecular response (MMR) rate by just shy of 20% (67.7% vs. 49%) compared to investigator-selected standard-of-care TKIs (imatinib, nilotinib, dasatinib, and bosutinib). Impressively, approximately 30% more patients achieved a 48-week MMR when treated with Scemblix compared to imatinib (69.3% vs. 40.2%), representing an unprecedented benefit. Although the second-generation TKIs have all demonstrated superiority over imatinib in their respective pivotal trials, the 48-week MMR benefit observed across these other trials sits approximately at the 20% mark, making these results from ASC4FIRST a considerable feat. As expected, the 48-week MMR benefit was less pronounced in the cohort that compared Scemblix to the second-generation TKIs, but nevertheless Scemblix still showed an 8% improvement over these reputably potent agents. While the trial was not powered to detect significance on this outcome, the numerical improvement supports the narrative that Scemblix can offer more durable and deeper responses for newly diagnosed CML patients compared to any of the TKIs currently on the market.

The safety profile of TKIs has a substantial influence on the agents' rankings within the CML market, and these safety data from ASC4FIRST continue to prime Scemblix to be the ideal candidate as the next standard-of-care treatment. Importantly, in these results, Scemblix demonstrated a favorable safety and tolerability profile, with fewer adverse events and treatment discontinuations versus both imatinib and second-generation TKIs. The importance of a positive safety profile in securing a label expansion into the front-line setting has been exemplified by Iclusig's turbulent attempt. The drug was initially considered to be the most potent TKI, and hopes were high for its potential as a front-line agent; however, following the discontinuation of the Phase III EPIC trial due to alarmingly high rates of arterial thrombotic events, the cost of Iclusig's high potency became apparent with unjustifiable safety risks. Considering this, there were concerns that ASC4FIRST may reveal Scemblix to face similar toxicity issues as Iclusig. However, altogether these results serve to dispel doubts on the STAMP inhibitor's benefit/risk profile and highlight Scemblix to have the potential to become the next standard-of-care treatment for newly diagnosed CML patients.

While the results mark another impressive win for CML drug pioneers Novartis, uptake of Scemblix in the front-line setting may be more lackluster than the data predict due to the impending genericization of the CML market. Despite demonstrating superiority over Gleevec, both Sprycel and Tasigna have struggled due to price competition with imatinib generics. Moreover, both of these second-generation TKIs have looming patent cliffs, with Tasigna already off-patent in the US. Considering this, price competition in a soon-to-be genericized market may hinder Scemblix's otherwise anticipated rapid ascent to standard of care, especially in cost-conservative settings. To overcome this, the drug will need to be afforded positive recommendations by health technology assessment bodies such as NICE. However, regardless of these uptake barriers, the positive data from ASC4FIRST will certainly still be celebrated by Novartis as a victory in bringing Scemblix closer to a label expansion and advancing on the company's strategy to offset anticipated generic erosion to Tasigna.

Source:

Globe Newswire 05/31/2024 (NVS)
American Society of Clinical Oncology (ASCO) 05/31/2024 (Abstract LBA6500)
Investor Presentation 06/02/2024 (NVS)
Citeline Analysis

Keytruda for Colorectal Cancer (CRC)

Event Date:	06/02/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - NEOPRISM-CRC (UK)
Market Group:	Oncology
Lead Company:	Merck & Co., Inc. (MRK)
Partner Companies:	DRI Capital
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Treatment	Treatment	Treatment
Treatment Description	TMB High or Medium	TMB Low	All Patients
Number of Patients	31	1	32
Number of Evaluable Patients	N/A	N/A	N/A
Intent-to-treat pCR Rate ***(Endpoint=Primary)***	55 %	0 %	53 %
Evaluable Tumours pCR Rate ***(Endpoint=Primary)***	59 %	0 %	58 %

The abstract entitled, "NEOPRISM-CRC: Neoadjuvant pembrolizumab stratified to tumour mutation burden for high risk stage 2 or stage 3 deficient-MMR/MSI-high colorectal cancer," was presented at the 2024 American Society of Clinical Oncology (ASCO) Annual meeting on June 2, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Context

Longer follow up is needed to assess relapse free survival and translational biomarker work is ongoing.

Design

The trial population included patients (pts) with operable high-risk stage 2 or stage 3 dMMR/MSI-High CRC. Pts with tumours that were TMB high or medium (≥6 mutations/Mb on FoundationOneCDx test) received 3 cycles of pembrolizumab (200mg every 3 weeks) and underwent surgery within 4-6 weeks of last cycle. Pts with TMB low tumours (≤5 mutations/Mb) underwent surgery 4-6 weeks after 1 cycle of pembrolizumab. The trial also incorporated translational endpoints to explore relationships between possible predictive novel biomarkers and response to pembrolizumab in blood, tumour tissue and microbiome. Researchers required 19 pts with TMB high or medium tumours to detect a pCR after 3 cycles of neoadjuvant pembrolizumab of 33% (minimum of 10%), with one-sided 5% significance level and 80% power (A'Hern single stage). The trial would be considered a success if ³5/19 of those pts achieved pCR. To achieve this number, researchers aimed to recruit 32 patients in total.

Endpoints

The primary end point was pathological complete response rate (pCR). Secondary endpoints included 3-year relapse free survival, overall

survival, safety, and health-related quality of life.

Results

The trial opened on July 20, 2022 and 32 pts were rapidly enrolled. The pCR primary endpoint analysis was performed on March 1, 2024. The primary endpoint was exceeded with the pCR in the intent to treat pts (N=32) as well as the pCR in evaluable tumours. Median TMB was 42 mutations/Mb (4-82). There was only 1 TMB low tumour and no TMB medium tumours. In the TMB high-medium cohort there were 32 evaluable resected tumours as 1 pt had 3 synchronous primaries, and 1 pt did not undergo surgery due to toxicity as well as pt choice. At a median follow-up of 6 months (range 2-15), no pts have had disease recurrence.

Most Common Adverse Events

There were no immune-related toxicities >Grade 3.

Conclusion

Neoadjuvant pembrolizumab for early stage deficient-MMR/MSI-High CRC is highly efficacious and safe.

Comment

Administering checkpoint inhibition before surgery, known as neoadjuvant therapy, presents a promising approach to treating bulky but operable cancers. The strategy can lead to high pathologic response rates, which are associated with better survival outcomes, and it is postulated that the higher the tumor mutational burden, the better the response. In the NICHE trial, neoadjuvant Opdivo + Yervoy treatment led to a pathological complete response (pCR) of 60% in dMMR colon cancer patients.

The Phase II NEOPRISM-CRC trial prospectively used tumor mutation burden (TMB) as a potential biomarker for clinical benefit to immunotherapy, as this is commonly used in the advanced/metastatic setting but not in the early stages of the disease. Thirty-two symptomatic CRC patients were stratified based on TMB, with medium or high TMB patients planned to receive three cycles of neoadjuvant Keytruda, and low TMB patients planned to receive only one cycle. The trial, however, had no medium TMB patients, with the vast majority being TMB high (n = 31). Surgery was performed 4-6 weeks after the last Keytruda cycle, with two patients receiving adjuvant chemotherapy with FOLFOX or CAPOX.

The trial showed that nine weeks of neoadjuvant Keytruda was effective in downstaging high-risk Stage II and III dMMR/MSI-high CRC, with 59% of patients (all high TMB) experiencing a pathological CR. At the median follow-up of 9.7 months, none of the treated patients had relapsed and the trial is currently being expanded to a 3-year relapse-free survival endpoint.

Treatment with Keytruda was safe, with no grade 5 events and with only 2% of patients experiencing a grade 3 immune-related adverse event. Given the setting, the trial also looked any surgical complications, and as highlighted by the presenter, there were few such complications and all were manageable. One patient did not proceed to surgery following Keytruda treatment and died for pneumonia six months later.

Neoadjuvant chemoradiotherapy is the current standard of care for early-stage/locally-advanced colon and rectal cancer, with immune checkpoint inhibitors Opdivo (with or without Yervoy), Keytruda and Jemperli (rectal cancer only) being recommended by the NCCN guidelines as neoadjuvant treatment options for dMMR/MSI-H patients. With up to 15% early-stage CRC patients harboring dMMR/MSI-H tumors, this is a commercially significant population, and the data presented at ASCO 2024 strengthens the case for the use of Keytruda in this setting.

Source:

American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract LBA3504)
Citeline Analysis

Etrumadenant for Colorectal Cancer (CRC)

Event Date:	06/02/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase Ib/II - ARC-9 (w/zimberelimab/FOLFOX +/- bevacizumab)
Market Group:	Oncology
Lead Company:	Arcus Biosciences, Inc. (RCUS)
Partner Companies:	Gilead Sciences (GILD) Otsuka (4578)
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	16% (5% Above Avg.)
Average Approval:	11%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Regorafenib	Etrumadenant + Zimberelimab + mFOLFOX-6 ± Bevacizumab **(EZFB)**	EZFB vs. Regorafenib
Number of Patients	37	75	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Median Progression-Free Survival ***(Endpoint=Primary)***	2.1 Months	6.2 Months	N/A (P<0.0001)
Median Overall Survival ***(Endpoint=Secondary)***	9.5 Months	19.7 Months	N/A (P=0.0003)
Comfirmed Objective Response Rate ***(Endpoint=N/A)***	2.7 %	17.3 %	N/A

Gilead Sciences and Arcus Biosciences announced new data from Cohort B of ARC-9, a Phase Ib/II study evaluating the safety and efficacy of etrumadenant, a dual A2a/b adenosine receptor antagonist, plus anti-PD-1 monoclonal antibody zimberelimab, FOLFOX chemotherapy and bevacizumab (EZFB) in third-line metastatic colorectal cancer (mCRC). An abstract entitled, "ARC-9: A randomized study to evaluate etrumadenant based treatment combinations in previously treated metastatic colorectal cancer (mCRC)," was presented at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 2, 2024.

Context

Data from Cohort A will be presented when they are mature.

Design

ARC-9 is a Phase Ib/II trial evaluating the safety and efficacy of etrumadenant (E), a dual A2a/A2b adenosine receptor antagonist, plus anti-PD-1 antibody zimberelimab (Z), FOLFOX and bevacizumab (if not contraindicated) in three cohorts of patients with mCRC.

Cohort B enrolled patients who previously progressed on both oxaliplatin- and irinotecan-containing chemotherapy in combination with anti-VEGF (R) therapy or anti-EGFR. Patients were randomized 2:1 to the etrumadenant plus zimberelimab regimen: E (150 mg orally [PO] once daily [QD]) + Z (240 mg intravenous [IV] once every 2 weeks [Q2W]) + mFOLFOX-6 + bevacizumab (5 mg/kg IV Q2W), or regorafenib (administered at a starting dose of 80 mg/day for the first week, followed by a dose escalation of 40 mg every week to 120 mg/day for the second week and 160 mg/day for the third week during Cycle 1 followed by 160 mg/day on Days 1-21 of each subsequent 28-day cycle). Patients who progressed on regorafenib were allowed to crossover to the etrumadenant plus zimberelimab regimen.

ARC-9 is a multi-cohort study in mCRC including Cohort A, which enrolled patients who previously progressed on FOLFOX/FOLFIRI in combination with anti-VEGF(R) or anti-EGFR. Patients were randomized 2:1 to the etrumadenant plus zimberelimab regimen, or FOLFOX-6 + bevacizumab.

Endpoints

The primary endpoint is PFS per RECIST 1.1, and OS is a key secondary endpoint.

Results

Cohort B of ARC-9 randomized 112 patients with comparable baseline characteristics between two arms: EZFB or regorafenib. At the time of data cut-off (November 13, 2023) median follow-up was 20.4 months. Patient baseline characteristics were similar to those of third-line patients who have progressed on oxaliplatin- and irinotecan-based regimens in mCRC. OS and PFS were consistently longer in the EZFB arm versus regorafenib, in all sub-groups analyzed, including in patients with liver metastases.

Per the abstract, EZFB demonstrated statistically significant improvement in PFS (HR 0.27, 95% CI 0.17-0.43, p<0.0001) and OS (HR 0.37, 95% CI 0.22-0.63, p=0.0003) vs regorafenib.

Most Common Adverse Events

The EZFB regimen had a safety profile consistent with the known safety profiles of each individual molecule to date, without unexpected toxicities. A higher percentage of patients treated with regorafenib (17%) had a treatment emergent adverse event (TEAE) leading to discontinuation of all study drugs than those treated with EZFB (5%). A lower percentage of patients experienced Grade ≥3 TEAEs attributed to etrumadenant or zimberelimab versus regorafenib (23.0% vs 25.7%).

Conclusion

Per the abstract, in this randomized Phase II clinical trial, EZFB significantly improved efficacy outcomes compared to rego in refractory mCRC pts previously treated with 5-FU, oxaliplatin and irinotecan regimens with no unexpected toxicities. Further investigation of this regimen is warranted given the clinically meaningful PFS and OS improvement.

Comment

Arcus Biosciences' etrumadenant is the first dual A2a/A2b adenosine receptor antagonist designed to maximally inhibit the adenosine-driven impairment of tumor-infiltrating lymphocytes (mainly CD8+ T cells and NK cells) and myeloid cells (dendritic cells, macrophages), mediated by A2aR and A2bR, respectively. Developed specifically for the oncology setting, etrumadenant achieves high penetration of tumor tissue, robust potency in the presence of high adenosine concentrations, and minimal shift in potency from non-specific protein binding. It is currently being evaluated in multiple trials across different indications, including prostate, NSCLC, and pancreatic cancers. Zimberelimab is a monoclonal antibody that binds to PD-1 on T/NK cells, preventing PD-L1-mediated immunosuppressive effects and resulting in tumor cell death. Since an anti-PD-1 molecule and A2R antagonists have complementary mechanisms of action and showcase synergistic effects, zimberelimab was in-licensed by Arcus to enable the development of precision combination regimens to be used in various registrational studies across different oncology indications.

Encouraging PFS and OS results from cohort B patients in the Phase II trial evaluating etrumadenant combined with zimberelimab and FOLFOX/bevacizumab regimens in the third-line treatment setting have brought hope for metastatic colorectal cancer (mCRC) patients with limited treatment options. The impressive results that will be presented at ASCO 2024, derived from a substantial patient sample size, underscore the need for further investigation of this promising regimen. Additionally, the trial compared this regimen against Stivarga, one of the current standards of care in this setting.

The standards of care for third-line mCRC patients include Stivarga, Fruzaqla, and Lonsurf either alone or with bevacizumab. The median PFS for these regimens ranges from 1.5 to six months, while the objective response rate (ORR) lies between 1% and 7%. In comparison, etrumadenant combined with zimberelimab and FOLFOX/bevacizumab regimens has demonstrated highly efficacious outcomes, with mPFS of 6.2 months and an ORR of 17.3%. Maintaining quality of life is also a crucial goal for third- and later-line treatments for mCRC patients. Despite the high rates of adverse events and increased hospitalizations due to treatment-related serious adverse events,

Fruzaqla achieved regulatory approval because of its promising efficacy (ORR of 1.7% and median PFS of 3.7 months) in this patient population with significant unmet need. Therefore, the future for the etrumadenant/ zimberelimab combination also looks promising. Additionally, the trial data indicate no unexpected toxicities and a safety profile comparable to that of Stivarga, but it will need to be monitored closely for widespread patient adoption. With Stivarga carrying a black box warning for severe hepatic toxicity, it would be interesting to see whether the etrumadenant/zimberelimab/bevacizumab/FOLFOX combination can offer a safer treatment option.

A substantial gap exists in addressing the treatment needs of mCRC patients irrespective of mutation status. Our epidemiology estimates a potential patient pool exceeding 40,000 individuals in 2023 in the US and five major European markets (France, Germany, Italy, Spain, and the UK) alone, representing a significant commercial opportunity. Therefore, given the favorable results, coupled with the substantial unmet need and the sizable addressable patient population, etrumadenant combined with zimberelimab has the potential to achieve significant success in this segment of CRC treatment.

Based on these results, we are raising etrumadenant's and zimberelimab's LOAs by an additional 5%.

Source:

American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract 3508)
Business Wire 06/02/2024 (GILD, RCUS)
Citeline Analysis

Zimberelimab for Colorectal Cancer (CRC)

Event Date:	06/02/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase Ib/II - ARC-9 (w/zimberelimab/FOLFOX +/- bevacizumab)
Market Group:	Oncology
Lead Company:	Arcus Biosciences, Inc. (RCUS)
Partner Companies:	Gilead Sciences (GILD) Harbin Gloria Pharmaceuticals (002437) Ligand (LGND) Strata Taiho WuXi Biologics (2269)
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	16% (5% Above Avg.)
Average Approval:	11%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Regorafenib	Etrumadenant + Zimberelimab + mFOLFOX-6 ± Bevacizumab **(EZFB)**	EZFB vs. Regorafenib
Number of Patients	37	75	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Median Progression Free Survival **95% CI** ***(Endpoint=Primary)***	2.1 Months	6.2 Months	N/A (P<0.0001)
Median Overall Survival **95% CI** ***(Endpoint=Secondary)***	9.5 Months	19.7 Months	N/A (P=0.0003)
Comfirmed Objective Response Rate **90% CI** ***(Endpoint=N/A)***	2.7 %	17.3 %	N/A

Gilead Sciences and Arcus Biosciences announced new data from Cohort B of ARC-9, a Phase Ib/II study evaluating the safety and efficacy of etrumadenant, a dual A2a/b adenosine receptor antagonist, plus anti-PD-1 monoclonal antibody zimberelimab, FOLFOX chemotherapy and bevacizumab (EZFB) in third-line metastatic colorectal cancer (mCRC). An abstract entitled, "ARC-9: A randomized study to evaluate etrumadenant based treatment combinations in previously treated metastatic colorectal cancer (mCRC)," was presented at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 2, 2024.

Context

Data from Cohort A will be presented when they are mature.

Design

ARC-9 is a Phase Ib/II trial evaluating the safety and efficacy of etrumadenant (E), a dual A2a/A2b adenosine receptor antagonist, plus anti-PD-1 antibody zimberelimab (Z), FOLFOX and bevacizumab (if not contraindicated) in three cohorts of patients with mCRC.

Cohort B enrolled patients who previously progressed on both oxaliplatin- and irinotecan-containing chemotherapy in combination with anti-VEGF (R) therapy or anti-EGFR. Patients were randomized 2:1 to the etrumadenant plus zimberelimab regimen: E (150 mg orally [PO] once daily [QD]) + Z (240 mg intravenous [IV] once every 2 weeks [Q2W]) + mFOLFOX-6 + bevacizumab (5 mg/kg IV Q2W), or regorafenib (administered at a starting dose of 80 mg/day for the first week, followed by a dose escalation of 40 mg every week to 120 mg/day for the second week and 160 mg/day for the third week during Cycle 1 followed by 160 mg/day on Days 1-21 of each subsequent 28-day cycle). Patients who progressed on regorafenib were allowed to crossover to the etrumadenant plus zimberelimab regimen.

ARC-9 is a multi-cohort study in mCRC including Cohort A, which enrolled patients who previously progressed on FOLFOX/FOLFIRI in combination with anti-VEGF(R) or anti-EGFR. Patients were randomized 2:1 to the etrumadenant plus zimberelimab regimen, or FOLFOX-6 + bevacizumab.

Endpoints

The primary endpoint is PFS per RECIST 1.1, and OS is a key secondary endpoint.

Results

Cohort B of ARC-9 randomized 112 patients with comparable baseline characteristics between two arms: EZFB or regorafenib. At the time of data cut-off (November 13, 2023) median follow-up was 20.4 months. Patient baseline characteristics were similar to those of third-line patients who have progressed on oxaliplatin- and irinotecan-based regimens in mCRC. OS and PFS were consistently longer in the EZFB arm versus regorafenib, in all sub-groups analyzed, including in patients with liver metastases.

Per the abstract, EZFB demonstrated statistically significant improvement in PFS (HR 0.27, 95% CI 0.17-0.43, p<0.0001) and OS (HR 0.37, 95% CI 0.22-0.63, p=0.0003) vs regorafenib.

Most Common Adverse Events

The EZFB regimen had a safety profile consistent with the known safety profiles of each individual molecule to date, without unexpected toxicities. A higher percentage of patients treated with regorafenib (17%) had a treatment emergent adverse event (TEAE) leading to discontinuation of all study drugs than those treated with EZFB (5%). A lower percentage of patients experienced Grade ≥3 TEAEs attributed to etrumadenant or zimberelimab versus regorafenib (23.0% vs 25.7%).

Conclusion

Per the abstract, in this randomized Phase II clinical trial, EZFB significantly improved efficacy outcomes compared to rego in refractory mCRC pts previously treated with 5-FU, oxaliplatin and irinotecan regimens with no unexpected toxicities. Further investigation of this regimen is warranted given the clinically meaningful PFS and OS improvement.

Comment

Arcus Biosciences' etrumadenant is the first dual A2a/A2b adenosine receptor antagonist designed to maximally inhibit the adenosine-driven impairment of tumor-infiltrating lymphocytes (mainly CD8+ T cells and NK cells) and myeloid cells (dendritic cells, macrophages), mediated by A2aR and A2bR, respectively. Developed specifically for the oncology setting, etrumadenant achieves high penetration of tumor tissue, robust potency in the presence of high adenosine concentrations, and minimal shift in potency from non-specific protein binding. It is currently being evaluated in multiple trials across different indications, including prostate, NSCLC, and pancreatic cancers. Zimberelimab is a monoclonal antibody that binds to PD-1 on T/NK cells, preventing PD-L1-mediated immunosuppressive effects and resulting in tumor cell death. Since an anti-PD-1 molecule and A2R antagonists have complementary mechanisms of action and showcase synergistic effects, zimberelimab was in-licensed by Arcus to enable the development of precision

combination regimens to be used in various registrational studies across different oncology indications.

Encouraging PFS and OS results from cohort B patients in the Phase II trial evaluating etrumadenant combined with zimberelimab and FOLFOX/bevacizumab regimens in the third-line treatment setting have brought hope for metastatic colorectal cancer (mCRC) patients with limited treatment options. The impressive results that will be presented at ASCO 2024, derived from a substantial patient sample size, underscore the need for further investigation of this promising regimen. Additionally, the trial compared this regimen against Stivarga, one of the current standards of care in this setting.

The standards of care for third-line mCRC patients include Stivarga, Fruzaqla, and Lonsurf either alone or with bevacizumab. The median PFS for these regimens ranges from 1.5 to six months, while the objective response rate (ORR) lies between 1% and 7%. In comparison, etrumadenant combined with zimberelimab and FOLFOX/bevacizumab regimens has demonstrated highly efficacious outcomes, with mPFS of 6.2 months and an ORR of 17.3%. Maintaining quality of life is also a crucial goal for third- and later-line treatments for mCRC patients. Despite the high rates of adverse events and increased hospitalizations due to treatment-related serious adverse events, Fruzaqla achieved regulatory approval because of its promising efficacy (ORR of 1.7% and median PFS of 3.7 months) in this patient population with significant unmet need. Therefore, the future for the etrumadenant/ zimberelimab combination also looks promising. Additionally, the trial data indicate no unexpected toxicities and a safety profile comparable to that of Stivarga, but it will need to be monitored closely for widespread patient adoption. With Stivarga carrying a black box warning for severe hepatic toxicity, it would be interesting to see whether the etrumadenant/zimberelimab/bevacizumab/FOLFOX combination can offer a safer treatment option.

A substantial gap exists in addressing the treatment needs of mCRC patients irrespective of mutation status. Our epidemiology estimates a potential patient pool exceeding 40,000 individuals in 2023 in the US and five major European markets (France, Germany, Italy, Spain, and the UK) alone, representing a significant commercial opportunity. Therefore, given the favorable results, coupled with the substantial unmet need and the sizable addressable patient population, etrumadenant combined with zimberelimab has the potential to achieve significant success in this segment of CRC treatment.

Based on these results, we are raising etrumadenant’s and zimberelimab's LOAs by an additional 5%.

Source:

American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract 3508)
Business Wire 06/02/2024 (GILD, RCUS)
Citeline Analysis

Opdivo for Colorectal Cancer (CRC)

Event Date:	06/02/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - CheckMate 8HW
Market Group:	Oncology
Lead Company:	Bristol Myers Squibb Company (BMY)
Partner Companies:	Ono Pharmaceutical (4528:JP)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Difference Between Treatment and Comparator
Treatment Description	Nivolumab + Ipilimumab vs. Chemptherapy
Number of Patients	N/A
Number of Evaluable Patients	255
Median Progression-Free Survival - HR ***(Endpoint=Primary)***	0.21 (P<0.0001)
Median Progression-Free Survival 2 - HR ***(Endpoint=Primary)***	0.27

Bristol Myers Squibb presented an abstract entitled "Nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) as first-line (1L) treatment for microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Expanded efficacy analysis from CheckMate 8HW" at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 2, 2024.

Data from the study were last seen in January 2024.

Design

Pts with unresectable or mCRC and MSI-H/dMMR status by local testing were enrolled across different lines of therapy and randomized 2:2:1 to NIVO (240 mg) + IPI (1 mg/kg) Q3W (4 doses, then NIVO 480 mg Q4W), NIVO (240 mg) Q2W (6 doses, then NIVO 480 mg Q4W), or chemo ± targeted therapies; treatments continued until disease progression or unacceptable toxicity (all arms) or for up to 2 years (NIVO ± IPI arms). In pts with blinded independent central review (BICR)–documented progression with chemo, crossover to NIVO + IPI was permitted.

Endpoints

Dual primary endpoints were PFS by BICR per RECIST v1.1 for NIVO + IPI vs chemo (1L) and NIVO + IPI vs NIVO (all lines) in pts with centrally confirmed MSI-H/dMMR mCRC. PFS2 (time from randomization to progression after subsequent systemic therapy, initiation of second subsequent systemic therapy, or death) was a key exploratory endpoint.

Results

Among 303 pts randomized to NIVO + IPI (n = 202) or chemo (n = 101), 171 pts in the NIVO + IPI arm and 84 pts in the chemo arm had centrally confirmed MSI-H/dMMR. At 31.5-months (mo) median follow-up (range 6.1–48.4), NIVO + IPI demonstrated superior PFS vs chemo (HR 0.21; 97.91% CI 0.13–0.35; *P*< 0.0001). Subsequent systemic therapy was received by 20 (12%) and 57 (68%) pts in the NIVO + IPI and chemo arms, respectively. In the chemo arm, 56 (67%) pts received subsequent immunotherapy (39 [46%] crossed over to NIVO + IPI on

study; 17 [20%] received non-study immunotherapy). Median PFS2 was not reached (NR) with NIVO + IPI and 29.9 mo with chemo (HR 0.27; 95% CI 0.17–0.44).

Most Common Adverse Events

Any grade and grade 3/4 treatment-related adverse events (TRAEs) are presented. Treatment-related deaths were reported for 2 pts in the NIVO + IPI arm.

Conclusion

Clinical benefit with 1L NIVO + IPI vs chemo was maintained after subsequent therapy, as shown by improved PFS2 in pts with centrally confirmed MSI-H/dMMR mCRC. No new safety concerns were identified with NIVO + IPI. These results further support NIVO + IPI as a standard-of-care 1L treatment option for pts with MSI-H/dMMR mCRC.

Comment

Positive interim results from the CheckMate 8HW trial, particularly in terms of PFS, bring renewed hope for patients with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC), who have limited treatment options. This market is primarily dominated by Keytruda, with some competition from Jemperli. Based on the CheckMate 142 trial, Opdivo was recommended for use in this patient population at any line of therapy, either as a monotherapy or in combination with the CTLA-4 inhibitor Yervoy. However, Keytruda gained wide acceptance in the front-line setting due to the larger population size in the KEYNOTE-177 trial and its use of an active comparator arm with the current standard of care (FOLFOX + Avastin/bevacizumab or Erbitux), limiting Opdivo's adoption in the first-line treatment setting.

Interim clinical data from the CheckMate 8HW trial that will be presented at ASCO 2024 provide promising insights and come from a sizable evaluable population of 303 first-line patients, a similar sample size to that of KEYNOTE-177 (n=307). The comparator arm in CheckMate 8HW, however, consists of investigator’s choice of chemotherapy, which is not as clinically relevant as a comparator as that used in KEYNOTE-177. It is important to note that the final analysis of KEYNOTE-177 showed that the median OS was not reached with Keytruda (vs. 36.7 months for the pooled comparator arms), with a median PFS of 16.5 months (vs. 8.2 months in the chemotherapy arm). Thus, combined data from CheckMate 142 and interim results from CheckMate 8HW support the use of Opdivo + Yervoy as a standard-of-care first-line treatment option for patients with MSI-H/dMMR mCRC. The combination’s potential for success is constrained by the fact that MSI-H/dMMR tumors account for only 5% of mCRC patients. Therefore, to achieve substantial commercial success in this segment of CRC treatment, the final results of the CheckMate 8HW trial need to be outstanding to replace Keytruda as the preferred treatment option.

Source:

Business Wire 05/23/2024 (BMY)
American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract 3503)
Citeline Analysis

PolyPEPI1018 for Colorectal Cancer (CRC)

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - OBERTO 301 - w/Atezolizumab
Market Group:	Oncology
Lead Company:	Treos Bio Limited
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	16% (5% Above Avg.)
Average Approval:	11%

Treos Bio presented results from the Phase II OBERTO-301 study of the PolyPEPI1018, in combination with atezolizumab in patients with late-stage microsatellite stable metastatic colorectal cancer (MSS mCRC) at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. The abstract entitled "A phase II, multicenter, open-label study of polyPEPI1018 in combination with atezolizumab in participants with relapsed or refractory microsatellite-stable metastatic colorectal (MSS mCRC) cancer (Oberto-301)" was presented at the Meeting on June 1, 2024.

Design

OBERTO-301 is a multicenter, open-label, Phase II clinical trial, conducted at the Mayo Clinic in Minnesota, Florida and Arizona, evaluating the combination treatment of PolyPEPI1018 and atezolizumab in patients with MSS mCRC who have progressed on two or three prior treatment regimens. The study enrolled 18 patients with refractory non-MSI-H metastatic colorectal cancer who were administered PolyPEPI1018 (1.2 mg) and atezolizumab (1,200 mg) every three weeks. Of these 44% had active liver metastasis.

Per the abstract, patients received PolyPEPI1018 (1.2 mg, sc) and atezolizumab (1,200 mg, iv) Q3W until disease progression or unacceptable toxicity. A Simon 2-stage design was applied. 18 patient (66% female) were enrolled for stage 1 of the study. Median age was 54 years (range 38–79), 50% had liver metastases and 67% received at least 3 lines of prior therapies.

Endpoints

The primary endpoint of the study is the incidence and severity of treatment-related adverse events. Secondary endpoints include objective response rate, duration of response, progression-free survival, and overall survival.

Results

- **Survival Benefits:** The median overall survival (mOS) was 12.8 months (95% CI 8.8 – NE) and the 12-months survival was 60%; this compares favorably to the historical data of 7.1 months and 27% respectively for atezolizumab monotherapy in a similar patient population. Differences between the survival of patients with and without liver metastasis were not statistically significant (HR: 0.58 [95% CI 0.18 – 1.90]; P=0.36):
  - Patients without active liver metastases (NLM) had a 12-month overall survival (OS) estimate of 67% and a median OS of 16.5 months.
  - Patients with active liver metastases (LM) had a 12-month OS estimate of 50% and a median OS of 8.6 months.
- **Progression-Free Survival (PFS) and Disease Control Rate (DCR)**: The median PFS was 2.7 months (95% CI 1.4-4.0), and the DCR was 61%. No tumor responses by RECIST 1.1 were observed.
- **Immune Response and Tumor Microenvironment:** PolyPEPI1018-specific CD8+ and/or CD4+ T cell responses were detected in 13 out of 16 subjects (ex vivo FluoroSpot), complemented by humoral responses against multiple PolyPEPI1018-antigens. Patients with available biopsy pairs (n=8) showed significant increases in average PD-L1 expression (IC%, p=0.029) and CD8+ tumor infiltrating lymphocytes (TILs, p=0.019) post-treatment, demonstrating an immune conversion from ‘cold’ to ‘hot’ tumor.

- **Correlation with PFS and Immunological Markers**: Patients with increased PFS (>12 weeks) showed significant increases in both post-treatment PD-L1 expression (p=0.007) and TILs (p=0.016) versus patients with PFS ≤ 12 weeks. Pre-treatment levels were not prognostic.
- **T Cell Responses and Survival**: Patients with CD8+ T cell responses had improved OS compared to patients with poor immunological responses (HR=0.13, p=0.022).

Most Common Adverse Events

PolyPEPI1018 in combination with atezolizumab was well tolerated, with no unexpected toxicities or serious adverse events related to treatment.

Per the abstract, most common side effect related to treatment was Grade (Gr) 1-2 local skin reaction (n=22). Gr 2 events (n=2) at least possibly related to treatment were nausea, pyrexia and increased blood alkaline phosphatase. There were no Gr 3-5 events or study discontinuation due to treatment AE.

Conclusions

Correlative data showing that the combination of PolyPEPI1018 and atezolizumab actually increased TILs and PD-L1 expression, which correlated with improved PFS.

Comment:

Treos Bio's PolyPEPI1018 is a ready-to-use vaccine composed of multiple peptides that trigger targeted immune responses to eliminate a wide range of cancer cells while sparing healthy ones. The vaccine comprises six lab-made polypeptides combined with the adjuvant Montanide, aiming to stimulate T cell reactions against 12 specific epitopes from seven cancer testis antigens commonly found in colorectal cancer. Promising results on OS and PFS from this Phase II trial assessing PolyPEPI1018 in the third-line or later treatment setting have instilled hope for microsatellite stable metastatic colorectal cancer (MSS mCRC) patients with few treatment alternatives. The consistent findings from three separate clinical trials - OBERTO-101, OBERTO-201, and OBERTO-301 - conducted in various MSS mCRC scenarios underscore the potential advantages of integrating PolyPEPI1018 into existing care protocols or incorporating it into a chemotherapy-free immunotherapy combination to address treatment-resistant MSS mCRC. OBERTO-101, OBERTO-201 demonstrated that this vaccine can prompt immune responses in both the body's periphery and within tumors, effectively transforming 'cold' tumors into 'hot' ones in early and advanced stages of MSS mCRC. This led to the exploration of combining PolyPEPI1018 with PD-(L)1 inhibitors such as Tecentriq as a potential treatment strategy in MSS mCRC.

It should be acknowledged, however, that these trials involved relatively small patient cohorts, . and further investigation involving larger patient groups is necessary to confirm and build upon these findings.

A substantial gap exists in addressing the treatment needs of CRC patients with microsatellite stable (MSS) tumors, comprising over 80% of metastatic colorectal cancer (mCRC) cases. Our epidemiology estimates a potential patient pool exceeding 20,000 individuals in 2023 for PolyPEPI1018 in the third-line and beyondtreatment settings in the US and EU5 alone, representing a significant commercial opportunity. Therefore, given the favourable preliminary results, coupled with the substantial unmet need and the sizable addressable patient population, PolyPEPI1018 has the potential to achieve significant success in this segment of CRC treatment.

Based on these results, we are raising PolyPEPI1018 LOA by 5%.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 3594)
American Society of Clinical Oncology (ASCO) 06/01/2024 (Poster 3594)
Globe Newswire 06/03/2024 (Treos)

Adcetris for Diffuse Large B-Cell Lymphoma (DLBCL) - NHL

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - ECHELON-3
Market Group:	Oncology
Lead Company:	Pfizer Inc. (PFE)
Partner Companies:	Takeda Pharmaceutical (TAK)
Former Companies:	Seagen (SGEN)
Change to Likelihood of Approval:	2%
Likelihood of Approval:	48% (4% Above Avg.)
Average Approval:	44%

	Placebo	Treatment
Treatment Description	Placebo + Lenalidomide + Rituximab	Adcetris + Lenalidomide + Rituximab
Number of Patients	118	112
Number of Evaluable Patients	N/A	N/A
Overall Survival (OS) ***(Endpoint=Primary)***	8.5 Months (P=0.0085)	13.8 Months (P<0.0001)
Median Progression-Free Survival (PFS) ***(Endpoint=Secondary)***	2.6 Months (P=0.0001)	4.2 Months (P<0.0001)
Overall Response Rate ***(Endpoint=Secondary)***	41.5 %	64.3 %
Complete Response Rate	18.6 %	40.2 %

Pfizer announced that data from the Phase III ECHELON-3 study of ADCETRIS were presented in an oral presentation entitled "Brentuximab vedotin in combination with lenalidomide and rituximab in patients with relapsed/refractory diffuse large B-cell lymphoma: Results from the phase 3 ECHELON-3 study" at the American Society of Clinical Oncology (ASCO) annual meeting on June 01, 2024.

Data from the study were last seen in March 2024.

Context

ADCETRIS is approved in the U.S. as monotherapy or in combination with chemotherapy for seven lymphomas including certain types of cHL.

Design

ECHELON-3 is an ongoing, randomized, double-blind, multicenter Phase III study evaluating ADCETRIS plus lenalidomide and rituximab versus lenalidomide and rituximab plus placebo in adult patients with relapsed/refractory DLBCL, regardless of CD30 expression, who have received two or more prior lines of therapy and are ineligible for stem cell transplant or CAR-T therapy. In this global study, 230 patients were randomized across North America, Europe and Asia-Pacific.

Per the abstract, patients with R/R DLBCL received BV+R2 or placebo+R2 (randomized 1:1). Pts received BV (1.2 mg/kg) or placebo q3w, R (375 mg/m^2) q3w, and len (20 mg) qd. The preplanned IA was performed at 134 OS events with a prespecified efficacy boundary of

2-sided P=0.0232.

Endpoints

The primary endpoint is OS in the intent-to-treat population, with key secondary endpoints of PFS and ORR as assessed by investigator. Other secondary endpoints include complete response rate, duration of response, safety and tolerability.

Results

Among 230 randomized patients in the trial, the interim analysis showed that median OS in patients randomized to receive ADCETRIS, lenalidomide and rituximab was 13.8 months (95% CI: 10.3-18.8) compared to 8.5 months (95% CI: 5.4-11.7) in patients randomized to lenalidomide and rituximab plus placebo. The study showed that the ADCETRIS combination reduced patients' risk of death by 37% compared to placebo in combination with lenalidomide and rituximab (HR 0.63 [95% CI: 0.445-0.891] p=0.0085). The overall survival benefit was consistent across levels of CD30 expression.

Median progression-free survival (PFS) was 4.2 months (95% CI: 2.9-7.1) in the ADCETRIS arm versus 2.6 months (95% CI: 1.4-3.1) in the lenalidomide and rituximab plus placebo arm (HR 0.527 [95% CI: 0.380-0.729] p<0.0001). The overall response rate for patients treated with the ADCETRIS regimen was 64.3% (95% CI: 54.7-73.1) versus 41.5% (95% CI: 32.5-51.0) in the lenalidomide and rituximab plus placebo arm. The complete response rate was 40.2% in ADCETRIS-treated patients (95% CI: 31.0%, 49.9%) compared to 18.6% (95% CI:12.1%, 26.9%) in the lenalidomide and rituximab plus placebo arm.

Per the abstract, 230 patients were randomized: 112 to BV+R2 and 118 to R2; all but 2 patients (both in R2 arm) received ≥1 dose of study drug. Median age was 71 yrs (range, 21-89), 56.5% were male, and 10.9% had an ECOG of 2. Median prior lines of therapy was 3 (range, 2-8); 29% had prior CAR T-cell therapy and 68% were CD30- (<1% CD30 tumor expression). At median follow-up of 16.4 months (mos) (range, 0.1-31.5) (cut-off: January 22, 2024), median OS benefit was consistent across key subgroups. In CD30+ vs CD30- subgroups, ORR/CR was 72.2%/38.9% vs 60.5%/40.8% with BV+R2, respectively, and 50.0%/26.3% vs 37.5%/15.0% with R2, respectively.

Most Common Adverse Events

The most frequently reported treatment-emergent adverse events (TEAEs) grade 3 or higher for the ADCETRIS versus placebo arms were: neutropenia (43% vs 28%), thrombocytopenia (25% vs 19%) and anemia (22% vs 21%). Peripheral sensory neuropathy was infrequent and low grade for each arm with grade 3 events of 4% vs 0%.

Per the abstract, the safety profile of BV+R2 was tolerable vs R2: grade (gr) ≥3 treatment-emergent adverse events (TEAEs) were 88% vs 77%, serious TEAEs were 60% vs 50%, and gr 5 TEAEs were 12% vs 8%, respectively. Most common TEAEs were neutropenia (46% vs 32%), anemia (29% vs 27%), and diarrhea (31% vs 23%). Rates of peripheral neuropathy for BV+R2 vs R2 were 31% vs 24% (all gr) and 6% vs 2% (gr 3). Median treatment duration was 3.6 mos with BV+R2 vs 2.0 mos with R2.

Conclusion

Per the abstract, treatment with BV+R2 triplet, compared to R2, demonstrated significant and clinically improvements in all key efficacy outcomes including OS in high-risk subgroups, with manageable safety.

Comment

These positive results in a Phase III trial should assure approval of this Adcetris regimen for third-line or later DLBCL and provide a new option for patients who are ineligible for CAR-T therapy or a bispecific antibody due to prior treatment exposure, co-morbidities, or access issues. The positives of this trial include having demonstrated significantly improved OS and PFS, although we note that the median PFS of 4.2 months for Adcetris combined with lenalidomide and rituximab is still very modest. Other positives include that a subgroup analysis showed activity in both CD30-positive and CD30-negative patients. For example, the complete response (CR) rate was 40.8% and 38.9% in CD30-negative (n=76) and CD30-positive (n=36) patients, respectively. Finally, this trial enrolled a highly pretreated population of patients who had a median of three prior lines of therapy, including ~55% who were primary refractory, ~30% with prior CD19 CAR-T therapy, ~15% with a prior bispecific antibody, and ~12% with a prior transplant. One drawback to this study is that the comparator, lenalidomide + rituximab, is not commonly used for DLBCL.

The Adcetris regimen also had some concerning safety signals. Compared to the lenalidomide + rituximab arm, the Adcetris arm reported higher rates of grade 5 adverse events (12% vs. 8%), as well as higher rates of peripheral neurotoxicity (31% vs. 24%).

If this regimen is approved, we expect that it will compete with Polivy combined with bendamustine + rituximab, Monjuvi combined with lenalidomide, and Zynlonta monotherapy. Monjuvi and Zynlonta were approved based on single-arm trials, while Polivy was approved based on a randomized Phase II trial. While Monjuvi was approved by the FDA for transplant-ineligible second-line or later patients, the other two agents were approved for third-line or later patients. For comparison, the CR rates (as reported on the FDA label) for the

Polivy and Monjuvi combinations were 40% and 37%, respectively, while Zynlonta reported a CR rate of 25%. The Polivy label notes that 48% of patients had a duration of response (DOR) of at least 12 months. The Monjuvi and Zynlonta labels list median DORs of 21.7 months and 10.3 months, respectively. For comparison, the median DOR for the Adcetris combination was 8.3 months vs 3.0 months for lenalidomide + rituximab (in patients with a CR, the median DOR was 18.9 months vs. not reached, respectively).

In the current treatment algorithm, third-line or later patients who have progressed on (or are ineligible for) CAR-T therapy or bispecifics end up cycling between all three of these regimens. If the Adcetris combination is approved, it will provide another option, albeit one with a novel target and that is supported by Phase III data.

As we await regulatory submissions, we are increasing the LOA by an additional 2%.

Source:

Business Wire 06/01/2024 (PFE)
American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract LBA7005)
Citeline Analysis

Zimberelimab for Gastric Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase II - EDGE-Gastric w/Domvanalimab
Market Group:	Oncology
Lead Company:	Arcus Biosciences, Inc. (RCUS)
Partner Companies:	Gilead Sciences (GILD) Harbin Gloria Pharmaceuticals (002437) Ligand (LGND) Strata Taiho WuXi Biologics (2269)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	44% (Same As Avg.)
Average Approval:	44%

Gilead Sciences and Arcus Biosciences announced longer-term efficacy and safety results from Arm A1 of the Phase II EDGE-Gastric study of various combinations of the Fc-silent anti-TIGIT antibody domvanalimab plus the anti-PD-1 monoclonal antibody zimberelimab and chemotherapy for the treatment of gastric cancer at the American Society of Clinical Oncology (ASCO) meeting. The abstract entitled "EDGE-Gastric Arm A1: Phase 2 study of domvanalimab, zimberelimab, and FOLFOX in first-line (1L) advanced gastroesophageal cancer" was presented on June 1, 2024.

Data from the study were last seen in November 2023.

Context

The updated data from Arm A1 of the Phase II EDGE-Gastric study support the ongoing Phase III STAR-221 study, in unresectable or metastatic upper GI cancers, which is expected to complete enrollment in the middle of 2024.

Design

The ongoing, multi-arm, multi-cohort global Phase II EDGE-Gastric trial is evaluating the safety and efficacy of various combinations of the Fc-silent anti-TIGIT antibody domvanalimab and the anti-PD-1 monoclonal antibody zimberelimab in patients with locally advanced unresectable or metastatic gastric (G), gastroesophageal junction (GEJ) or esophageal (E) adenocarcinoma. Patients in Arm A1, with previously untreated G/GEJ/E adenocarcinoma, received 1600 mg of domvanalimab intravenously (IV) every four weeks (Q4W) plus 480 mg of zimberelimab IV Q4W + FOLFOX (oxaliplatin 85 mg/m2 IV, leucovorin 400 mg/m2 IV, fluorouracil 400 mg/m2 IV bolus + 2400 mg/m2 continuous 46-48-hour IV infusion) every two weeks.

Results

At data cutoff (DCO, March 12, 2024), safety and efficacy were evaluated in all patients enrolled and treated (n=41). With a median time on treatment of 49.4 weeks (range: 0.4 - 79.4 weeks), the domvanalimab plus zimberelimab and chemotherapy regimen demonstrated sustained improvement across efficacy measures, including in those patients who have low PD-L1 expression.

Endpoint	Overall n=41	PD-L1-high (TAP ≥5%) n=16	PD-L1-low (TAP <5%) n=24
Progression-Free Survival (PFS)			

Median in Months (95% CI)	12.9 mos (9.8, 13.8)	13.8 mos (11.3, NE)	11.3 mos (5.5, 13.8)
12-month PFS Rate (95% CI)	57.6% (41.7,73.5)	68.8% (46.0, 91.5)	46.8% (24.7, 68.9)
Objective Response Rate (ORR) per RECIST v1.1			
Confirmed ORR (95% CI)	58.5% (42.1, 73.7)	68.8% (41.3, 89.0)	50.0% (29.1, 70.9)
Complete Response (%)	3 (7.3%)	1 (6.3%)	1 (4.2%)
Partial Response (%)	21 (51.2%)	10 (62.5%)	11 (45.8%)
Stable Disease (%)	14 (34.1%)	5 (31.3%)	9 (37.5%)
Progressive Disease Confirmed (%)	2 (4.9%)	0	2 (8.3%)
Not Evaluable (NE) (%)	1 (2.4%)	0	1 (4.2%)
Median Duration of Response (DOR) in Months	12.4 mos (9.9, NE)	NE (11.5, NE)	10.2 mos (4.0, 12.4)

Most Common Adverse Events

No unexpected safety signals were observed at the time of DCO. The domvanalimab plus zimberelimab and chemotherapy regimen was generally well tolerated and showed an overall safety profile consistent with the known safety profiles of each individual molecule to date. Infusion-related reactions were observed in 19.5% of the total subjects, and the majority were related to chemotherapy.

Conclusion

These updated data show consistent objective response rate (ORR) and provide mature progression-free survival (PFS) in patients with locally advanced unresectable or metastatic gastric, gastroesophageal junction or esophageal adenocarcinoma (upper GI cancers).

Comment

The numerical response data from the Phase II EDGE trial are positively supportive of dual blockade use in frontline gastric cancer, however, may look slightly lackluster when compared to data from single blockade trials. The EDGE trial is investigating the dual blockade regimen of PD-1 inhibitor zimberelimab and TIGIT inhibitor domvanalimab in frontline metastatic gastric cancer. The hopes for this dual blockade regimen are to improve upon the current sub-optimal two-year overall survival outcome offered by standard of care PD-1 blockade regimens Opdivo and Keytruda, both of which are used in conjunction with chemotherapy for patients with or without HER2 overexpression. In these results from EDGE the overall response rate (ORR) was reported at 58.5%, which looks comparable to the ORR seen with Opdivo in the Phase III CheckMate-649 (ORR 58%). Whilst the similarity between the response rates indicates the dual blockade regimen to have promising competitive efficacy, it comes as a slight disappointment and could call into question whether dual blockade does exert a more potent effect than singular blockade. Nevertheless, it should be noted that cross trial comparisons can be unreliable, with the EDGE trial being an earlier phase study conducted in a considerably smaller patient pool than CheckMate 649 (360 patients enrolled vs 2032). In order to better discern whether dual blockade can improve upon single blockade, more mature Phase III data will be key. Moreover, overall survival data will play a crucial role in determining the future of blockade in gastric cancer, and for now we await such data.

The median progression free survival data reported at 12.9 months does help the regimen's outlook and is encouraging. Furthermore, the median duration of response indicates the combination treatment to have promising durability. Whilst comparison at this stage is difficult, especially without overall survival data, the dual blockade regimen certainly looks to meet the bar for entry set by single dual blockade. Though the response data may be tinged with anticlimax, the data still serves to warrant further exploration of this blockade in frontline gastric cancer. Data from the Phase III Star-221 trial is now eagerly awaited and will prove more telling of the combination's future in this space.

Source:

Business Wire 06/01/2024 (GILD & RCUS)
American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 433248)
Citeline Analysis

DHP107 for Gastric Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - China
Market Group:	Oncology
Lead Company:	Daehwa Pharmaceutical Co Ltd (067080:KS)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	0% (Same As Avg.)
Average Approval:	N/A

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Paclitaxel IV	Paclitaxel Oral	Paclitaxel Oral vs Paclitaxel IV
Number of Patients	268	N/A	N/A
Number of Evaluable Patients	N/A	268	N/A
Median BIRC-Assessed Progression-Free Survival (PFS) ***(Endpoint=Primary)***	2.89 Months	3.02 Months	N/A
Progression-Free Survival (PFS) - Hazard Ratio	N/A	N/A	0.894 (P=0.311)
Median Overall survival (OS) ***(Endpoint=Primary)***	6.54 Months	9.13 Months	N/A
Overall survival (OS) - Hazard Ratio	N/A	N/A	0.770 (P=0.006)

An abstract entitled "Paclitaxel oral solution versus paclitaxel injection as second-line therapy in advanced gastric cancer: A randomized, open-label, non-inferiority phase 3 trial" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Context

This study aimed to determine non-inferiority in efficacy and safety profile of paclitaxel oral solution versus paclitaxel IV, as monotherapy in larger population with unresectable locally advanced, recurrent or metastatic gastric cancer in China.

Design

This is a randomized, open-label, non-inferiority Phase III trial conducted at 53 centers in China. Patients with unresectable or recurrent or metastatic gastric cancer progressed after fluoropyrimidine- or fluoropyrimidine plus platinum-based first-line therapy were randomly assigned

1:1 (stratified by gastrectomy, ECOG PS and prior chemotherapy) to receive oral paclitaxel (200mg/m2 twice daily on days 1, 8, 15 every 4 weeks) or paclitaxel IV (175mg/m2 on day 1 every 3 weeks).

Endpoints

The co-primary endpoints were blind independent review committee (BIRC)-assessed progression-free survival (PFS) and overall survival (OS), with non-inferiority margin of hazard ratio (HR) of 1.18 and 1.16 in statistical comparison, respectively.

Results

From April 22, 2019, to January 31, 2022 (data cut-off), 536 patients were randomized to oral paclitaxel (n=268) or paclitaxel IV (n=268), with median follow-up of 13.4 vs. 12.6 months, respectively. The PFS showed non-inferiority of oral paclitaxel to paclitaxel IV with median BIRC-assessed PFS 3.02 months (95% confidence interval [CI]: 2.69, 3.71) in oral paclitaxel vs. 2.89 months (95% CI: 2.53, 3.48) in paclitaxel IV (HR 0.894, 95% CI: 0.719, 1.112, p=0.311). The OS (cutoff on February 15, 2023) showed of oral paclitaxel over paclitaxel IV with median OS 9.13 months (95% CI: 7.72, 10.97) in oral paclitaxel vs. 6.54 months (95% CI: 5.75, 7.26) in paclitaxel IV (HR 0.770, 95.5% CI: 0.635, 0.934, p=0.006).

Most Common Adverse Events

For the treatment-related adverse events (TRAEs), oral paclitaxel decreased neuropathy incidence (22.3% vs. 38.7% all grade) and no hypersensitivity occurred in oral paclitaxel without premedication. The most common ≥Grade 3 TRAEs were neutrophil count decreased (47.9% in oral paclitaxel vs. 54.5% in paclitaxel IV), white blood cell count decreased (41.5% vs. 35.3%) and anemia (16.6% vs. 10.9%). Grade 5 TRAEs were at low with comparable incidences (four [1.5%] vs. three [1.1%]).

Conclusion

The study showed statistical non-inferiority of paclitaxel oral solution in PFS and statistically significant and clinical improvement in OS as compared to paclitaxel IV, with clinically manageable safety profile, supporting paclitaxel oral solution as second-line treatment option for patients with gastric cancer.

Comment

These data bode well for Daehwa Pharmaceutical's oral paclitaxel agent, DHP107, and set the agent in good stead for a likely approval into the Chinese market. For metastatic gastric cancer patients who have progressed on frontline therapy, options are limited, and paclitaxel-based regimens are the standard of care (SoC). Oral administration of paclitaxel offers key quality of life benefits over IV administration, affording less hospital visits and improving patients' independence, as well as eliminating the risk of IV-related infections. In these data presented at ASCO 2024, the safety benefits of oral formulation are underpinned, with decreased neuropathy incidence compared to the IV formulation. Considering the quality of life and safety benefits oral administration can offer, it is likely that an oral formulation would be favored by patients and physicians alike, compared to IV.

It should be considered that the SoC second-line therapy across many western and eastern markets is Cyramza in combination with paclitaxel. Although only receiving approval within China in 2022, the Cyramza + paclitaxel regimen was given priority as the recommended second-line therapy option in the 2023 update of the Chinese Society of Clinical Oncology (CSCO) guidelines and is expected to assume position as SoC swiftly. Considering Cyramza is administered intravenously every two weeks, patients receiving this SoC regimen would still require hospital visitation, despite potentially having the option of oral paclitaxel. Nevertheless, IV paclitaxel is dosed weekly when in combination with Cyramza, and thus, an oral formulation would decrease the IV visits for patients receiving the SoC Cyramza regimen by half.

With the drug's launch in Korea marking DHP107 the world's first oral formulation of paclitaxel to be approved, the company has been keen to bring the drug to a wider market. So far, the company has not stated plans to explore DHP107 in western markets, but if they were to launch the drug in ex-Asian markets, price competition could play a critical role in uptake. To enhance uptake in western markets, it would serve the agent well to not come in at a price premium. Though physicians and patients may prefer an oral formulation, with non-inferiority data, pricing and reimbursement plans will likely take precedence, especially in cost-conservative settings. It would be imperative that Health technology assessment (HTA) bodies, such as NICE, favorably recommend the agent in order to see use across Europe. Negotiations with insurance companies would also be key to secure payer coverage within the US.

Overall, these data are positive and support the expansion of DHP107 outside of Korean markets.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 4051)
Citeline Analysis

Petosemtamab for Head and Neck Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase I/II - Dose Finding/Expansion
Market Group:	Oncology
Lead Company:	Merus N.V. (MRUS)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	2%
Likelihood of Approval:	13% (2% Above Avg.)
Average Approval:	11%

Merus announced that interim clinical data from the Phase I/II trial of the bispecific antibody petosemtamab in combination with pembrolizumab was presented in an abstract entitled "Petosemtamab (MCLA-158) with pembrolizumab as first-line (1L) treatment of recurrent/metastatic (r/m) head and neck squamous cell carcinoma (HNSCC): Phase 2 study." at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting on June 3, 2024.

Data from this study were last seen in April 2023.

Design

Per the abstract, key eligibility criteria were r/m HNSCC with no prior systemic therapy, PD-L1 combined positive score ≥1, ECOG PS 0–1, measurable disease, and primary tumor location in oropharynx (regardless of p16 status), oral cavity, hypopharynx, or larynx.

Endpoints

Per the abstract, primary endpoints are safety and investigator-assessed ORR (RECIST v1.1). Secondary endpoints include DOR, progression-free survival (per investigator), and overall survival.

Results

As of a March 6, 2024 data cutoff date, 45 patients (pts) were treated

- 26 patients were enrolled as of the abstract cutoff date
  - The efficacy population consisted of 24 patients who had the opportunity for 4 or more months follow up, with ≥2 treatment cycles and ≥1 post-baseline tumor assessment; or who discontinued early due to disease progression or death
  - Two patients were not included: One patient withdrew consent prior to first tumor assessment and the other patient discontinued due to toxicity with less than 2 cycles of treatment
- Response rates overall (N=24): 67%, including 1 confirmed complete response, 12 confirmed partial responses (PRs) and 3 unconfirmed PRs (all of whom confirmed after the data cutoff) by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. per investigator assessment, including
  - 3 of 4 patients with HPV associated cancer responded
  - Responses observed across PD-L1 levels (CPS 1-19: 60% [6/10]; CPS ≥ 20: 71% [10/14])
- At the time of data cutoff, 32 patients of the 45 enrolled, remained on treatment, including 14 of 16 responders and 18 of the initial 26 patients enrolled
- Median follow up of 3.6 months for the 45 patients

Most Common Adverse Events

In 45 patients the combination was well tolerated and no significant overlapping toxicities with pembrolizumab were observed. Treatment-emergent adverse events (AEs) were reported in 45 pts.

- Most were Grade (G) 1 or 2 in severity (no G4–5 were observed)
- Infusion-related reactions (composite term) were reported in 38% (all Gs) and 7% (G3) of pts, most occurred during the first infusion and resolved

Conclusion

This interim dataset, petosemtamab in combination with pembrolizumab has demonstrated clinically meaningful activity in first line head and neck cancer with safety.

Comment

With an ORR of 67% (n=24), these are positive results for petosemtamab combined with Keytruda for first-line recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). All but three of the 16 responses have been confirmed. Looking at subgroups, the ORR was similar for the four human papilloma virus (HPV) p16-positive patients and for the 20 HPV p16-negative patients (75% and 65% ORR, respectively). Although the number of HPV-positive patients is small, this is encouraging as traditional EGFR targeting drugs such as Erbitux typically do not work in such patients. However, petosemtamab is a bispecific antibody that targets both EGFR and LGR5 (a receptor of WNT signaling upregulated in many cancer types) which may give it activity in HPV-positive patients. The ORR was also similar for the 10 PD-L1 CPS 1-19 patients and the 14 PD-L1 CPS ≥20 patients (60% and 71% ORR, respectively).

The most common grade 3 adverse events (there were no grade 4/5 events) were asthenia (fatigue) which was reported in 7% of patients and infusion related reactions which was also seen in 7% of patients. Discontinuation due to treatment related adverse events was reported in two (4%) of patients, one with grade 2 asthenia, the other with grade 1 diarrhea.

Class competitor BCA101 is a bispecific antibody that targets both EGFR and TGF-beta and is currently in Phase I development. In a Phase Ib trial enrolling first-line R/M patients, BCA101 combined with Keytruda reported an ORR of 48% (3% CR). Subgroup analysis showed that BCA101 was substantially more active in HPV-negative patients (65% ORR in 20 patients) compared to HPV-positive patients (18% ORR in 11 patients). While the BCA101 and petosemtamab combinations report similar activity in HPV-negative patients, the petosemtamab combination has the advantage of also being highly active in HPV-positive patients.

In the US, the current standard-of-care for this setting is Keytruda monotherapy for patients with a PD-L1 CPS ≥1 or Keytruda combined with chemotherapy for patients regardless of CPS. The Keytruda FDA label reports a 19% ORR (5%CR)/20.9 month median duration of response (mDOR) for Keytruda monotherapy and a 36% ORR (6% CR rate)/6.7 month mDOR for Keytruda combined with chemotherapy. The 67% ORR (4% CR rate) for petosemtamab + Keytruda compares well to historical data for Keytruda. The historical data shows that while the addition of chemotherapy to Keytruda increases the ORR, those extra-responders don't have a long DOR suggesting that the two agents are more additive than synergistic. With a current median follow-up of 3.6 months, we will need longer follow-up to see if petosemtamab + Keytruda retains the long DOR seen with Keytruda monotherapy.

Next steps include updated data for all 45 first-line patients treated with petosemtamab + Keytruda including duration of response data. Merus has indicated that they expect to initiate two pivotal Phase III trials in 2024. The first trial, expected to initiate in mide-2024, will evaluate petosemtamab monotherapy for second- or third-line R/M HNSCC. The comparator for this first trial will be physician's choice of chemotherapy or Erbitux. Merus has previously reported an ORR of 37% (n=43) for petosemtamab monotherapy in this setting. The median duration of response was 6.0 months while median PFS and OS were 5.3 months and 11.5 months, respectively.

The second Phase III trial will evaluate petosemtamab + Keytruda for first-line R/M HNSCC. The comparator will be Keytruda monotherapy and the trial is expected to initiate by the end of 2024. Merus may have to raise additional funds to complete this second trial with company officials noting in the conference call that a supply deal is not in place with Merck and the costs for supplying Keytruda will run into the high tens of millions of dollars.

Some key late phase pipeline drugs being developed for the R/M HNSCC setting include ficlatuzumab, an antibody that blocks signaling through the HGF/c-MET pathway. A small Phase II study enrolled second-line R/M patients refractory to Erbitux and either refractory or ineligible for checkpoint inhibitors and chemotherapy. In a subgroup of HPV-negative patients, the median PFS for ficlatuzumab combined with Erbitux was 4.1 months and the ORR was 38% (n=16). A Phase III trial, FIERCE-HN, is enrolling HPV-negative, second-line R/M patients who have failed prior therapy with a checkpoint inhibitor and platinum-based chemotherapy given in combination or sequentially. The trial is comparing ficlatuzumab combined with Erbitux to placebo combined with Erbitux, and is expected to readout in 2027. Another agent being evaluated for R/M HNSCC is eftilagimod alpha (efti), a soluble form of the LAG-3 cell surface protein. At ASCO 2023, Immutep presented final data from Part C of TACTI-002, which evaluated efti combined with Keytruda in checkpoint inhibitor-naïve second-line patients. The trial reported an ORR of 38% and a median OS of 12.6 months in 25 patients with CPS ≥1. A randomized Phase IIb trial, TACTI-003, is evaluating efti combined with Keytruda, and is enrolling first-line R/M HNSCC patients who have

PD-L1-positive tumors (CPS ≥1). The comparator is Keytruda monotherapy and a topline readout is expected in 2024.

As we await updated data for petosemtamab and initiation of a Phase III trial, we are increasing the LOA by 2%.

Source:

Globe Newswire 05/23/2024 (MRUS)
Globe Newswire 05/28/2024 (MRUS)
American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 6014)
Company Conference Call 05/28/2024 (MRUS)
Company Conference Call Slides 05/28/2024

Tivdak for Head and Neck Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - innovaTV 207
Market Group:	Oncology
Lead Company:	Pfizer Inc. (PFE)
Partner Companies:	Genmab (GMAB) Zai Lab (ZLAB)
Former Companies:	Seagen (SGEN)
Change to Likelihood of Approval:	1%
Likelihood of Approval:	12% (1% Above Avg.)
Average Approval:	11%

Genmab announced that data from the Phase II innovaTV 207 trial, Part C (n=40), investigating tisotumab vedotin, an antibody-drug conjugate directed to tissue factor, was presented at the 2024 ASCO Annual Meeting. An abstract entitled "Tisotumab vedotin in head and neck squamous cell carcinoma: Updated analysis from innovaTV 207 Part C" was presented on June 3, 2024.

Methods

The innovaTV 207 trial is an open-label, global, Phase II, multicohort, multicenter study evaluating tisotumab vedotin monotherapy or in combination for advanced solid tumors. In Part C, patients with recurrent or metastatic HNSCC received tisotumab vedotin monotherapy (1.7 mg/kg IV once every two weeks). All patients were required to have received a platinum-based regimen, either in the recurrent/metastatic setting, or to have persistent disease following platinum-based chemoradiation and a checkpoint inhibitor, if eligible.

Endpoints

The primary endpoint of the trial is confirmed objective response rate (cORR) per RECIST 1.1 per investigator, defined as the proportion of patients who achieve a confirmed complete or partial response. Selected secondary endpoints include duration of response (DOR), time-to-response (TTR), and safety.

Results

In the HNSCC cohort of innovaTV 207 Part C (n=40), median duration of response (DOR) was 5.6 months and median time-to-response (TTR) was 1.4 months. All patients were required to have received a platinum-based regimen in the recurrent or metastatic setting or have persistent disease following platinum-based chemoradiation and a checkpoint inhibitor (CPI), if eligible. The study also showed that among patients with no more than one or two lines of therapy in the recurrent or metastatic setting (n=25), 40% had achieved a cORR at the time of data cut-off.

As of December 2023, 40 patients with recurrent or metastatic HNSCC were treated with tisotumab vedotin monotherapy (1.7 mg/kg intravenously, once every two weeks). In this cohort, 32 (80%) received prior platinum-based therapy, 19 (47.5%) received at least two prior lines of systemic therapy (median: 2; range: 1-3), 40 (100%) received prior CPI, 23 (57.5%) received prior taxane, and 27 (67.5%) received prior cetuximab. The primary sites at diagnosis were oropharynx (n=16), larynx (n=13), and oral cavity (n=9).

Most Common Adverse Events

The safety findings were consistent with previous tisotumab vedotin trials, and no new safety signals were observed. Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 67.5% of patients, and the most common were peripheral neuropathy events (40%). Adverse events of special interest (of any grade) were prespecified for ocular, peripheral neuropathy, and bleeding events, and occurred in 52.5%, 47.5%, and 40% patients, respectively.

Conclusions

Per the abstract, TV demonstrated encouraging antitumor activity in a heavily pretreated r/m HNSCC population with a manageable safety profile consistent with previous TV monotherapy data. The study is ongoing; TV represents a promising treatment option for pts with r/m

HNSCC who have progressed after prior platinum-based therapy and immunotherapy.

Comment

With an ORR of 40% in 25 second- or third-line recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) patients, these are encouraging results for the antibody-drug conjugate Tivdak. In a wider group of 40 second- to fourth-line patients, the ORR was lower at 32.5% with a median follow-up of 16.9 months. There was one complete response with all the other responses being partial responses. The median duration of response for both the wider group and the subgroup of 25 patients was 5.6 months.

Adverse events of special interest for Tivdak are ocular events, peripheral neuropathy, and bleeding. The most common ocular events were conjunctivitis (30%) and dry eye (17.5%). Similarly, the most common peripheral neuropathy events were peripheral sensory neuropathy (40%) while the most common bleeding events were nose bleeds (17.5%). Grade ≥3 ocular events, peripheral neuropathy, and bleeding, occurred in 5.0%, 10.0%, and 2.5% of patients. Finally, adverse events led to discontinuation in 20% of patients while drug-related adverse events led to discontinuation in 15% of patients (7.6% due to ocular events, 5% due to peripheral neuropathy, and 2.5% due to bleeding events).

The standard-of-care for R/M HNSCC is Keytruda, either as monotherapy or in combination with chemotherapy. Once patients progress on Keytruda there is no agreed upon standard-of-care although many patients receive Erbitux or chemotherapy. Another drug being developed for this setting is ficlatuzumab. A small Phase II study enrolled patients refractory to Erbitux and either refractory or ineligible for checkpoint inhibitors and chemotherapy. In a subgroup of HPV-negative patients, the median PFS for ficlatuzumab combined with Erbitux was 4.1 months and the ORR was 38% (n=16). A Phase III trial, FIERCE-HN, is enrolling HPV-negative R/M patients who have failed prior therapy with a checkpoint inhibitor and platinum-based chemotherapy given in combination or sequentially. The trial is comparing ficlatuzumab combined with Erbitux to placebo combined with Erbitux, and is expected to readout in 2027. The 32.5-40% ORR reported at ASCO for Tivdak compares well to the 38% ORR reported for ficlatuzumab, especially considering that Tivdak was evaluated as monotherapy while ficlatuzumab was evaluated in combination with Erbitux. Furthermore, Erbitux is known to not be active in HPV+ve patients which is why the ficlatuzumab combination is only being evaluated in HPV-ve patients. The innovaTV 207 trial enrolled both HPV-positive and HPV-negative patients and among the 16 oropharynx patients enrolled, 75% were HPV-positive. One drawback for Tivdak is that it appears less active in patients previously treated with a taxane in the recurrent/metastatic setting. While such patients responded, their responses were not as deep. This is likely because both taxanes and the Tivdak payload (MMAE) disrupt microtubules.

At ASCO we saw results for part C of the innovaTV 207 trial. Enrollment in the trial continues and part E will evaluate Tivdak monotherapy in second- or third-line R/M HNSCC patients while part F will evaluate Tivdak combined with Keytruda for first-line R/M HNSCC. At the 2024 JPMorgan Healthcare Conference, Genmab officials announced that pending regulatory feedback, they intend to initiate a Phase III trial for Tivdak in head and neck cancer (likely for second- or third-line R/M HNSCC).

As we await for updated data from innovaTV 207, we are increasing the LOA by 1%.

Source:

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 6012)
Press Release 06/03/2024 (GMAB)
Citeline Analysis

PRGN-2012 for Head and Neck Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase I/II - U.S.
Market Group:	Oncology
Lead Company:	Precigen, Inc. (PGEN)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	4%
Likelihood of Approval:	15% (4% Above Avg.)
Average Approval:	11%

Precigen announced updated data from the pivotal Phase I/II study of PRGN-2012 in recurrent respiratory papillomatosis patients. The abstract entitled "PRGN-2012, a novel gorilla adenovirus-based immunotherapy, provides the first treatment that leads to complete and durable responses in recurrent respiratory papillomatosis patients" at the American Society of Clinical Oncology (ASCO) annual meeting on June 03, 2024.

Data from the study were last seen in October 2023.

Design

The Phase I/II clinical study evaluated safety and efficacy of PRGN-2012. The study design included an initial 3+3 dose escalation cohort to identify the recommended Phase II dose (RP2D). Adult RRP patients who had three or more surgeries in the prior 12 months were eligible for the study. The Phase I/II study enrolled a total of 38 patients. Of these, 3 patients received four administrations of PRGN-2012 at 1x 10^{11} particle units (PU)/dose and 35 patients received four administrations of PRGN-2012 at RP2D (5 x 10^{11} PU/dose) over a 12 week treatment period via subcutaneous injection.

Baseline patient characteristics of the 35 adult patients included a median age of 49 years (range: 20-88); 20 of the patients were male and 15 were female. Patients had a median of 4 surgeries (range: 3-10) in the 12 months before PRGN-2012 treatment initiation. Average years since RRP diagnosis was 20 (range: 1-65) with 12 and 23 patients with juvenile and adult onset RRP, respectively.

Endpoints

Primary endpoints included safety and Complete Response rate defined as the percentage of patients who require no RRP surgeries in the 12-month period after PRGN-2012 treatment completion. Key secondary endpoints included HPV-specific immune responses, extent of papilloma growth as measured by Derkay scoring, and quality of life measurement as measured by Vocal Handicap Index-10 (VHI-10).

Results

Primary efficacy endpoint analysis demonstrated that 51% (18 out of 35) (95% CI: 34-69) patients achieved Complete Response, defined as no need for RRP surgeries in the 12-month period following completion of PRGN-2012 treatment. The Complete Response rate was 50% (6 out of 12) and 52% (12 out of 23) in the Phase I and Phase II portions of the study, respectively. Complete Responses were durable. Median durability of response has not yet been reached with median follow up of 20 months as of the data cutoff date of May 20, 2024. PRGN-2012 treatment significantly ($p<0.0001$) reduced the need for surgeries in RRP patients compared to pre-treatment history. PRGN-2012 treatment reduced the need for RRP surgeries in 86% (30 out of 35) of patients compared to their pre-treatment history. RRP surgeries were reduced from a median of 4 (range: 3-10) in the 12 months pre-treatment to 0 (range: 0-7) in the 12 months post PRGN-2012 treatment completion .

PRGN-2012 treatment showed significant ($p<0.0001$) improvement in anatomical Derkay scores, a tool used for research purposes to quantify RRP severity based on involvement of laryngeal structures, with mean Derkay scores reducing from 9 (range: 5-19) at baseline to 1 (range: 0-5) at 24 weeks post-treatment in patients with Complete Response. Quality of life, as evaluated using the validated VHI-10, significantly ($p<0.0001$) improved from a mean of 25 (range: 12-38) at baseline to 7 (range: 0-30) at 24 weeks post PRGN-2012 treatment in patients with

Complete Response. PRGN-2012 treatment induced HPV 6/11-specific T cell responses in RRP patients with a significantly greater expansion of peripheral HPV-specific T cells observed in responders compared with non-responders.

Most Common Adverse Events

PRGN-2012 treatment was well-tolerated with no dose-limiting toxicities and no treatment-related adverse events (TRAEs) greater than Grade 2. All patients received four administrations of PRGN-2012 at the intended dose levels. TRAEs were mostly mild with no treatment-related serious adverse events reported. The most common TRAE was injection site reaction. Other common TRAEs occurring in more than one subject were fatigue, chills, and fever. There was no meaningful anti-drug antibody response with repeat administrations of PRGN-2012.

Conclusion

Per the abstract, these data demonstrate the overall favorable safety profile and significant clinical benefit of PRGN-2012 in adult RRP patients. These findings support PRGN-2012 as a potential therapeutic option for this patient population where no FDA-approved therapeutics exist.

Comment

With a CR rate of 51% and no grade ≥3 adverse events, this is a straightforward win for PRGN-2012 for the treatment of recurrent respiratory papillomatosis (RRP), a disease with no approved systemic therapies. RRP is a rare, lifelong disease caused by infection with HPV6 or HPV11. Benign papillomas grow in the respiratory tract and can cause severe voice disturbance. In certain cases, RRP can be life threatening due to the risk of papillomas blocking the airway, growing in the lungs, or undergoing malignant transformation. The current standard-of-care is repeat surgical debulking of papilloma which can lead to irreversible scarring of the trachea.

PRGN-2012 is a gene therapy based therapeutic vaccine that uses a replication incompetent gorilla adenoviral vector to express HPV6 and HPV11 antigens and elicit a T-cell immune response. The trial enrolled patients who had at least three surgeries in the prior 12 months. Three patients were treated at dose level 1 and 35 patients were treated at dose level 2. Patients enrolled at dose level 2 had a mean of 4.5 surgeries in the previous 12 months with a range of 3-10 surgeries. A CR was defined as no surgeries in the 12 months after completing a course of four subcutaneous injections of PRGN-2012 (day 0, day 15, day 43 and day 85). PRGN-2012 at dose level 2 reported a 51% CR rate. These responses were durable and with a median follow-up of 20 months (range of ~12 months to ~32 months), the median duration of response has not been reached; all patients with a CR remain in response and have not had surgery. Patients with a CR also saw an improvement compared to baseline in papilloma secerity as measured by the anatomic Derkay score at week 24 as well as an improvement in voice quality as measured by the VHI-10 index at week 24. In addition to the 51% of patients with a CR, an additional 35% of patients reported fewer surgeries in the 12 months following treatment compared to the 12 months preceding treatment.

During the Q&A, the investigator Dr Scott Norberg was asked if there were any factors that could explain why some patients respond while others do not and he exmentioned that a 2023 paer suggested that the papilloma microenvironemt may play a role with some papillomas not allow maenigful mmigration of T cells. In response to another question, Dr Norberg explained that there were some responders where the papilloma was still present but had not grown.

In the second-half of 2024, Precigen is expected to initiate a confirmatory trial and then submit regulatory applications seeking accelerated approval. The confirmatory trial design has been approved by the FDA and will be a single-arm trial very similar to the pivotal Phase II trial but will also evaluate retreatment with PRGN-2012.The requirements for the BLA submission have also been approved by the FDA.

During the conference call, KOL Dr Clint Allen from the NCI noted that if approved, PRGN-2012 will likely become the standard of care for first-line RRP regardless of the number of baseline surgeries. Dr Allen also noted that no clinically meaningful anti-drug antibodies have been detected so repeated treatment may be possible.

This study helps validate the company's off-the-shelf gene therapy/therapeutic vaccine technology. Products being developed with this technology include PRGN-2009 targeting HPV 16/18. PRGN-2009 is being evaluated in Phase II studies in combination with bintrafusp alfa for HPV-positive solid tumors and in combination with Keytruda for newly diagnosed HPV-positive oropharyngeal head and neck cancer and recurrent or metastatic cervical cancer.

As we await a regulatory submission and a potential commercial launch in 2025, we are increasing the LOA by 4%.

Source:

PR Newswire 06/03/2024 (PGEN)

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract LBA6015)
Company Conference Call 06/03/2024 (PGEN)
Company Conference Call Slides 06/03/2024 (PGEN)
Citeline Analysis

Opdivo for Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)

Event Date:	06/04/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - CheckMate 9DW (w/Ipilimumab)
Market Group:	Oncology
Lead Company:	Bristol Myers Squibb Company (BMY)
Partner Companies:	Ono Pharmaceutical (4528:JP)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	LEN/SOR	NIVO + IPI	NIVO + IPI vs LEN/SOR
Number of Patients	333	335	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Median Overall Survival HR=0.79, 95% CI ***(Endpoint=Primary)***	20.6 Months	23.7 Months	N/A (P=0.0180)
Objective Response Rate 95% CI ***(Endpoint=Secondary)***	13 %	36 %	N/A (P<0.0001)
Complete Response Rate	2 %	7 %	N/A
Median Duration of Response 95% CI ***(Endpoint=Secondary)***	12.9 Months	30.4 Months	N/A
Risk of Symptom Deterioration HR=076, 95% CI	N/A	N/A	-24 % (P=0.0059)

Bristol Myers Squibb announced the first presentation of results from the Phase III CheckMate -9DW trial evaluating the dual immunotherapy combination of Opdivo (nivolumab) plus Yervoy (ipilimumab) compared to investigator's choice of lenvatinib or sorafenib as a first-line treatment for patients with unresectable hepatocellular carcinoma (HCC). An abstract entitled, "nivolumab (nivolumab) plus ipilimumab (IPI) vs lenvatinib (LEN) or sorafenib (SOR) as first-line treatment for unresectable hepatocellular carcinoma (uHCC): First results from CheckMate 9DW," was presented at the 2024 ASCO Meeting on June 4, 2024.

Data from this study were last seen in March 2024.

Design

CheckMate -9DW is a Phase III randomized, open-label trial evaluating the combination of Opdivo plus Yervoy compared to investigator's choice of lenvatinib or sorafenib monotherapy in patients with advanced hepatocellular carcinoma who have not received prior systemic therapy.

Approximately 668 patients were randomized to receive Opdivo plus Yervoy (Opdivo 1mg/kg plus Yervoy 3 mg/kg Q3W for up to four doses, followed by Opdivo monotherapy 480 mg Q4W) infusion, or single agent lenvatinib or sorafenib as oral capsules in the control arm.

Per the abstract, pts were randomly assigned 1:1 to receive nivolumab (NIVO) 1 mg/kg + ipilimumab (IPI) 3 mg/kg Q3W (up to 4 cycles) followed by NIVO 480 mg Q4W or investigator's choice of lenvatinib (LEN) 8 mg or 12 mg QD or sorafenib (SOR) 400 mg BID until disease progression or unacceptable toxicity. nivolumab was given for a maximum of 2 years.

Endpoints

The primary endpoint of the trial is overall survival and key secondary endpoints include objective response rate and time to symptom deterioration.

Results

With a median follow-up of approximately 35.2 months, treatment with Opdivo plus Yervoy demonstrated:

- A statistically significant and clinically meaningful improvement in the primary endpoint of overall survival (OS). Median OS was 23.7 months (95% CI: 18.8–29.4) for Opdivo plus Yervoy compared to 20.6 months (95% CI: 17.5–22.5) with lenvatinib or sorafenib (HR: 0.79 (0.65–0.96); p=0.018). The overall survival benefit was generally consistent across patient subgroups.
- A statistically significant and clinically meaningful improvement in the key secondary endpoint of objective response rate (ORR), which was 36% (95% CI: 31-42) for Opdivo plus Yervoy compared to 13% (95% CI: 10-17) with lenvatinib or sorafenib.
- A higher complete response (CR) rate of 7% for Opdivo plus Yervoy vs. 2% with lenvatinib or sorafenib. Responses were durable; among responders, median duration of response was 30.4 months for Opdivo plus Yervoy (95% CI: 21.2-NE) and 12.9 months for lenvatinib or sorafenib (95% CI: 10.2-31.2).
- Opdivo plus Yervoy demonstrated a significantly reduced risk of symptom deterioration of 24% compared to lenvatinib or sorafenib (HR: 0.76, 95% CI: 0.62-0.93; p=0.0059)

Most Common Adverse Events

The safety profile for the combination of Opdivo plus Yervoy remained consistent with previously reported data and was manageable with established protocols. Treatment-related adverse events (TRAEs) of any grade were reported in 84% of patients with Opdivo plus Yervoy and 91% in patients with lenvatinib or sorafenib. Grade 3/4 TRAEs occurred in 41% and 42% of patients, respectively.

Conclusion

These data from CheckMate -9DW confirm the efficacy of the combination of nivolumab and ipilimumab and its ability to extend survival.

Per the abstract, nivolumab + ipilimumab demonstrated statistically significant OS benefit vs lenvatinib/sorafenib in pts with previously untreated uHCC, as well as higher ORR and durable responses with a manageable safety profile. These results support this combination as a potential new first-line SOC for uHCC.

Comment:

The impressive outcomes in terms of the OS indicate that the combination of Opdivo and Yervoy may establish itself as the next SoC for patients with unresectable hepatocellular carcinoma (uHCC). It is worth noting that a similar median OS was observed in the CARES-310 trial, where Jiangsu Hengrui's camrelizumab (in combination with Elevar's rivoceranib) led to a median OS of 23.8 months in the same patient population. The camrelizumab/rivoceranib combination may have a regulatory advantage, however, despite the issuance of a complete response letter (CRL) by the FDA in May 2024.

The CRL primarily addressed manufacturing issues and did not raise concerns related to the trial's clinical data. While it's anticipated that these manufacturing issues will be resolved in the near future, some additional time may be necessary for regulatory considerations.

Building upon the results from the CheckMate-040 trial, the combination of Opdivo and Yervoy has already established itself as a second-line treatment for patients with advanced HCC. Consequently, there is a strong likelihood that this combination therapy will receive a label expansion into the first-line setting, with the company intending to discuss the findings of the CheckMate9DW trial with regulatory authorities and submit marketing approval applications. With its physician familiarity that stems from its use in the second-line setting and now compelling efficacy data from its use in the first line, the Opdivo plus Yervoy combination holds significant potential for achieving considerable commercial success in HCC. It remains to be seen, however, which of the two combinations—Opdivo/Yervoy or

camrelizumab/rivoceranib—will pass the FDA approval hurdle first.

Source:

Business Wire 06/04/2024 (BMY)
American Society of Clinical Oncology (ASCO) 06/04/2024 (Abstract LBA4008)

Camrelizumab for Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - w/Rivoceranib
Market Group:	Oncology
Lead Company:	Jiangsu Hengrui Pharmaceuticals (600276:SS)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	1%
Likelihood of Approval:	99% (7% Above Avg.)
Average Approval:	92%

An abstract entitled "Camrelizumab plus rivoceranib vs sorafenib as first-line therapy for unresectable hepatocellular carcinoma (uHCC): Final overall survival analysis of the phase 3 CARES-310 study" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data in this event has been created solely from the abstract program.

Background

The phase 3 CARES-310 trial is the first to demonstrate significant progression-free survival (PFS) and overall survival (OS) benefits with immunotherapy plus an anti-angiogenic tyrosine kinase inhibitor (TKI) over standard TKI as first-line treatment for uHCC. In the primary analysis of PFS (data cut-off [DCO], May. 10, 2021) and interim analysis of OS (DCO, Feb. 8, 2022), significant improvements were observed with camrelizumab (C; anti-PD-1 antibody) + rivoceranib (R; VEGFR2-TKI) vs. sorafenib (S). Here, we report updated data at the final analysis (FA), after an additional follow-up of ~16 mo.

Methods

In this international, randomized, open-label, phase 3 trial, 543 patients with uHCC who had not previously received systemic treatment were randomized 1:1 to receive either C (200 mg, iv, q2w) + R (250 mg, po, qd) or S (400 mg, po, bid). As of Jun.14, 2023, 351 (65%) deaths occurred, and a protocol-specified FA was performed.

Results

272 patients were allocated to C+R and 271 to S. At DCO of FA, median follow-up was 22.1 mo in C+R group and 14.9 mo in S group. After end of study treatment, 36% of patients in C+R group and 42% in S group received subsequent targeted therapy; 17% and 36% received immunotherapy, respectively. Median OS was significantly prolonged with C+R vs. S (23.8 mo [95% CI 20.6-27.2] vs. 15.2 mo [95% CI 13.2-18.5]; hazard ratio (HR) 0.64 [95% CI 0.52-0.79]; 1-sided p <0.0001). OS rate with C+R vs.S was 49.0% vs. 36.2% at 24 mo, and 37.7% vs. 24.8% at 36 mo. OS benefits with C+R was generally consistent across subgroups, regardless of geographical region, race, and aetiology. Benefits in PFS, objective response rate (ORR) and duration of response (DoR) with C+R were also sustained after prolonged follow-up. Safety data aligned with the interim OS analysis, with no new signals noted.

Conclusions

At the protocol-specified FA, C+R continued to show clinically meaningful survival improvement compared with S, with manageable safety. The extended follow-up further confirmed the favorable benefit-to-risk profile of C+R, supporting it as a new first-line treatment option for uHCC.

Comment:

Impressive overall survival (OS) results from the CARES-310 trial indicate that the camrelizumab + rivoceranib combination could emerge as the favored first-line treatment for patients with unresectable hepatocellular carcinoma (uHCC). With a median overall survival (mOS) of 23.8 months, this trial boasts the longest mOS reported in any global Phase III trial for uHCC. As a result, this combination has the potential to surpass the current standard of care, Tecentriq plus bevacizumab. However, it is to be noted that in May 2024, the FDA issued a complete response letter (CRL) to Jiangsu Hengrui Pharma and Elevar Therapeutics' respective applications for PD-1 inhibitor camrelizumab and the VEGFR inhibitor rivoceranib in uHCC. The two major issues highlighted the in CRL were-

- Deficiencies related to the developer's manufacturing site
- FDA's inability to fully assess the combination within the review period due to travel restrictions at sites such as Russia and Ukraine

The FDA plans to conduct a thorough evaluation based on the companies' responses to the manufacturing shortfalls. Meanwhile, the developers intend to continue discussions with the FDA and resubmit their marketing application. There is a high likelihood of these issues being resolved soon, given the impressive trial results and the fact that the CRL does not cite any concerns related to the trial or clinical data.

Multiple PD-1/PD-L1 combinations are in development for the first-line treatment of metastatic HCC. These include Opdivo + Yervoy, tiragolumab + bevacizumab + Tecentriq, Loqtorzi + Lenvima, and Lenvima + nofazinlimab. Additionally, tislelizumab is under development as a first-line monotherapy, though its efficacy seems weaker compared to combination regimens. Nonetheless, with a first-to-market advantage and notable efficacy data, the camrelizumab plus rivoceranib combination therapy could achieve substantial commercial success.

Based on these results, we are raising camrelizumab's and rivoceranib's LOA by 1% each.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 4110)

SCT-510A for Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II/III - w/SCT-I10A (China)
Market Group:	Oncology
Lead Company:	Sinocelltech Group Limited
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	0% (Same As Avg.)
Average Approval:	N/A

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Sorafenib	SCT-I10A + SCT510	SCT-I10A + SCT510 Vs Sorafenib
Number of Patients	116	230	N/A
Number of Evaluable Patients	116	230	N/A
Median Overall survival (OS) ***(Endpoint=Primary)***	14.2 Months	22.1 Months	N/A (P=0.0008)
Median Progression-free Survival (PFS) ***(Endpoint=Primary)***	2.9 Months	7.1 Months	N/A (P<0.0001)
Objective response rate (ORR) ***(Endpoint=Secondary)***	4.3 %	32.8 %	N/A

An abstract entitled "SCT-I10A combined with a bevacizumab biosimilar (SCT510) versus sorafenib in the first-line treatment of advanced hepatocellular carcinoma: A randomized phase 3 trial" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

In this open-label, multicenter, Phase III trial conducted in China, patients with advanced HCC who had not received prior system therapy were enrolled and randomly assigned (2:1) to receive SCT-I10A (200 mg every three weeks [Q3W]) plus SCT510 (a bevacizumab biosimilar, 15 mg/kg Q3W) or sorafenib (400 mg orally twice daily) until no clinical benefit or unacceptable toxicity. Randomization was stratified by ECOG performance status (0 vs. 1), baseline alpha-fetoprotein level (<400ng/ml vs. ≥400ng/ml), macrovascular invasion or extrahepatic metastasis (yes vs. no).

Endpoints

The co-primary endpoints were overall survival (OS) and progression-free survival (PFS) as assessed by the blinded independent central review (BICR) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 in the full analysis set.

Results

At the data cutoff for the interim analysis (November 2, 2023), a total of 346 patients were enrolled and received at least one dose (SCT-I10A plus SCT510 group, n=230; sorafenib group, n=116), and the median follow-up was 19.7 months. The SCT-I10A plus SCT510 group exhibited a significantly longer median OS than that in the sorafenib group (22.1 vs. 14.2 months, hazard ratio [HR] 0.60; 95% confidence interval [CI]: 0.44, 0.81; p=0.0008). Median PFS was prolonged significantly in the SCT-I10A plus SCT510 group compared to the sorafenib group (7.1 vs. 2.9 months; HR 0.50; 95%CI: 0.38, 0.65; p<0.0001). The objective response rate (ORR) was higher in the SCT-I10A plus SCT510 group (32.8% [75/229]) than in the sorafenib group (4.3% [5/116]).

Most Common Adverse Events

Grade ≥3 treatment-related adverse events (TRAEs) were observed in 42.6% (98/230) of patients in the SCT-I10A plus SCT510 group and 33.6% (39/116) of patients in the sorafenib group. The most common grade ≥3 TRAE was hypertension (SCT-I10A plus SCT510 group vs. sorafenib group: 7.8% [18/230] vs. 4.3% [5/116]). Three drug-related deaths (unknown cause, hemorrhage intracranial, or upper gastrointestinal hemorrhage in 1 patient each) occurred and were related to SCT510.

Conclusions

The combination of SCT-I10A and SCT510 showed substantial clinical advantages and an acceptable safety profile in patients with advanced HCC, thereby supporting its suitability as a first-line treatment option for HCC.

Comment:

Positive interim results for progression-free survival (PFS) and overall survival (OS) from the Phase 2/3 trial evaluating SCT-I10A combined with SCT510 in the first-line treatment of advanced hepatocellular carcinoma (HCC) showcase the regimen's potential as a first-line treatment option for HCC. It is important to note that the trial was conducted in China, and the results would need to be replicated in a Western population to qualify for FDA regulatory approval.

Additionally, the Phase III CARES-310 results, presented at ASCO 2024, demonstrated that the camrelizumab plus rivoceranib combination achieved a median overall survival (mOS) of 23.8 months—the highest ever reported in any global Phase III trial for HCC. Despite the issuance by the FDA of a complete response letter (CRL) for the marketing applications of camrelizumab and rivoceranib, it is highly likely that the manufacturing issues which led to the CRL will be resolved soon, leading to an FDA regulatory approval for the combination in near future. With a first-to-market advantage and notable efficacy data, the camrelizumab plus rivoceranib combination therapy will likely achieve substantial commercial success and become the standard of care in this setting.

The commercial outlook for the combination of SCT-I10A with SCT510 therefore appears less promising, even after a potential approval. This is due to the anticipated delay in achieving regulatory approval and the robust efficacy data already demonstrated by the camrelizumab plus rivoceranib combination.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 4092)
Citeline Analysis

SCT-I10A for Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II/III - w/(SCT510) (China)
Market Group:	Oncology
Lead Company:	Sinocelltech Group Limited
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	0% (Same As Avg.)
Average Approval:	N/A

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Sorafenib	SCT-I10A + SCT510	SCT-I10A + SCT510 Vs Sorafenib
Number of Patients	116	230	N/A
Number of Evaluable Patients	116	230	N/A
Median Overall survival (OS) ***(Endpoint=Primary)***	14.2 Months	22.1 Months	N/A (P=0.0008)
Median Progression-free Survival (PFS) ***(Endpoint=Primary)***	2.9 Months	7.1 Months	N/A (P<0.0001)
Objective response rate (ORR) ***(Endpoint=Secondary)***	4.3 %	32.8 %	N/A

An abstract entitled "SCT-I10A combined with a bevacizumab biosimilar (SCT510) versus sorafenib in the first-line treatment of advanced hepatocellular carcinoma: A randomized phase 3 trial" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

In this open-label, multicenter, Phase III trial conducted in China, patients with advanced HCC who had not received prior system therapy were enrolled and randomly assigned (2:1) to receive SCT-I10A (200 mg every three weeks [Q3W]) plus SCT510 (a bevacizumab biosimilar, 15 mg/kg Q3W) or sorafenib (400 mg orally twice daily) until no clinical benefit or unacceptable toxicity. Randomization was stratified by ECOG performance status (0 vs. 1), baseline alpha-fetoprotein level (<400ng/ml vs. ≥400ng/ml), macrovascular invasion or extrahepatic metastasis (yes vs. no).

Endpoints

The co-primary endpoints were overall survival (OS) and progression-free survival (PFS) as assessed by the blinded independent central review (BICR) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 in the full analysis set.

Results

At the data cutoff for the interim analysis (November 2, 2023), a total of 346 patients were enrolled and received at least one dose (SCT-I10A plus SCT510 group, n=230; sorafenib group, n=116), and the median follow-up was 19.7 months. The SCT-I10A plus SCT510 group exhibited a significantly longer median OS than that in the sorafenib group (22.1 vs. 14.2 months, hazard ratio [HR] 0.60; 95% confidence interval [CI]: 0.44, 0.81; p=0.0008). Median PFS was prolonged significantly in the SCT-I10A plus SCT510 group compared to the sorafenib group (7.1 vs. 2.9 months; HR 0.50; 95%CI: 0.38, 0.65; p<0.0001). The objective response rate (ORR) was higher in the SCT-I10A plus SCT510 group (32.8% [75/229]) than in the sorafenib group (4.3% [5/116]).

Most Common Adverse Events

Grade ≥3 treatment-related adverse events (TRAEs) were observed in 42.6% (98/230) of patients in the SCT-I10A plus SCT510 group and 33.6% (39/116) of patients in the sorafenib group. The most common grade ≥3 TRAE was hypertension (SCT-I10A plus SCT510 group vs. sorafenib group: 7.8% [18/230] vs. 4.3% [5/116]). Three drug-related deaths (unknown cause, hemorrhage intracranial, or upper gastrointestinal hemorrhage in 1 patient each) occurred and were related to SCT510.

Conclusions

The combination of SCT-I10A and SCT510 showed substantial clinical advantages and an acceptable safety profile in patients with advanced HCC, thereby supporting its suitability as a first-line treatment option for HCC.

Comment:

Positive interim results for progression-free survival (PFS) and overall survival (OS) from the Phase 2/3 trial evaluating SCT-I10A combined with SCT510 in the first-line treatment of advanced hepatocellular carcinoma (HCC) showcase the regimen's potential as a first-line treatment option for HCC. It is important to note that the trial was conducted in China, and the results would need to be replicated in a Western population to qualify for FDA regulatory approval.

Additionally, the Phase III CARES-310 results, presented at ASCO 2024, demonstrated that the camrelizumab plus rivoceranib combination achieved a median overall survival (mOS) of 23.8 months—the highest ever reported in any global Phase III trial for HCC. Despite the issuance by the FDA of a complete response letter (CRL) for the marketing applications of camrelizumab and rivoceranib, it is highly likely that the manufacturing issues which led to the CRL will be resolved soon, leading to an FDA regulatory approval for the combination in near future. With a first-to-market advantage and notable efficacy data, the camrelizumab plus rivoceranib combination therapy will likely achieve substantial commercial success and become the standard of care in this setting.

The commercial outlook for the combination of SCT-I10A with SCT510 therefore appears less promising, even after a potential approval. This is due to the anticipated delay in achieving regulatory approval and the robust efficacy data already demonstrated by the camrelizumab plus rivoceranib combination.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 4092)

Rivoceranib for Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)

Event Date:	05/30/2024
Event Type:	Trial Data - Final Results (Clinical Analysis)
Trial Name:	Phase III - w/Camrelizumab
Market Group:	Oncology
Lead Company:	Elevar Therapeutics, Inc.
Partner Companies:	Advenchen Laboratories Bukwang Pharmaceutical (003000) HLB LifeScience (067630) Hengrui Pharmaceuticals (600276:SS)
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	98% (6% Above Avg.)
Average Approval:	92%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Sorafenib (S)	Camrelizumab (C) + Rivoceranib (R)	C + R vs S
Number of Patients	N/A	N/A	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Median OS ***(Endpoint=Primary)***	15.2 Months	23.8 Months	N/A (P<0.0001)
OS Rate at 24 Months ***(Endpoint=Primary)***	36.2 %	49.0 %	N/A
OS Rate at 36 Months ***(Endpoint=Primary)***	24.8 %	37.7 %	N/A

Elevar Therapeutics has announced that the overall survival (OS) analysis of camrelizumab and rivoceranib as a first-line treatment for unresectable hepatocellular carcinoma (uHCC) will be presented in an abstract entitled "Camrelizumab plus rivoceranib vs sorafenib as first-line therapy for unresectable hepatocellular carcinoma (uHCC): Final overall survival analysis of the Phase 3 CARES-310 study" at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2024. Additional data were published on the ASCO website in an abstract entitled "Role of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte-ratio (PLR) in unresectable hepatocellular carcinoma (uHCC): Subgroup analysis of patients treated with camrelizumab (cam) + rivoceranib (rivo) in the CARES-310 trial".

Data from this study were last seen in July 2023.

"Camrelizumab plus rivoceranib vs sorafenib as first-line therapy for unresectable hepatocellular carcinoma (uHCC): Final overall

survival analysis of the Phase 3 CARES-310 study" - Abstract 4110

Design
CARES-310 was a randomized, open-label, international Phase III study, which included 543 patients with unresectable or metastatic HCC who had not received prior systemic therapy. Patients were randomized 1:1 to receive the combination of camrelizumab + rivoceranib or sorafenib (400 mg orally twice daily), a standard-of-care first-line multi-kinase inhibitor treatment for uHCC. Camrelizumab was administered intravenously (190 mg) every two weeks and rivoceranib was administered orally (250 mg) once daily. The study was conducted at 95 study sites across 13 countries/regions.

Endpoints
The co-primary endpoints were overall survival and progression-free survival. Secondary endpoints included objective response rate and duration of response.

Results
The interim analysis of CARES-310 OS was completed after data cut-off on February 8, 2022. For the final analysis, 16 months later, camrelizumab + rivoceranib continued to show clinically meaningful survival improvement compared with sorafenib.

In the final analysis, median OS was significantly prolonged with camrelizumab + rivoceranib vs. sorafenib (23.8 mo [95% CI 20.6-27.2] vs. 15.2 mo [95% CI 13.2-18.5]; hazard ratio 0.64 [95% CI 0.52-0.79]; 1-sided p < 0.0001). OS rate with camrelizumab + rivoceranib vs. sorafenib was 49.0% vs. 36.2% at 24 mo, and 37.7% vs. 24.8% at 36 mo. OS benefits with camrelizumab + rivoceranib were generally consistent across subgroups, regardless of geographical region, race and etiology.

Most Common Adverse Events
Camrelizumab + rivoceranib demonstrated a manageable safety profile.

Conclusion
The CARES-310 final OS analysis confirmed statistically superior and clinically meaningful survival improvement with a manageable safety profile for the combination of camrelizumab and rivoceranib as a first-line treatment for patients suffering from unresectable hepatocellular carcinoma. These data confirm that the novel combination therapy represents a clinically differentiated improvement to the standard of care in first-line treatments for uHCC.

"Role of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte-ratio (PLR) in unresectable hepatocellular carcinoma (uHCC): Subgroup analysis of patients treated with camrelizumab (cam) + rivoceranib (rivo) in the CARES-310 trial" - Abstract e16197

Design
Per the abstract, the subgroup of pts treated with cam+rivo and BL NLR < 5 or ≥5 and PLR < 300 or ≥300 were evaluated for mOS, mPFS, overall response rate (ORR), disease control rate (DCR), and safety.

Results
Per the abstract, of 272 pts treated with cam+rivo, 64.3% of pts had extrahepatic spread, median AFP was 84.1 ng/mL, 86.8% were Child-Pugh (CP) class A5, 13.2% were CP class A6, 73.5% were ALBI grade 1, 26.5% were ALBI grade 2. Additionally, 249 pts had NLR < 5, 10 pts had NLR ≥5, 252 pts had PLR < 300, and 7 pts had PLR ≥300. Pts with BL NLR < 5 and PLR < 300 demonstrated improved outcomes in mOS, mPFS, ORR, and DCR vs pts with BL NLR ≥5 and PLR ≥300.

Most Common Adverse Events
Per the abstract, rates of any-grade treatment-related adverse events (TRAEs) and grade ≥3 TRAEs were comparable between pts with BL NLR <5 and ≥5 and PLR <300 and ≥300.

Conclusion
Per the abstract, these results suggest that NLR and PLR may serve as a prognostic marker in patients with uHCC, but larger studies are needed to validate these findings.

Comment
Impressive OS results from the CARES-310 trial indicate that the camrelizumab + rivoceranib combination could emerge as the favored first-line treatment for patients with unresectable HCC (uHCC). With a median OS (mOS) of 23.8 months, this trial boasts the longest mOS reported in any global Phase III trial for uHCC. As a result, this combination has the potential to surpass the current standard of care, Tecentriq + bevacizumab. However, it is to be noted that in May 2024, the FDA issued a complete response letter (CRL) to Jiangsu Hengrui Pharma and Elevar Therapeutics' respective applications for PD-1 inhibitor camrelizumab and VEGFR inhibitor rivoceranib in

uHCC. The two major issues highlighted in the CRL were:

- deficiencies related to the developer’s manufacturing site
- FDA’s inability to fully assess the combination within the review period due to travel restrictions at sites such as Russia and Ukraine.

The FDA plans to conduct a thorough evaluation based on the companies' responses to the manufacturing shortfalls. Meanwhile, the developers intend to continue discussions with the FDA and resubmit their marketing applications. There is a high likelihood of these issues being resolved soon, given the fact that the CRL does not cite any concerns related to the trial or clinical data.

Multiple PD-1/PD-L1 combinations are in development for the first-line treatment of metastatic HCC. These include Opdivo + Yervoy, tiragolumab + bevacizumab + Tecentriq, Loqtorzi + Lenvima, and Lenvima + nofazinlimab. Additionally, tislelizumab is under development as a first-line monotherapy, though its efficacy seems weaker compared to combination regimens. With a first-to-market advantage and notable efficacy data, the camrelizumab + rivoceranib combination therapy could achieve substantial commercial success.

Based on these results, we are raising camrelizumab’s and rivoceranib’s LOAs by 5% each.

Source:

Globe Newswire 05/30/2024 (Elevar Therapeutics)
American Society of Clinical Oncology (ASCO) (Abstract 4110)
American Society of Clinical Oncology (ASCO) (Abstract e16197)

Camrelizumab for Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)

Event Date:	05/30/2024
Event Type:	Trial Data - Final Results (Clinical Analysis)
Trial Name:	Phase III - w/Rivoceranib
Market Group:	Oncology
Lead Company:	Jiangsu Hengrui Pharmaceuticals (600276:SS)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	98% (6% Above Avg.)
Average Approval:	92%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Sorafenib (S)	Camrelizumab (C) + Rivoceranib (R)	C + R vs S
Number of Patients	N/A	N/A	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Median OS ***(Endpoint=Primary)***	15.2 Months	23.8 Months	N/A (P<0.0001)
OS Rate at 24 Months ***(Endpoint=Primary)***	36.2 %	49.0 %	N/A
OS Rate at 36 Months ***(Endpoint=Primary)***	24.8 %	37.7 %	N/A

Elevar Therapeutics has announced that the overall survival (OS) analysis of camrelizumab and rivoceranib as a first-line treatment for unresectable hepatocellular carcinoma (uHCC) will be presented in an abstract entitled "Camrelizumab plus rivoceranib vs sorafenib as first-line therapy for unresectable hepatocellular carcinoma (uHCC): Final overall survival analysis of the Phase 3 CARES-310 study" at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2024. Additional data were published on the ASCO website in an abstract entitled "Role of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte-ratio (PLR) in unresectable hepatocellular carcinoma (uHCC): Subgroup analysis of patients treated with camrelizumab (cam) + rivoceranib (rivo) in the CARES-310 trial".

Data from this study were last seen in July 2023.

"Camrelizumab plus rivoceranib vs sorafenib as first-line therapy for unresectable hepatocellular carcinoma (uHCC): Final overall survival analysis of the Phase 3 CARES-310 study" - Abstract 4110

Design

CARES-310 was a randomized, open-label, international Phase III study, which included 543 patients with unresectable or metastatic HCC who

had not received prior systemic therapy. Patients were randomized 1:1 to receive the combination of camrelizumab + rivoceranib or sorafenib (400 mg orally twice daily), a standard-of-care first-line multi-kinase inhibitor treatment for uHCC. Camrelizumab was administered intravenously (190 mg) every two weeks and rivoceranib was administered orally (250 mg) once daily. The study was conducted at 95 study sites across 13 countries/regions.

Endpoints
The co-primary endpoints were overall survival and progression-free survival. Secondary endpoints included objective response rate and duration of response.

Results
The interim analysis of CARES-310 OS was completed after data cut-off on February 8, 2022. For the final analysis, 16 months later, camrelizumab + rivoceranib continued to show clinically meaningful survival improvement compared with sorafenib.

In the final analysis, median OS was significantly prolonged with camrelizumab + rivoceranib vs. sorafenib (23.8 mo [95% CI 20.6-27.2] vs. 15.2 mo [95% CI 13.2-18.5]; hazard ratio 0.64 [95% CI 0.52-0.79]; 1-sided p < 0.0001). OS rate with camrelizumab + rivoceranib vs. sorafenib was 49.0% vs. 36.2% at 24 mo, and 37.7% vs. 24.8% at 36 mo. OS benefits with camrelizumab + rivoceranib were generally consistent across subgroups, regardless of geographical region, race and etiology.

Most Common Adverse Events
Camrelizumab + rivoceranib demonstrated a manageable safety profile.

Conclusion
The CARES-310 final OS analysis confirmed statistically superior and clinically meaningful survival improvement with a manageable safety profile for the combination of camrelizumab and rivoceranib as a first-line treatment for patients suffering from unresectable hepatocellular carcinoma. These data confirm that the novel combination therapy represents a clinically differentiated improvement to the standard of care in first-line treatments for uHCC.

"Role of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte-ratio (PLR) in unresectable hepatocellular carcinoma (uHCC): Subgroup analysis of patients treated with camrelizumab (cam) + rivoceranib (rivo) in the CARES-310 trial" - Abstract e16197

Design
Per the abstract, the subgroup of pts treated with cam+rivo and BL NLR < 5 or ≥5 and PLR < 300 or ≥300 were evaluated for mOS, mPFS, overall response rate (ORR), disease control rate (DCR), and safety.

Results
Per the abstract, of 272 pts treated with cam+rivo, 64.3% of pts had extrahepatic spread, median AFP was 84.1 ng/mL, 86.8% were Child-Pugh (CP) class A5, 13.2% were CP class A6, 73.5% were ALBI grade 1, 26.5% were ALBI grade 2. Additionally, 249 pts had NLR < 5, 10 pts had NLR ≥5, 252 pts had PLR < 300, and 7 pts had PLR ≥300. Pts with BL NLR < 5 and PLR < 300 demonstrated improved outcomes in mOS, mPFS, ORR, and DCR vs pts with BL NLR ≥5 and PLR ≥300.

Most Common Adverse Events
Per the abstract, rates of any-grade treatment-related adverse events (TRAEs) and grade ≥3 TRAEs were comparable between pts with BL NLR <5 and ≥5 and PLR <300 and ≥300.

Conclusion
Per the abstract, these results suggest that NLR and PLR may serve as a prognostic marker in patients with uHCC, but larger studies are needed to validate these findings.

Comment
Impressive OS results from the CARES-310 trial indicate that the camrelizumab + rivoceranib combination could emerge as the favored first-line treatment for patients with unresectable HCC (uHCC). With a median OS (mOS) of 23.8 months, this trial boasts the longest mOS reported in any global Phase III trial for uHCC. As a result, this combination has the potential to surpass the current standard of care, Tecentriq + bevacizumab. However, it is to be noted that in May 2024, the FDA issued a complete response letter (CRL) to Jiangsu Hengrui Pharma and Elevar Therapeutics' respective applications for PD-1 inhibitor camrelizumab and VEGFR inhibitor rivoceranib in uHCC. The two major issues highlighted in the CRL were:

- deficiencies related to the developer's manufacturing site
- FDA's inability to fully assess the combination within the review period due to travel restrictions at sites such as Russia and

Ukraine.

The FDA plans to conduct a thorough evaluation based on the companies' responses to the manufacturing shortfalls. Meanwhile, the developers intend to continue discussions with the FDA and resubmit their marketing applications. There is a high likelihood of these issues being resolved soon, given the fact that the CRL does not cite any concerns related to the trial or clinical data.

Multiple PD-1/PD-L1 combinations are in development for the first-line treatment of metastatic HCC. These include Opdivo + Yervoy, tiragolumab + bevacizumab + Tecentriq, Loqtorzi + Lenvima, and Lenvima + nofazinlimab. Additionally, tislelizumab is under development as a first-line monotherapy, though its efficacy seems weaker compared to combination regimens. With a first-to-market advantage and notable efficacy data, the camrelizumab + rivoceranib combination therapy could achieve substantial commercial success.

Based on these results, we are raising camrelizumab's and rivoceranib's LOAs by 5% each.

Source:

Globe Newswire 05/30/2024 (Elevar Therapeutics)
American Society of Clinical Oncology (ASCO) (Abstract 4110)
American Society of Clinical Oncology (ASCO) (Abstract e16197)

ARX788 for HER2+ Breast Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase II/III - ACE-Breast-02 (China)
Market Group:	Oncology
Lead Company:	Johnson & Johnson (JNJ)
Partner Companies:	Zhejiang Medicine (600216)
Former Companies:	Ambrx
Change to Likelihood of Approval:	0%
Likelihood of Approval:	11% (Same As Avg.)
Average Approval:	11%

Johnson & Johnson announced data from the Phase II/III ACE-Breast-02 study of ARX788 for HER2+ advanced breast cancer (ABC) at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. The abstract entitled "ACE-Breast-02: A pivotal Phase 2/3 trial of ARX788, a novel anti-HER2 antibody-drug conjugate (ADC), versus lapatinib plus capecitabine for HER2+ advanced breast cancer (ABC)" was presented at the meeting on June 3, 2024.

Data from this study were last seen in March 2023.

Design

This randomized study was conducted in HER2+ (FISH+ or IHC3+) ABC in 85 centers in China. Patients with unresectable or metastatic breast cancer pretreated with trastuzumab and taxane were randomized 1:1 to receive ARX788 (1.5mg/kg, IV, Q3W) or lapatinib plus capecitabine (LC, lapatinib 1250mg, QD; capecitabine 1000mg/m^2 BID, d1-14, Q3W), stratified by previous chemotherapy lines (0-1 vs. >1) and visceral metastasis (yes vs. no). ARX788 was not pre-medicated with any prophylactic measures.

Endpoints

The primary endpoint was progression-free survival (PFS) determined by Independent Review Committee (IRC).

Results

As of December 21, 2022, 221 patients were randomly assigned to ARX788 and 220 to LC, and 240 PFS events occurred. The median PFS was 11.33 months with ARX788 versus 8.25 months with LC as per IRC (HR 0.64, p=0.0006).

Most Common Adverse Events

Treatment-related adverse events (TRAEs) of any grade occurred in 98.6% (217/220) and 99.1% (213/215) of patients, respectively. TRAEs of grade 3–5 were similar in the two groups (41.4% and 40.0%, respectively), commonest being blurred vision (12.3%), dry eye (9.1%), keratopathy (5.9%) and interstitial lung disease (5.9%) with ARX788, and hand-foot syndrome (18.1%), hypokalemia (5.1%), and diarrhea (4.2%) with LC. 71 patients (32.3%) had interstitial lung disease with ARX788, primarily grade 1 or 2 (26.8%), with three (1.4%) possibly having drug-related deaths. 164 patients (74.5%) had ocular events related to ARX788, primarily grade 1 or 2 (55.5%) with no grade 4 or 5.

Conclusion

ARX788 significantly prolonged PFS compared to LC in patients with HER2+ ABC previously treated with trastuzumab and taxane. While ocular toxicity and interstitial lung disease were common and manageable, its hematological and GI toxicities under no prophylactic premedication compared favorably with already available ADCs.

Comment

Ambrx's novel HER2-targeting antibody-drug conjugate (ADC) candidate ARX788 joins the approved and emerging agents looking to

enter the earlier stages of the HER2+ breast cancer treatment paradigm. The first numerical results for the drug in the Phase II/III ACE-Breast-02 trial are favorable and highlight the potential for ARX788 to become a second-line and beyond treatment option for patients who have progressed on trastuzumab and taxane therapy, which is currently the first-line standard of care.

The 2024 ASCO presentation details the ACE-Breast-02 study to have met its primary endpoint, with a statistically significant median PFS of 11.33 months vs. 8.25 months in the Tykerb + capecitabine control arm. In the subgroup analysis, efficacy was positive in all key subgroups. As expected, stronger PFS benefit was shown in patients that had received fewer lines of chemotherapy and was broadly consistent in HR+ and HR- patients. So, as of yet, it seems there is no market niche for ARX788 to enter.

Notably, this trial has a similar design to Kadcyla's Phase III EMILIA trial, which led to Kadcyla becoming the standard of care for HER2+ breast cancer patients with residual invasive disease after taxane treatment. In that trial, Kadcyla showed a median PFS of 9.6 months (vs. 6.4 months in the control arm), which is encouraging for ARX788, and outlines the strong efficacy data in the ACE-Breast-02 trial. Since Kadcyla's approval, however, Enhertu has effectively replaced it as the standard of care in the second-line setting following the vast median PFS benefit of 28.8 months seen in the DESTINY-Breast-03 trial. While Enhertu's efficacy data are far superior to those seen in the ACE-Breast-02 trial, there are associated poor treatment outcomes and high toxicity rates in post-trastuzumab and taxane patients, leaving this patient population in an area of unmet need, with few treatment options left if Enhertu is not well tolerated.

Grade ≥3 treatment-related adverse effects were similar between ARX788 and the control arm (41.4% and 40.0%, respectively), which bodes well for ARX788, as in the DESTINY-Breast03 trial of Enhertu, 56% of patients treated experienced grade ≥3 treatment-related adverse effects. Interstitial lung disease is a common adverse reaction in Enhertu therapy and leads to increased discontinuation rates, with the drug carrying a black box warning for this toxicity. While detailed levels of discontinuation rates were not disclosed for ARX788, treatment-related concerns and increasing patient adherence have become increasingly important in physician decision-making, and a strong tolerability profile could be key for ARX788's uptake.

Overall, these results represent a step in the right direction for finding effective and well-tolerated therapies for pretreated HER2+ patients. However, these data come from a Chinese-only patient population, so it remains to be seen as to whether the results will be translated into a Western population, should a similar trial be set up.

Source:

Press Release 05/23/2024 (JNJ)
American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 1020)
Citeline Analysis

Enhertu for HER2+ Breast Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase I/II - DESTINY-Breast07
Market Group:	Oncology
Lead Company:	Daiichi Sankyo Co., Ltd. (4568)
Partner Companies:	AstraZeneca (AZN)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Treatment	Treatment
Treatment Description	T-DXd	T-DXd + P
Number of Patients	75	50
Number of Evaluable Patients	75	50
Confirmed ORR ***(Endpoint=Secondary)***	77.3 %	82 %
PFS rate at 12 months ***(Endpoint=Secondary)***	77.3 %	89.4 %

Daiichi Sankyo announced data from the Phase Ib/II DESTINY-Breast07 study of ENHERTU alone or in combination with other anticancer therapies as a first-line treatment for HER2 positive metastatic breast cancer. An abstract entitled "DESTINY-Breast07: Dose-expansion interim analysis of T-DXd monotherapy and T-DXd + pertuzumab in patients with previously untreated HER2+ mBC" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data from this study were last seen in December 2022.

Design

Per the abstract, pts had locally assessed HER2+ mBC with measurable disease and no or stable brain metastases. A disease-free interval of ≥12 months from (neo)adjuvant therapy was required; no prior therapy for mBC was allowed. Pts were stratified by hormone receptor and disease status (recurrent vs de novo), and PD-L1 expression. Pts received T-DXd 5.4 mg/kg intravenously (IV) every 3 weeks (Q3W) as monotherapy or in combination with P 420 mg IV Q3W, with an 840 mg loading dose.

Endpoints

Per the abstract, primary endpoints were safety and tolerability; key secondary endpoints included objective response rate (ORR) and progression-free survival (PFS), per RECIST 1.1 by investigator.

Results

Confirmed ORR in the ENHERTU monotherapy arm was 76.0% (80% CI: 68.5-82.4) with six CRs and 51 PRs. In the ENHERTU plus pertuzumab combination arm, confirmed ORR was 84.0% (80% CI: 75.3-90.5) with 10 CRs and 32 PRs. The 12-month PFS rate was 80.8% (80% CI: 73.7-86.1) in the ENHERTU monotherapy arm and 89.4% (80% CI: 81.9-93.9) in the ENHERTU plus pertuzumab combination arm.

Per the abstract, seventy-five pts were treated in the T-DXd module and 50 pts in the T-DXd + P module; median follow up was 19.2 months (range 8.7–29.2) and 20.6 months (range 13.3–26.7), respectively. Median age was 57 years in both modules. The confirmed ORR was 77.3% (80% confidence interval [CI] 70.0, 83.6) with T-DXd and 82.0% (80% CI 73.1, 88.8) with T-DXd + P. PFS rate at 12 months was 77.3% (80% CI 69.0, 83.7) with T-DXd and 89.4% (80% CI 81.9, 93.9) with T-DXd + P.

Most Common Adverse Events

The safety of ENHERTU as a monotherapy and in combination with pertuzumab was consistent with known safety profiles of each therapy. Grade 3 or higher TEAEs occurred in 52.0% of patients in the ENHERTU monotherapy arm and 62.0% of patients in the ENHERTU plus pertuzumab combination arm. The most common grade 3 or higher TEAEs occurring in 5% or more of patients were neutropenia (27.0% in ENHERTU monotherapy arm; 24% in ENHERTU plus pertuzumab arm), anemia (4.0% in ENHERTU monotherapy arm; 14.0% in ENHERTU plus pertuzumab arm) and diarrhea (3.0% in ENHERTU monotherapy arm; 6.0% in ENHERTU plus pertuzumab arm). The majority of ILD or pneumonitis events were low grade (grade 1 or 2). In the ENHERTU monotherapy arm, there were two (2.7%) grade 1 events and five (6.7%) grade 2 events. There were no grade 3 or higher events observed in the ENHERTU monotherapy arm. In the ENHERTU plus pertuzumab combination arm, there were six (12.0%) grade 2 events and one (2.0%) grade 3 event. There were no grade 4 or 5 events observed in the ENHERTU plus pertuzumab combination arm.

Per the abstract, as of August 1, 2023, the most common adverse event (AE) was nausea (T-DXd, 70.7% [4.0% Grade 3]; T-DXd + P, 68.0% [0% Grade 3]). Diarrhea was reported in 34.7% (2.7% Grade 3) and 60.0% (6.0% Grade 3) of pts in the T-DXd and T-DXd + P modules, respectively. There were no Grade ≥4 nausea or diarrhea events. Adjudicated drug-related interstitial lung disease (ILD) / pneumonitis was reported in six (8.0%) and five (10.0%) pts in the T-DXd and T-DXd + P modules, respectively (all Grade ≤2). One non-treatment-related AE with outcome of death was reported in the T-DXd module (post-acute COVID-19 syndrome); none with T-DXd + P.

Conclusions

In the analysis, ENHERTU demonstrated promising activity as a monotherapy (n=75) and in combination with pertuzumab (n=50).

Per the abstract, safety profiles were consistent with the known profiles for T-DXd and P, with no Grade ≥3 ILD events. Early data showed promising efficacy in both modules. The DESTINY-Breast07 study is ongoing; analyses from the Phase III DESTINY-Breast09 clinical trial will provide definitive data on TDXd ± P in 1L HER2+ mBC.

Comments

Astra Zeneca and Daiichi Sankyo's blockbuster drug Enhertu is being investigated in the Phase Ib/II DESTINY-Breast07 trial as a monotherapy and in combination with Perjeta (pertuzumab) in HER2+ breast cancer patients as a first-line therapy. The current standard of care for first-line HER2+ breast cancer is the combination of Perjeta, Herceptin (trastuzumab) and docetaxel, which is based off the pivotal Phase III CLEOPATRA trial. The results of this study showed the combination to have a median OS of 56.5 months versus 40.8 months and mPFS of 18.7 versus 12.4 months in the trastuzumab + docetaxel arm. Importantly, Perjeta and trastuzumab are anti-HER2 monoclonal antibodies and there is emerging resistance to anti-HER2 agents, outlining the need for more effective therapeutic agents in the first-line.

Enhertu has already demonstrated impressive efficacy in the Phase III DESTINYBreast-03 trial, which investigated the drug in the second-line setting in patients who had progressed on trastuzumab and taxanes, and demonstrated a PFS of 28.8 months. ASCO 2024 highlights the first dataset released for Enhertu monotherapy and Enhertu in combination with Perjeta as a first-line treatment for HER2+ breast cancer. The interim analysis of DESTINY-Breast07 details a positive objective response rate (ORR) of 77.3% in the Enhertu monotherapy arm and 82.0% in the Enhertu and Perjeta combination arm. While this is not a far cry from the standard of care combination's ORR of 80.2%, the PFS data has the potential to be very positive given Enhertu's historically strong efficacy in the breast cancer space. Notably, the rate of adjudicated drug-related interstitial lung disease or pneumonitis, which is a common cause of discontinuation for Enhertu, was concordant with those of DESTINYBreast-03.

The same regimens are being investigated in the Phase III DESTINY-Breast09 trial, with topline data expected in 2025. While late-phase PFS data on the utility of Enhertu in the first-line is confirmed, the positive ORR supports the expectation that Enhertu will move up the treatment ladder into the first-line setting and will potentially reshape the standard sequence of anti-HER2–targeted agents in the HER2+ treatment algorithm.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 1009)

Business Wire 06/02/2024 (Daiichi Sankyo)
Business Wire 06/02/2024 (AZN)
Citeline Analysis

Ibrance for HER2+ Breast Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - PATRICIA II (Spain)
Market Group:	Oncology
Lead Company:	Pfizer Inc. (PFE)
Partner Companies:	Amgen (AMGN) Royalty Pharma (RPRX)
Former Companies:	Onyx
Change to Likelihood of Approval:	0%
Likelihood of Approval:	44% (Same As Avg.)
Average Approval:	44%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Treatment of Physician's Choice (TPC)	Palbociclib + T + ET	Palbociclib + T + ET vs TPC
Number of Patients	N/A	N/A	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Progression-Free Survival (PFS) ***(Endpoint=Primary)***	7.5 Months	9.1 Months	N/A (P=0.031)
12-Month PFS Rate ***(Endpoint=Primary)***	21.4 %	43.7 %	N/A
Overall Response Rate	8.3 %	18.9 %	N/A

The abstract entitled "Primary results from PATRICIA cohort C (SOLTI-1303), a randomized phase II study evaluating palbociclib with trastuzumab and endocrine therapy in pretreated HER2-positive and PAM50 luminal advanced breast cancer" was presented at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2024.

Data summarized in this event are solely based on data contained in the abstract from the ASCO abstract website.

Design

PATRICIA (cohort C) is a randomized, open-label, Phase II study conducted at 34 sites in Spain recruiting from August 2019 to August 2023. Pts with HER2+/HR+ and centrally tested PAM50 Luminal A or B intrinsic subtype ABC who had received at least one prior line of anti-HER2-based regimens were eligible. Pts were randomized 1:1 to Cohort C1 (Palbociclib 125 mg/day orally 3 weeks/1 week off + T + ET) or Cohort C2 (TPC, including T + any ET or chemotherapy (CT) + T, or T-DM1). The stratification factors were number of previous regimens for ABC and presence of visceral disease. The trial was designed to recruit a total of 102 pts, having an 80% power with one-sided alpha=0.1 to detect a HR of 0.62 in favor of the palbociclib cohort. The study was closed after 73 pts were randomized due to slow recruitment.

Endpoints

The primary endpoint was progression-free survival (PFS).

Results

At data cut-off, 264 pts were pre-screened, and 73 pts were randomized. In cohort C1, 50% of the pts received fulvestrant and 50% aromatase inhibitor as ET. In cohort C2, 37.1% of pts were treated with TDM-1, 45.7% with CT+ T, 11.4 % with ET + T and two pts withdrew their consent before starting the treatment.

Palbociclib + T + ET was associated with longer PFS compared to TPC (median 9.1 vs 7.5 months, stratified HR=0.52 [95%CI 0.29-0.94]; two-sided p=0.031); 12-months PFS rates were 43.7% and 21.4%, respectively. The overall response rate was 18.9% (95% CI 8.6-35.7) in cohort C1 and 8.3% (95% CI 1.4-28.5) in cohort C2.

Most Common Adverse Events

Grade ≥3 adverse events occurred in 63.2% of pts in C1 and 45.5% in C2 cohort. The most frequent grade ≥3 adverse event in the experimental arm was neutropenia (55.3%).

Conclusion

The combination of palbociclib, T and ET showed a statistically significant improvement in PFS in patients with previously treated PAM50 luminal A or B HER2+ advanced breast cancer, as compared to TPC.

Comment

Pfizer's CDK4/6 inhibitor Ibrance is a gold-standard therapy in hormone receptor-positive (HR+)/HER2- breast cancer, but its role in the HER2+ breast cancer space remains unclear due to the lack of late-phase data. The Phase II PATRICIA study highlights the efficacy of the CDK4/6 inhibitor in combination with an anti-HER2 treatment and endocrine therapy in HER2+ patients who have progressed on at least one line of systemic treatment. The release of the ASCO 2024 abstract with topline results for the PATRICIA study highlights the potential for Ibrance to have limited success in a restricted setting in HER2+ pretreated patients.

Currently, the key recommended therapies for HER2+ breast cancer patients in the second- and third-line settings are Enhertu, and Tukysa in combination with Herceptin and Xeloda. In this pretreated setting, the Ibrance combination showed a significantly longer median PFS (mPFS) compared with the physician's choice of therapy arm (9.1 months vs. 7.5 months) in patients who had received a median of two prior lines of treatment, with 12-month PFS rates of 43.7% vs. 21.4%, respectively. Although these efficacy data are not negative, they are less impressive when compared to the data released for Enhertu's Phase III DESTINY-Breast02 trial, which showed an mPFS of 17.8 months vs. 6.9 months for the physician's choice group, in patients who had received two or more prior anti-HER2-based regimens. Ibrance's data look more competitive when compared to the Tukysa combination's data from the Phase II HER2CLIMB trial, however, which showed an mPFS of 7.8 months (vs. 5.6 months for the comparator) in patients who had received one or more prior anti-HER2-based regimens. However, subgroup analysis of patients with brain metastases firmly solidified Tukysa's place as a standard-of-care therapy for these pretreated HER2+ patients.

The Ibrance/trastuzumab/endocrine therapy combination also faces fierce competition from pipeline therapies that are aiming to reveal the benefits of an anti-HER2 + CDK4/6 inhibitor + endocrine therapy triplet combination in HER2+ breast cancer. In the PATRICIA cohort, the Ibrance combination showed slightly inferior efficacy to zanidatamab in combination with Ibrance plus fulvestrant, which had an mPFS of 11.7 months and a PFS rate of 67% at six months in a Phase II trial for HER2+ patients who had progressed on two lines of therapy. The safety profiles from the PATRICIA trial and Phase II zanidatamab combination trial look manageable and similar, with grade ≥3 adverse events occurring in 63.2% and 67% of patients, respectively. Both of these rates are higher than the 57.1% of patients who had grade ≥3 adverse events in Enhertu's DESTINY-Breast02 trial.

Although still in the early phases of investigation, the results from the SOLTI-1303 trial are not hugely promising when compared to both established and pipeline therapies in the pretreated setting. However, Enhertu's prominence on the market may not be a complete dealbreaker for the uptake of Ibrance, as Enhertu aiming to establish an earlier position in the treatment algorithm could provide a key opportunity for the Ibrance/trastuzumab/endocrine therapy combination to become a treatment option for patients who progress on or do not tolerate Enhertu. However, late-phase data would be needed to confirm this possibility in a larger trial.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 1008)
Citeline Analysis

Adcetris for Hodgkin's Lymphoma

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - BrECADD (Germany)
Market Group:	Oncology
Lead Company:	Pfizer Inc. (PFE)
Partner Companies:	Takeda Pharmaceutical (TAK)
Former Companies:	Seagen (SGEN)
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

Takeda and Pfizer announced that the German Hodgkin Study Group (GHSG) announced results from the Phase III HD21 trial evaluating ADCETRIS (brentuximab vedotin) in combination with chemotherapy at the 60 th American Society of Clinical Oncology (ASCO) Annual Meeting. The abstract entitled "Tolerability and efficacy of BrECADD versus BEACOPP in advanced stage classical Hodgkin lymphoma: GHSG HD21, a randomized study" was presented at the meeting on June 1, 2024.

Context

Takeda will be responsible for submission of regulatory filings based on the HD21 study outside of the U.S. and Canada. Under the terms of the collaboration agreement, Pfizer has U.S. and Canadian commercialization rights and Takeda has rights to commercialize ADCETRIS in the rest of the world. At a preplanned three-year analysis, the study met its co-primary endpoints, with the ADCETRIS combination regimen demonstrating significantly improved safety as assessed by treatment-related morbidity (TRMB) and non-inferior PFS.

Per the abstract, this is the report of the confirmative analysis of the HD21 trial.

Design

The HD21 study is a Phase III, multi-country, prospective, open-label, randomized, multicenter trial sponsored by the German Hodgkin Study Group (GHSG) with a PET-response adapted designed to assess the feasibility, efficacy, safety and tolerability of BrECADD rationally designed, CD30-intensified frontline regimen for patients with advanced classical Hodgkin lymphoma. Enrolled patients with newly diagnosed, Stage IIb with large mediastinal mass and/or extranodal lesions, Stage III or IV Hodgkin lymphoma were randomized to receive two cycles of either escalated BEACOPP or BrECADD, respectively, followed by interim PET staging. A decision is then made if patients received a further two or four cycles of escalated BEACOPP or BrECADD. The HD21 trial aims to evaluate a modified treatment regimen to minimize side effects, while maintaining similar responses to treatment. The HD21 study is supported by Takeda, designed to evaluate ADCETRIS in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine and dexamethasone (BrECADD) in comparison to a standard of care treatment escalated doses of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone (eBEACOPP) in patients with newly diagnosed Stage IIb/III/IV classical Hodgkin lymphoma.

Per the abstract, HD21 is an international, Phase III trial including AS-cHL patients 18-60 years at diagnosis. Patients were randomized to receive individualized 4 or 6 cycles of either BEACOPP or BrECADD guided by PET2 results.

Endpoints

The study has co-primary endpoints: safety is assessed by treatment-related morbidity (TRMB) (superiority), a novel endpoint focused on clinically relevant, acute toxicities of primary chemotherapy, and efficacy is assessed by PFS (non-inferiority). Secondary endpoints are tumor response (complete response [CR] rate), overall survival (OS), infertility rate at one year, second malignancies, frequency of adverse events, therapy adherence and quality of life.

Results

After 48 months, BrECADD showed good efficacy to BEACOPP (94.3% PFS for BrECADD and 90.9% PFS for eBEACOPP; hazard ratio [HR]:

0.66 [95% CI:88.7-93.1]; p<0.035). The study found that the addition of ADCETRIS to this chemotherapy regimen improved the risk-to-benefit profile of the combination treatment, maintaining efficacy with significantly fewer acute and long-lasting treatment-related toxicities than the comparator arm.

Per the abstract, the ITT (intention-to-treat) cohort for the efficacy analysis consisted of 1482 patients, of which 742 were randomized to receive BrECADD and 740 to BEACOPP. Median age was 31.1 years (range 18 to 60), 44% were female. PET2 was negative in 424 (57.5%) and 426 (58.2%) patients for BrECADD or eBEACOPP, respectively, and these were scheduled for 4 treatment cycles. With median follow-up of 48 months, 4y-PFS was 94.3% for BrECADD (95%-CI 92.6-96.1), and 90.9% for BEACOPP (95%-CI 88.7-93.1). The hazard ratio was 0.66 [95% CI 0.45-0.97], p=0.035). PFS benefit of BrECADD was driven by a reduction in early treatment failures, i.e., primary progression within 3 months (5 vs. 15) or early relapse between months 3 and 12 (11 vs. 23) and observed across all investigated subgroups. PET2-negative patients in the BrECADD group showed a 4-year PFS of 96.5%. 4-year OS was 98.5% for BrECADD and 98.2% for BEACOPP. Analyses of gonadal function demonstrated higher follicle stimulating hormone recovery rates after one year in both men (67% vs. 24%) and women (89% vs. 68%) with higher birth-rates in the BrECADD group (n=60 vs. n=43).

Most Common Adverse Events

Treatment with BrECADD was also associated with a significant reduction in the incidence of TRMB compared with BEACOPP (n=738; 42% vs 59%; p<0.001), as well as clinically meaningful reductions in adverse events (AEs). The safety profile of ADCETRIS in patients receiving BrECADD remained consistent with other approved ADCETRIS combination regimens, and no new safety signals were identified.

Conclusion

The four-year analysis presented by the GHSG showed superior progression-free survival (PFS) and improved tolerability for patients compared to a current standard of care regimen used in Europe in this setting.

Comment

These are excellent, mature (four-year), results from the HD21 Phase III trial. Escalated BEACOPP (eBEACOPP) is a standard of care for frontline, advanced stage, classic Hodgkin lymphoma that is widely used in the EU but is not routinely used in the US due to toxicity concerns. The goal of the HD21 trial was to increase the safety of the eBEACOPP regimen by replacing bleomycin (which is associated with pulmonary toxicity) and vincristine (which is associated with neuropathy) with Adcetris while retaining doxorubicin, cyclophosphamide, and etoposide. This new BrECADD regimen also replaces procarbazine with the less geno- and gonadotoxic dacarbazine and replaces 14 days of prednisone with four days of dexamethasone. The HD21 trial had an interim PET/CT staging after two cycles of therapy and patients who were PET-negative received two additional cycles of treatment while patients who were PET-positive received four additional cycles.

With regards to safety, the trial met its co-primary endpoint of superior tolerability for the BrECADD regimen as defined by treatment-related morbidity (TRMB) which includes grade 2-4 peripheral sensory neuropathy, grade 4 anemia, thrombopenia, or infection, or grade 3-4 organ toxicity. TRMB events occurred in 42% of patients in the BrECADD arm compared to 59% of patients in the eBEACOPP arm (relative risk 0.72, 95% CI 0.65-0.79). Resolution of TRMB events at 12 months was also improved with only one patient with persistent TRMB at in the BrECADD arm compared to seven patients in the eBEACOPP arm (n=657).

The significant reduction of TRMB was also accompanied by a reduction in the BrECADD arm of transfusion frequency for red blood cells (24% vs 52%) and platelets (17% vs 34%) as well as a reduction in peripheral sensory neuropathy whether it was all grade (39% vs 49%), grade ≥2 (6% vs 14%), or grade ≥3 (1% vs 2%).

Recovery of gonadal function is an important endpoint as median patient age was 31 years. At four years of follow-up, the percent of patients with FSH improved in the BrECADD arm (95.7% vs 73.4% for women and 87% vs 40% for men).

With regards to efficacy, at an interim analysis conducted after a median of three years of follow-up, the trial met the second coprimary endpoint of demonstrating non-inferiority of BrECADD compared to eBEACOPP as determined by PFS (3-year PFS of 94.9% vs 92.3%, respectively). With four years of follow-up, the trial has now demonstrated superiority on the PFS endpoint (4-year PFS of 94.3% vs 90.9%; p=0.035). OS was similar between the two arms with 4-year OS at 98.2% and 98.6%, respectively.

The discussant, Dr Ranajana Advani from Stanford University, noted that in Hodgkin lymphoma, there has been a lot of work to improve tolerability by adding novel agents such as Adcetris or Opdivo to deintensified regimens of radiotherapy and chemotherapy. She noted that while the N-AVD regimen has shown superiority to the Bv-AVD regimen in the SWOG S1826 trial (1 year PFS of 94% vs 86%), the 4-year PFS for BrECADD (94.3%) is comparable to what was reported for N-AVD. She further added that comparison of Adcetris and Opdivo regimens will have to consider that the BrECADD regimen still requires transfusions (RBC transfusions in 24% of patients, platelet

transfusions in 17% of patients) while the risk that acute immune-oncology toxicities associated with Opdivo (such as endocrinopathies, arthritis, xerostemia, neurotixicities, or ocular events) become chronic (>12 weeks beyond treatment cessation) is unknown. Finally, Dr Advani noted that the BrECADD regimen has not been evaluated in the pediatric or elderly population.

In summary, the BrECADD regimen showed superior tolerability and efficacy compared to the eBEACOPP regimen. We await a submission to EU authorities based on the HD21 trial and if approved, we expect that the Adcetris regimen will become a standard of care in the EU.

Source:

Business Wire 06/01/2024 (TAK)
Press Release 06/01/2024 (PFE)
American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract LBA7000)
Citeline Analysis

H3B-6545 for HR+/HER2- Breast Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase I/II - Monotherapy (HER2 Negative Subjects)
Market Group:	Oncology
Lead Company:	Eisai Co., Ltd. (4523:JP)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	2%
Likelihood of Approval:	14% (3% Above Avg.)
Average Approval:	11%

An abstract entitled "H3B-6545 in women with locally advanced/metastatic estrogen receptor-positive (ER+), HER2 negative (–) breast cancer (BC)" was presented at the American Society of Clinical Oncology Annual Meeting on June 3, 2024.

Data in this event has been created solely from the abstract program.

Background

H3B-6545 is a novel selective ER covalent antagonist (SERCA) that inactivates wild-type and mutant ERα. This phase 1/2 study aimed to identify the maximum tolerated dose (MTD)/recommended phase 2 dose (RP2D), and characterize safety and efficacy of H3B-6545 in women with advanced/metastatic ER+, HER2– BC.

Methods

This multicenter, open-label study included dose-escalation [ph1] and -expansion [ph2] phases. Females (postmenopausal or concurrently receiving a luteinizing hormone-releasing hormone agonist) with ER+, HER2–BC who had disease progression on standard therapy were eligible. Prior therapy must have included a minimum of 2 hormonal therapies (HTs), or 1 HT + 1 chemotherapy, or 1 HT + a CDK4/6 inhibitor. H3B-6545 was administered orally QD at doses of 100-600 mg. The MTD was the highest dose at which ≤1 of 6 patients (pts) had a dose-limiting toxicity (DLT). In ph2, efficacy of the RP2D was examined. The primary endpoints were determination of RP2D (ph1) and efficacy (ph2; including objective response rate [ORR], duration of response [DOR], and progression-free survival [PFS] per RECIST v1.1 by investigator, and overall survival [OS]). Safety and PK were secondary endpoints.

Results

At data cutoff (30 Nov 22), 151 pts received ≥1 dose of H3B-6545 during ph1 or ph2. Pts had a median (m [range]) of 2 (1-7) prior endocrine- and 1 (1-6) non-endocrine–containing therapies; 90.1% of pts received prior CDK4/6 inhibitors. During ph1, DLTs of grade (G) 3 rash (n=1) and G 3 fatigue (n=1) were observed at 600 mg; thus, 450 mg was determined to be the MTD/RP2D. In the full analysis set (N=151), 100% and 50.3% of pts had any grade and G ≥3 treatment-emergent adverse events (TEAEs), respectively. TEAEs leading to drug interruption, dose reduction, and withdrawal occurred in 38.4%, 20.5%, and 8.6% of pts, respectively. Nausea (45.7% [2.0% G ≥3]), sinus bradycardia (44.4% [0% G ≥3]), and diarrhea (41.1% [1.3% G ≥3]) were the most common TEAEs. QT prolongation occurred in 9.9% [3.3% G ≥3] of pts. Among 94 response-evaluable pts treated at 450 mg, ORR was 20.2% (95% CI 12.6–29.8) and clinical benefit rate (CBR) was 41.5% (95% CI 31.4–52.1); mPFS (95% CI) was 5.06 (3.15–7.26) months. Among all pts treated at 450 mg (n=115), mOS (95% CI) was 21.52 (16.56–25.46) months. Plasma concentration of H3B-6545 increased as dose increased. Additional results are shown (Table).

Conclusions

H3B-6545 had a low rate of G ≥3 TEAEs and showed clinically meaningful antitumor activity in heavily pretreated female patients with ER+, HER2– BC.

Comments

Anti-estrogen therapy targeting the estrogen-mediated signaling pathway is a key component of treatment in both early and advanced-stage HR+/HER2- breast cancer. For the past three decades, treatment of HR+/HER2- breast cancer has included selective estrogen receptor modulators (SERMs) including tamoxifen and selective estrogen receptor degraders (SERDS) including fulvestrant. Oserdu, which has a hybrid mechanism of being both a SERD and a SERM, was approved in 2023 based on the Phase III Emerald study. Although patients do almost universally benefit from these treatments, resistance to this class of drugs is common, especially in patients with an *ESR1*-mutation, which is associated with high levels of endocrine resistance. Furthermore, *ESR1* mutations often occur concurrently with other genomic alterations, which collectively are associated with a worse prognosis.

To address these resistance mechanisms, novel next-generation anti-estrogen therapies are being developed, including selective estrogen receptor covalent antagonists (SERCAs). Eisai's H3B-6545 is a first-in-class SERCA that antagonizes both wild-type and mutant Erα. It is being investigated in the Phase I/II study in the third-line and beyond in pre- and post-menopausal women who have locally advanced or metastatic disease and have progressed on prior therapy. Results from this one-arm study, presented at ASCO 2024, showed a 450 mg dose of H3B-6545 to have positive antitumor activity in the heavily pre-treated population, with an median PFS of 5.06 months and median OS of 21.52 months. Interestingly, prior SERD treatment did not negatively affect the median PFS for patients (mPFS of 7.33 months), highlighting the potential for H3B-6545 to be a therapeutic option for patients who have progressed on prior SERDs. The mPFS was also 7.33 months in *ESR1*-mutant patients, highlighting the potential for H3B-6545 to be efficacious in patients who have endocrine resistance, an area of high unmet need. Furthermore, the tolerability profile of the agent was strong, with a discontinuation rate of 1.7% due to treatment-related adverse events.

While this is still early-phase, these results are encouraging given that SERDs have not had much luck in the heavily pre-treated HR+/HER2- breast cancer space. Data from both the Phase II AMEERA-3 trial of amcenestrant and the Phase II acelERA trial of giredestrant showed that the drugs failed to meet their respective primary endpoints of significant PFS in second- and third-line metastatic patients, which may reflect badly on this emerging class. However, the Phase Ib/II trial, which investigated palazestrant, a next-generation complete estrogen receptor antagonist (CERAN) and SERD, showed a clinical benefit rate (CBR) of 85% in patients who had received zero to two prior therapies. In a cautious comparison, while this is higher than the CBR of 41.5% demonstrated by H3B-6545, it is natural that H3B-6545's data looks less strong, as palazestrant was given in combination with an approved breast cancer drug in a less heavily pre-treated population. Therefore, in totality, the results of this trial are very encouraging with the potential for an exciting new drug class to enter the breast cancer market. We are increasing the LOA by 2%.

Source:

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 1015)

Ibrance for HR+/HER2- Breast Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase IV - PALMARES-2
Market Group:	Oncology
Lead Company:	Pfizer Inc. (PFE)
Partner Companies:	Amgen (AMGN) Royalty Pharma (RPRX)
Former Companies:	Onyx
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

An abstract entitled, "Comparison of antitumor efficacy of first-line palbociclib, ribociclib, or abemaciclib in patients with HR+/HER2- aBC: Results of the multicenter, real-world, Italian study PALMARES-2," was presented at the American Society of Clinical Oncology annual meeting on June 3, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

The multicenter, population-based study PALMARES-2 evaluated the antitumor efficacy of 1st line Palbociclib, Ribociclib or Abemaciclib in combination with ET in consecutive HR+/HER2- aBC patients treated in 18 Italian cancer centers between January 1, 2016 and September 1, 2023.

Endpoints

The primary study endpoint was real-world Progression-Free Survival (rwPFS), as defined as the time interval between ET plus CDK4/6i initiation and disease progression. Multivariate Cox regression model was used to adjust the association between individual CDK4/6i and rwPFS for clinically relevant variables.

Results

With a data cut-off date of January 1, 2024, investigators enrolled 1850 patients, 750 (40.6%), 676 (36.5%) and 424 (22.9%) of whom received Palbociclib, Ribociclib and Abemaciclib, respectively. Among 1226 (66.3%) patients with endocrine-sensitive disease, 1087 (89%) received concomitant Aromatase Inhibitors, whereas 441 (70.7%) out of 624 (33.7%) patients with endocrine-resistant disease received concomitant Fulvestrant. Patients treated with Abemaciclib were more likely to have endocrine-resistant disease, liver metastases, lobular tumor histology and lower PgR tumor expression, and less likely to have *de novo* metastatic disease (p<0.001). Median rwPFS in the whole study cohort was 34.9 months (95% CI 32.0-37.4). Abemaciclib and Ribociclib were independently associated with better rwPFS when compared to Palbociclib, whereas Abemaciclib and Ribociclib showed no significantly different efficacy (aHR 0.91, 95% CI 0.70-1.19; p=0.505).

Conclusion

The real-world study PALMARES-2 revealed different antitumor efficacy of individual CDK4/6i in HR+/HER2- aBC patients. Longer follow-up is required to study if Palbociclib, Ribociclib and Abemaciclib are associated with different overall survival.

Comments

The treatment paradigm for patients with HR+/HER2- breast cancer has been transformed by the availability of cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors. The approved CDK4/6 inhibitors, Ibrance (palbociclib), Kisqali (ribociclib) and Verzenio (abemaciclib), in

combination with endocrine therapy (ET) represent the standard-of-care treatment for first-line HR+/HER2- metastatic breast cancer patients. CDK4/6 inhibitors generate therapeutic benefit through inhibiting the phosphorylation of proteins which activate the cell cycle, thereby promoting cell cycle arrest. There is widespread clinical experience with CDK4/6 inhibitors and all the agents have enjoyed success with high uptake following approval.

Pfizer's Ibrance was first approved in 2015 based on an improved PFS of 20.2 months versus 10.2 months in the letrozole control arm in the Phase III PALOMA-1 trial. Novartis' Kisqali, which has a CDK6 binding affinity somewhat below Ibrance but comparable to Ibrance for CDK4, followed suit in 2017, based on positive results in the Phase III MONALEESA-2 trial, which showed an improved PFS of 19.3 months versus 14.7 months in the letrozole control arm. Notable, the MONALEESA-2 trial was designed very similarly to PALOMA-1, using letrozole as the control arm. The third CDK4/6 inhibitor to enter market was Eli Lilly's Verzenio in 2018, which is the current market leader, and shows more potent activity against CDK4 and CDK6 than Ibrance and Kisqali. The approval came following the results of Phase III MONARCH-3, which showed a PFS improvement of 28.2 months versus 14.8 months in the aromatase inhibitor control arm. To date, the CDK4/6 inhibitor market is constantly shifting as the CDK4/6 inhibitors' differentiation from each other is limited, with response rates and safety profiles being largely similar.

The Phase II PALMARES-2 trial is the first real-world study to compare the efficacy of the CDK4/6 inhibitors in a clinical setting and first to assess the specific clinical utility of the three CDK4/6 inhibitors in subgroup analyses. The results, presented at ASCO 2024, revealed that Verzenio and Kisqali were independently associated with better real-world PFS when compared to Ibrance, while Verzenio and Kisqali showed no significant difference in efficacy. Interestingly, Verzenio and Kisqali were more effective in endocrine-resistant and pre-menopausal patients and Ibrance was more effective than the other agents in patients with de novo metastatic disease. The results from this study will be meaningful in helping the drugs distinguish themselves and carve out their own prospective niche in the market. For Ibrance, the data from this trial explains the shift away from Ibrance that is currently being seen in clinical practice. Overall, the results of this study represent an important step in identifying which of the CDK4/6 inhibitors are more effective in specific clinical contexts, which will thereby improve patient outcomes.

Source:

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 1014)

Enhertu for HR+/HER2- Breast Cancer

Event Date:	06/02/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - DESTINY-Breast06
Market Group:	Oncology
Lead Company:	Daiichi Sankyo Co., Ltd. (4568)
Partner Companies:	AstraZeneca (AZN)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment
Treatment Description	T-DXd, HER2-low	TPC, HER2-low	T-DXd, ITT	TPC, ITT	T-DXd, HER2-ultralow	TPC, HER2-ultralow
Number of Patients	359	354	436	430	76	76
Number of Evaluable Patients	N/A	N/A	N/A	N/A	N/A	N/A
Modified Progression-free Survival (mPFS) ***(Endpoint=Primary)***	13.2	8.1	13.2	8.1	13.2	8.3
Progression-free Survival (PFS) Hazard Ratio ***(Endpoint=Primary)***	0.62 (P<0.0001)	N/A	0.63 (P<0.0001)	N/A	0.78	N/A
12 Month Overall Survival Rate ***(Endpoint=Secondary)***	87.6 %	81.7 %	87.0 %	81.1 %	84.0 %	78.7 %
Overall Survival (OS) Hazard Ratio ***(Endpoint=Secondary)***	0.83 (P=0.1181)	N/A	0.81	N/A	0.75	N/A
Confirmed Objective Response Rate (ORR)	56.5 %	32.2 %	57.3 %	31.2 %	61.8 %	26.3 %

Daiichi Sankyo announced results from the Phase III DESTINY-Breast06 study of ENHERTU (trastuzumab deruxtecan)in patients with HR positive, HER2 low (IHC 1+ or IHC 2+/ISH-) metastatic breast cancer. The abstract entitled "Trastuzumab deruxtecan (T-DXd) vs physician's choice of chemotherapy (TPC) in patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-low or HER2-ultralow metastatic breast cancer (mBC) with prior endocrine therapy (ET): Primary results from DESTINY-Breast06 (DB-06)" was presented at the 2024 American Society of Clinical Oncology Scientific meeting on June 2, 2024.

Data from this study was last seen in April 2024.

Design

DESTINY-Breast06 is a global, randomized, open-label, Phase III trial evaluating the efficacy and safety of ENHERTU (5.4 mg/kg) versus investigator's choice of chemotherapy (capecitabine, paclitaxel or nab paclitaxel) in patients with HR positive, HER2 low (IHC 1+ or IHC 2+/ISH-) or HER2 ultralow (defined as IHC 0 with membrane staining) advanced or metastatic breast cancer. Patients in the trial had no prior chemotherapy for advanced or metastatic disease and received at least two lines of prior endocrine therapy in the metastatic setting. Patients also were eligible if they had received one prior line of endocrine therapy combined with a CDK4/6 inhibitor in the metastatic setting and experienced disease progression within six months of starting first-line treatment or received endocrine therapy as an adjuvant treatment and experienced disease recurrence within 24 months.

DESTINY-Breast06 enrolled 866 patients (n=713 for HER2 low and n=153 for HER2 ultralow) at multiple sites in Asia, Europe, North America, Oceania and South America.

Per the abstract, pts with HER2-low or -ultralow, HR+ mBC were randomized 1:1 to T-DXd 5.4 mg/kg or TPC. Pts had no prior CT for mBC, with ≥2 lines of ET for mBC, or 1 line of ET for mBC if PD occurred ≤24 months (mo) of adjuvant ET or ≤6 mo of ET+CDK4/6i for mBC.

Endpoints

The primary endpoint is PFS in the HR positive, HER2 low patient population as measured by BICR. Key secondary endpoints include PFS by BICR in the overall trial population (HER2 low and HER2 ultralow), OS in patients in the HER2 low patient population and OS in the overall trial population. Other secondary endpoints include ORR, DOR, time to first subsequent treatment or death, time to second subsequent treatment or death and safety. Analysis of the HER2 ultralow subgroup was not powered to demonstrate statistical significance.

Results

In the primary endpoint analysis of patients with HR positive, HER2 low metastatic breast cancer, ENHERTU reduced the risk of disease progression or death by 38% versus chemotherapy (hazard ratio [HR]: 0.62; 95% confidence interval [CI]: 0.51-0.74; p<0.0001). Median PFS was 13.2 months in the ENHERTU arm compared to 8.1 months in the chemotherapy arm as assessed by blinded independent central review (BICR).

In the key secondary endpoint analysis of PFS by BICR in the overall trial population, ENHERTU achieved a similar 37% reduction in the risk of disease progression or death versus chemotherapy with a median PFS of 13.2 months in the ENHERTU arm versus 8.1 months with chemotherapy (HR: 0.63; 95% CI: 0.53-0.75; p<0.0001).

A prespecified exploratory analysis showed the clinically meaningful improvement in PFS was consistent between patients with HER2 low and HER2 ultralow expression. In patients with HER2 ultralow expression, ENHERTU showed a 22% reduction in the risk of disease progression or death compared to chemotherapy with a median PFS of 13.2 months with ENHERTU versus 8.3 months with chemotherapy (HR: 0.78; 95% CI: 0.50-1.21).

In patients with HER2 low expression, confirmed objective response rate (ORR) was 56.5% in the ENHERTU arm with nine complete responses (CRs) and 194 partial responses (PRs) versus 32.2% in the chemotherapy arm with zero CRs and 114 PRs. In the overall trial population, confirmed ORR in the ENHERTU arm was 57.3% with 13 CRs and 237 PRs versus 31.2% in the chemotherapy arm with zero CRs and 134 PRs. In patients with HER2 ultralow expression, the confirmed ORR in the ENHERTU arm was 61.8% with four CRs and 43 PRs versus 26.3% in the chemotherapy arm with zero CRs and 20 PRs.

Patients in the DESTINY-Breast06 trial received a median of two prior lines of endocrine therapy in each treatment arm. In the overall trial population, 14.9% of patients (n=65) in the ENHERTU arm had received one prior line of endocrine therapy and 67.8% (n=295) had received two prior lines of endocrine therapy. No patients in the trial had received prior chemotherapy treatment in the metastatic setting. Median duration of follow-up was 18.2 months. As of the data cut-off of March 18, 2024, a total of 119 patients (14.0%) remained on study treatment, with 89 (20.5%) receiving ENHERTU and 30 (7.2%) receiving chemotherapy.

Per the abstract, as of Mar 18, 2024, 866 pts (HER2-low, n=713; HER2-ultralow, n=153) were randomized; 90.4% had prior CDK4/6i. TPC group pts were selected for capecitabine (59.8%), nab-paclitaxel (24.4%) or paclitaxel (15.8%). T-DXd significantly improved PFS vs TPC in HER2-low (HR, 0.62 [95% CI 0.51, 0.74], p<0.0001; median, 13.2 vs 8.1 mo). ITT and HER2-ultralow results were consistent with HER2-low. Median treatment duration was 11.0 mo (T-DXd) vs 5.6 mo (TPC). OS was immature at first interim analysis (HER2-low HR, 0.83 [95% CI 0.66, 1.05], P=0.1181; median follow up, 18.6 mo).

Most Common Adverse Events

The safety profile of ENHERTU in DESTINY-Breast06 was consistent with previous breast cancer clinical trials with no new safety concerns identified. The most common grade 3 or higher treatment related treatment emergent adverse events (TEAEs) occurring in 5% or more of

patients treated with ENHERTU were neutropenia (20.7%), leukopenia (6.9%) and anemia (5.8%). Interstitial lung disease (ILD) or pneumonitis occurred in 11.3% of patients treated with ENHERTU. The majority of ILD or pneumonitis events were low grade (grade 1 [n=7; 1.6%] or grade 2 [n=36; 8.3%]). There were three grade 3 ILD events (0.7%), zero grade 4 events and three grade 5 events (0.7%) as determined by an independent adjudication committee.

Per the abstract, Grade (Gr) ≥3 drug-related adverse events occurred in 40.6% (T-DXd) vs 31.4% (TPC). Adjudicated interstitial lung disease / pneumonitis occurred in 49 (11.3%; 0.7% Gr 3/4, 0.7% Gr 5) vs 1 (0.2% Gr 2) pts receiving T-DXd vs TPC.

Conclusion

Per the abstract, T-DXd showed a statistically significant and clinically meaningful PFS benefit vs TPC (CT) in HER2-low mBC. HER2-ultralow results were consistent with HER2-low. Safety was in line with known profiles. DB-06 establishes T-DXd as a standard of care following ≥1 endocrine-based therapy for pts with HER2-low and -ultralow, HR+ mBC.

Comments

Daiichi Sankyo's and Astra Zeneca's Enhertu is a HER2-targeting monoclonal antibody-drug conjugate (ADC) currently investigated in HR+/HER2-low and ultra-low metastatic breast cancer patients who have progressed on one or more lines of endocrine therapy. Enhertu has most recently been approved in HR+/HER2-low metastatic breast cancer patients who have received one or two lines of prior chemotherapy based off the resounding success of the DESTINY-Breast04 Phase III trial, which showed a 10-month PFS benefit versus 5.5 months with chemotherapy. The DESTINY-Breast06 Phase III trial differs from the DESTINY-Breast04 trial in its chemo-naïve patient population and inclusion of the HER2-ultralow patient group, which makes the trial more clinically relevant and commercially meaningful. Approval of the drug in this setting would expand the use of Enhertu into the key HER2-ultra low metastatic breast cancer population, which accounts for ~25% of the HR+ metastatic breast cancer subtype and is associated with very poor outcomes.

Endocrine therapies remain the backbone of treatment for HR+/HER2- metastatic breast cancer but after two lines of treatment, further efficacy is limited due to endocrine resistance, and a novel treatment class is needed for subsequent lines of therapy. The current standard of care following endocrine therapies is systemic chemotherapy, with anthracyclines, taxanes and anti-metabolites being the preferred options. However, these are associated with poor treatment outcomes and high toxicity, leaving this population in an area of high unmet patient need .

The primary results from the highly anticipated DESTINY-Breast06 trial were presented at ASCO 2024, and they showed that Enhertu treatment led to a statistically significant and clinically meaningful PFS benefit versus chemotherapy, in both HR+/HER2-low and HR+/HER2-ultralow patient cohorts. Enhertu improved PFS by 5.1 months compared to the chemotherapy arm (13.2 months verus 8.1 months) in HER2-low patients, and improved the PFS by 4.9 months compared to the chemotherapy arm (13.2 months versus 8.3 months) in HER2-ultralow patients. Importantly, subgroup analysis was very encouraging, with significantly improved PFS following Enhertu treatment in all subgroups, including in those who had received more than three line of prior endocrine therapy and those who had endocrine resistance. At 12 months, OS data were not mature but were trending towards significant.

Trodelvy, the TROP1-targeting ADC, is also seeking a label expansion into the post-endocrine HR+/HER2- setting. It is being investigated in the Phase III ASCENT-07 trial with a primary completion expected in September 2025. While no data are available from this trial yet, Trodelvy has shown positive efficacy data in the in the HR+/HER2- heavily pre-treated space, with a clinically meaningful PFS of 5.5 months and an OS of 14 months versus chemotherapy in the Phase III TROPICS-02 trial. The robust efficacy highlighted in DESTINY-Breast06's primary analysis, will translate into incremental competitive pressure on Trodelvy and will set a high benchmark. The approval of one or both of these therapies will cause a significant shift away from chemotherapy in the second-line and beyond treatment paradigm of HR+/HER2- metastatic breast cancer.

A determining factor discerning Enhertu and Trodelvy could come down to their tolerability in the ongoing studies. In the DESTINY-Breast06 trial, Enhertu had a 14.3% discontinuation rate, primarily due to pneumonitis. The presented also noted that interstitial lung disease remains a key safety risk with Enhertu treatment, given the rate of any grade drug-related interstitial lung disease was high (11.3%) and caused three patient deaths. ASCENT-07 safety data have not yet been published, but to afford an (indirect) comparison, Trodelvy has two black box warnings but a lower discontinuation rate (6%), primarily due to Grade 3 or higher neutropenia, in the TROPICS-02 study.

The results from this study are highly supportive of Enhertu in earlier line treatment and in HER2-ultralow patients, and following this success, it can be expected that there will be a shift in the treatment algorithm away from chemotherapy and towards Enhertu in earlier-lines of therapy. Investigators have noted that their attention will now turn to the HER2 0 patient population, for which the Phase II DAISY trial has been initiated, in the hopes of further increasing the commercial viability of Enhertu. However, it remains a question as

to whether the HER2-ultra low data suggests that Enhertu can be given to all patients irrespective of HER2 status, given the limited accuracy of IHC testing to detect a true HER2-ultra low and HER2 0 patient.

Source:

American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract LBA1000)
Business Wire 06/02/2024 (Daiichi Sankyo)
Business Wire 06/02/2024 (AZN)
Citeline Analysis

Padcev for HR+/HER2- Breast Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - KEYNOTE-F21
Market Group:	Oncology
Lead Company:	Astellas Pharma, Inc. (4503:JP)
Partner Companies:	Pfizer (PFE)
Former Companies:	Seagen (SGEN)
Change to Likelihood of Approval:	-4%
Likelihood of Approval:	7% (4% Below Avg.)
Average Approval:	11%

	Treatment	Treatment
Treatment Description	TNBC Cohort	HR+/HER2- Cohort
Number of Patients	42	45
Number of Evaluable Patients	42	45
Confirmed ORR ***(Endpoint=Primary)***	19.0 %	15.6 %
Confirmed DCR ***(Endpoint=Secondary)***	57.1 %	51.1 %
Time to response, mo, median	1.8 Months	3.5 Months
DOR ***(Endpoint=Secondary)***	3.8 Months	7.2 Months
PFS ***(Endpoint=Secondary)***	3.5 Months	5.4 Months
OS ***(Endpoint=Secondary)***	12.9 Months	19.8 Months

An abstract entitled "Enfortumab vedotin (EV) in triple-negative breast cancer (TNBC) and HR+/HER2- breast cancer (BC) cohorts of EV-202" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data in this event has been created solely from the abstract program.

Methods

In this open-label, multicohort, Phase II trial, eligible adults had locally advanced or metastatic (la/m) solid tumors, measurable disease, and ECOG PS 0–1. In BC cohorts, patients (pts) had prior taxanes or anthracyclines, ≥1 standard-of-care cytotoxic regimen and ≤2 lines (L) of cytotoxic therapy for la/mBC, and prior PD-1/L1 inhibitor (TNBC) or endocrine treatment (tx) with a CDK4/6 inhibitor (HR+/HER2- BC). Nectin-4 expression was not required but was assessed retrospectively. Pts received EV 1.25 mg/kg intravenously days 1, 8, and 15 of each 28-d cycle until discontinuation criteria (eg, disease progression, unacceptable toxicity) were met.

Endpoints

Primary endpoint was confirmed objective response rate (ORR); ≥10 (TNBC) or ≥12 (HR+/HER2- BC) responders out of 40 evaluable pts were needed to claim promising antitumor activity. Secondary endpoints were duration of response (DOR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and safety/tolerability. Antitumor activity was investigator-assessed per RECIST v1.1.

Results

In the TNBC cohort, 42 female pts received EV as of March 3, 2023 (median follow-up, 11.8 mo). Median age was 53 y, 64% had ≥2L systemic tx for metastatic BC, and 33% had prior sacituzumab govitecan. ORR was 19.0%.

In the HR+/HER2- BC cohort (median age, 57.0 y), 45 female pts received EV as of December 3, 2022 (median follow-up, 11.2 mo). Most (73%) had ≥3L systemic tx for metastatic BC. ORR was 15.6%.

Most Common Adverse Events

In the TNBC cohort, Grade ≥3 tx-related adverse events (TRAEs) in >1 pt were decreased neutrophil count (n=3, 7%), decreased white blood cell count (n=2, 5%), and increased aspartate aminotransferase (n=2, 5%). Selected TRAEs of special interest were skin reactions (n=25, 60%), peripheral neuropathy (n=11, 26%), and hyperglycemia (n=2, 5%).

In the HR+/HER2- BC cohort, Grade ≥3 TRAEs in >1 pt were maculopapular rash (n=7, 16%), pruritus and increased aspartate aminotransferase (both n=3, 7%), and abdominal pain and erythema (both n=2, 4%). Selected TRAEs of special interest were skin reactions (n=28, 62%), peripheral neuropathy (n=12, 27%), and hyperglycemia (n=5, 11%).

Conclusions

EV showed antitumor activity in heavily pretreated TNBC. Safety in both cohorts was manageable and consistent with previous reports.

Comments

Astella Pharma's Padcev (enfortumab vedotin) is a nectin-4-directed antibody drug conjugate (ADC). Following the success of Padcev in combination with Keytruda in urothelial cancer, the Phase II EV-202 trial was initiated to investigate Padcev as third-line and beyond treatment option in locally advanced and metastatic solid tumors, in which there were two breast cancer cohorts; HR+/HER2- breast cancer and triple negative breast cancer (TNBC). Later-line chemotherapy is associated with low response rates, poor quality of life, and substantial toxicity and there remains an unmet clinical need for novel, effective therapies for both subtypes of breast cancer .

Although Padcev demonstrated antitumor activity, data released at ASCO 2024 showed that the prespecified ORR threshold was not met in either cohort. In the heavily pre-treated TNBC cohort, in which 7.1% of patients had received more than three lines of cytotoxic therapy, the primary endpoint of confirmed objective response rate (ORR) was 19.0% and mPFS as per investigator assessment was 3.52 months. This does not compare favorably to ADC Trodevly's ORR of 31% in the Phase III ASCENT trial for patients who had received at least two systemic therapies. The toxicity profile was very positive, however, given the poor patient outcomes generally associated with the TNBC treatment, with a 0% rate of adverse events leading to discontinuation.

In the heavily pre-treated HR+/HER2- breast cancer cohort, in which 17.8% of patients had received three or more lines of cytotoxic therapy, the ORR was 15.6% and mPFS as per investigator assessment was 5.39 months. This data continues to look slightly disappointing when (cautiously) compared to the current standard of care in later lines of treatment, Trodelvy, which achieved an ORR of 21% in the Phase III TROPICS-02 trial. Further competition will arise from the pipeline ADC datopotamab deruxtecan, which is being investigated in the third-line and beyond setting in the Phase III TROPION-Breast01 trial and which showed an impressive ORR of 36.4%, and from Enhertu, which is seeking a label expansion from the Phase III DESTINY-Breast06 trial, which showed a very strong ORR of 56.5% in HER2-low patients and 61.8% in HER2-ultralow patients. Following the release of this data at ASCO 2024, Enhertu sets a very high benchmark and is expected to dominate the market in this setting. The HR+/HER2- had a slightly higher level of treatment related adverse effects, although still clinically manageable, and these led to a discontinuation rate of 11.1%.

While efficacy was weak in both cohorts, Padcev's safety profile was strong in both cohorts. This is notably different to Trodelvy's two black box warnings, which leaves the current standard of care vulnerable to competitors with better tolerability profiles. However, based on the high levels of upcoming competition, it is unlikely that Padcev will be able to differentiate itself enough to be approved. We await to see if a Phase III trial is initiated as future development opportunities for Padcev are evaluated. In the meantime, we decrease the LOA by 4%.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 1005)
Citeline Analysis

Verzenio for HR+/HER2- Breast Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - postMONARCH
Market Group:	Oncology
Lead Company:	Eli Lilly and Company (LLY)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Placebo + Fulvestrant	Abemaciclib + Fulvestrant	A + F vs Pbo vs F
Number of Patients	186	182	N/A
Number of Evaluable Patients	186	182	N/A
Improved in investigator-assessed PFS (Interim Analysis) ***(Endpoint=Primary)***	N/A	N/A	N/A (P=0.01)
PFS rates at 6 months	37 %	50 %	N/A
ORR ***(Endpoint=Secondary)***	7 %	17 %	N/A

An abstract entitled "Abemaciclib plus fulvestrant vs fulvestrant alone for HR+, HER2- advanced breast cancer following progression on a prior CDK4/6 inhibitor plus endocrine therapy: Primary outcome of the phase 3 postMONARCH trial" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

postMONARCH was a global, double-blind, placebo-controlled study with pts randomized 1:1 to abemaciclib + fulvestrant or placebo + fulvestrant. Eligible pts had disease progression on a CDK4/6i + AI as initial therapy for ABC or relapse on/after a CDK4/6i + ET as adjuvant therapy for early breast cancer. No other prior treatment for ABC was permitted.

Endpoints

Primary endpoint was investigator-assessed PFS; secondary endpoints included PFS by blinded independent central review (BICR), overall survival (OS), objective response rate (ORR), and safety. Assuming a hazard ratio (HR) of 0.7, the study had ~80% power to detect superiority for abemaciclib, with a cumulative 2-sided type I error of 0.05. Kaplan-Meier method was used to estimate PFS curves and treatment effect was

estimated using a stratified Cox proportional hazard model.

Results

A total of 368 pts were randomized to abemaciclib + fulvestrant (n = 182) or placebo + fulvestrant (n= 186). Most pts (99%) enrolled directly after CDK4/6i + ET as initial therapy for ABC. Prior CDK4/6i was 59% palbociclib, 33% ribociclib, and 8% abemaciclib.

At interim analysis, the study reached the pre-specified criteria for significantly improved investigator-assessed PFS with abemaciclib + fulvestrant compared to placebo + fulvestrant (169 events, HR = 0.66; 95% CI 0.48 – 0.91; p = 0.01). At primary analysis (258 events), the HR was 0.73 (95% CI 0.57 – 0.95), with PFS rates at 6 months of 50% vs 37% for the abemaciclib and placebo arms, respectively. Consistent effect was seen across major clinical and genomic subgroups, including pts with baseline*ESR1* or *PIK3CA* mutations. ORR was improved with abemaciclib compared to placebo (17% vs 7%, respectively, in pts with measurable disease). PFS according to BICR was also improved with HR = 0.55 (95% CI 0.39 - 0.77). OS remains immature (20.9% event rate).

Most Common Adverse Events

Safety was consistent with the known profile of abemaciclib.

Conclusion

Abemaciclib + fulvestrant demonstrated statistically significant PFS improvement in pts with ABC progression on prior CDK4/6i-containing therapy.

Comments

Currently, in the treatment landscape for patients with HR+/HER2- metastatic breast cancer, inhibitors of cyclin-dependent kinases 4 and 6 (CDK4/6) in combination with anti-estrogen endocrine therapies are the standard of care in the first-line setting. There are three CDK4/6 inhibitors that are FDA-approved, namely Ibrance (palbociclib), Kisqali (ribociclib), and Verzenio (abemaciclib), but despite widespread clinical experience with these agents, there is limited insight into the role of continued CDK4/6 inhibition in patients who have received a prior CDK4/6 inhibitor, and trials have had varied results with inconsistent benefit. The Phase II PACE trial showed that the addition of Ibrance to fulvestrant did not significantly improved PFS in metastatic breast cancer patients who had progressed on CDK4/6 inhibitors, while the Phase II MAINTAIN trial demonstrated Kisqali to significantly increase PFS in combination with fulvestrant versus the control arm (5.33 versus 2.76 months) in post CDK4/6 inhibitor patients.

The Phase III postMONARCH trial is investigating the efficacy of Verzenio in combination with fulvestrant in patients who have progressed on a CDK4/6 inhibitor plus endocrine therapy, and will provide insight into the utility of Verzenio in this setting. Verzenio has already demonstrated efficacy in combination with fulvestrant in the Phase III MONARCH-2 trial in advanced breast cancer in advanced breast cancer patients who had progressed on an endocrine therapy. However, none of the patients in the MONARCH-2 trial had received a prior CDK4/6 inhibitor and therefore the results did not provide clarity on the role of Verzenio in post CDK4/6 inhibitor patients. Despite the lack of data, clinicians do administer a second course of CDK4/6 blockade in the second line setting and therefore, establishing the potential activity of Verzenio following disease progression on any of the CDK4/6 inhibitors, represents a key unmet need in the treatment landscape.

The highly anticipated results from this trial, presented at ASCO 2024, show that at interim analysis, the study reached the pre-specified criteria for significantly improved investigator-assessed PFS, and PFS rates at six months were 50% versus 37% with Verzenio and fulvestrant versus fulvestrant alone, respectively. The secondary analysis at 12 months, presented at ASCO 2024, showed a median PFS of 12.9 versus 5.6 months in the control group. Furthermore, there was consistent PFS benefit across clinically relevant subgroups at 12 months, including patients with baseline *ESR1* or *PIK3CA* mutations. However, it is important to note, that at 6 months, patients who had received previous Kisqali treatment did not have a statistically significant PFS. OS data at this time were not commented on. The safety profile was encouraging, with a 6% discontinuation rate due to treatment-related adverse events. Key Grade 3+ toxicities included leukopenia/neutropenia, fatigue and diarrhoea, which are in line with safety profile demonstrated in MONARCH-2.

Given the extensive use of CDK4/6 inhibitors in the large HR+/HER2- metastatic breast cancer population, these results provide a highly lucrative opportunity for Verzenio to establish its place as the key CDK4/6 inhibitor for a large biomarker unrestricted patient population, who have progressed on CDK4/6 blockade.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract LBA1001)

Inavolisib for HR+/HER2- Breast Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase II/III - INAVO120 (w/Palbociclib/Fulvestrant, PIK3CA-Mutant/HR+/HER2-)
Market Group:	Oncology
Lead Company:	Roche Holding AG (RHHBY)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	100% (8% Above Avg.)
Average Approval:	92%

	Placebo	Treatment
Treatment Description	Pbo	Inavo
Number of Patients	164	161
Number of Evaluable Patients	164	161
Increase in median PFS2	15.1 Months	24.0 Months
Increase in median TTFC	15.0 Months	N/A

An abstract entitled "First-line inavolisib/placebo + palbociclib + fulvestrant (Inavo/Pbo+Palbo+Fulv) in patients (pts) with PIK3CA-mutated, hormone receptor-positive, HER2-negative locally advanced/metastatic breast cancer who relapsed during/within 12 months (mo) of adjuvant endocrine therapy completion: INAVO120 Phase III randomized trial additional analyses" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data from this study were last seen in December 2023.

Data in this event has been created solely from the abstract program.

Background

INAVO120 showed significantly and meaningfully improved investigator-assessed progression-free survival (PFS; stratified hazard ratio 0.43) with Inavo+Palbo+Fulv v Pbo+Palbo+Fulv, and manageable safety and tolerability. To further characterize the substantial benefit/risk of the Inavo triplet, researchers assessed additional clinically relevant efficacy endpoints, detailed safety data of key adverse events (AEs) for Inavo (hyperglycemia [HG], diarrhea, rash, stomatitis), and pt-reported outcomes (PROs).

Endpoints

Efficacy endpoints included time from randomization to end of next-line treatment (tx; proxy for PFS2) and to first chemotherapy (TTFC). Key AEs were reported by grouped terms. PROs were assessed by PRO-CTCAE, an overall bother item, BPI-SF, and EORTC QLQ-C30.

Results

Increases in median “PFS2” (24.0 v 15.1 mo; unstratified hazard ratio: 0.59 [95% CI, 0.42–0.83]) and TTFC (NE v 15.0 mo; unstratified hazard ratio: 0.53 [95% CI, 0.37–0.78]) were observed in the Inavo v Pbo arm (median follow-up: 21.3 mo). Pts receiving Inavo experienced a longer duration of time without worsening pain severity and maintained their day-to-day functioning and health-related quality of life on tx.

Most Common Adverse Events

Key AEs were mostly G1–2 and had resolved. No key AEs were G4–5. In the Inavo arm, among pts who experienced key AEs (HG, diarrhea, rash, stomatitis), median time to first onset was 7, 15, 29, and 13 days, respectively. The key AEs were managed with standard supportive care and Inavo dose interruptions/reductions. One pt discontinued Inavo due to HG; one, due to stomatitis. Most pts in both arms reported levels of selected symptomatic AEs from the PRO-CTCAE and overall tx bother as moderate or less, indicating that Inavo does not contribute additional tx burden.

Conclusions

Inavo+Palbo+Fulv was associated with sustained benefit beyond disease progression, delaying chemotherapy administration, with manageable safety and tolerability that was reflected in PROs; hence, supporting it as a new standard of care.

Comments

Combination therapy with cyclin-dependent kinases 4 and 6 (CDK4/6) inhibitors and endocrine therapy (ET) is the current standard of care for metastatic HR+/HER2- metastatic breast cancer patients in the adjuvant setting. However, acquired resistance to the doublet therapy is highly common, and given the same combination therapy is used extensively in the first-line setting, there is a high unmet need for more efficacious treatments in the first-line setting, especially for patients who are resistant to the CDK4/6 and ET combination. Furthermore, chemotherapy, the standard of care for patients who no longer respond to ET, is associated with poor outcomes.

Roche's inavolisib, is a potent and selective PI3Kα inhibitor that also promotes the degradation of mutant p110α. It is currently being investigated in the Phase III INAVO120 trial in combination with Ibrance (a CDK4/6 inhibitor) and Faslodex (an ET) versus placebo with Ibrance and Faslodex as a first-line therapy for patients with *PIK3CA*-mutant HR+/HER2- locally advanced or metastatic breast cancer. It is hypothesized that a PI3K inhibitor in combination with the current standard of care ET and CDK4/6 inhibitor will show a synergistic anti-tumor effect. *PIK3CA* is one of the most frequently mutated oncogenes in breast cancer, with up to 40% of HR+HER2- patients having the mutation, and contributes to both chemotherapy and endocrine therapy resistance. Therefore, the patient population studied in the INAVO120 trial has an additional element of unmet need.

PI3K inhibitors have had limited success in the past due to poor efficacy and tolerability, and low combinability with CDK4/6 inhibitors. To date, the only approved PI3K inhibitor in this space is Piqray in combination with Faslodex, for patients who had progressed on endocrine therapy in the second-line and beyond. This approval was based off the success of the Phase III SOLAR-1 trial, which showed a statistically significant improvement in PFS of 11.0 months versus 5.7 months in the placebo arm. In a cautious comparison, the primary analysis of INAVO120, which was presented at SABCS 2023, was promising compared to that of SOLAR-1. The inavolisib/Ibrance/Faslodex combination showed a statistically significant PFS of 15.0 months vs 7.3 months in placebo/Ibrance/Faslodex control arm. Data presented at ASCO 2024 highlights the next stage of analysis, with a PFS2 of 24.0 v 15.1 months, which is described as time from randomization to end of next-line treatment. At this time, OS data were immature but a clear positive trend has been observed.

The common adverse events in the INAVO120 trial were in line with those of the PI3K inhibitor drug class and clinically manageable. Compared to Piqray in the SOLAR-1 trial, rates of the most common grade 3 adverse events were lower; hyperglycemia (6% versus 33.1%) and diarrhea (4% versus 7%). The high rates of toxicity associated with Piqray leave room for inavolisib to be a more well-tolerated and selective PI3K inhibitor in the first-line setting.

The efficacy of the inavolisib combination seems robust and based on the strength of the data, Roche has initiated the Phase III INAVO122 trial in pre-treated *PIK3CA*-mutated HER2+ breast cancer patients. In addition, the FDA has granted priority review to the combination, which could lead to an accelerated approval for endocrine refractory *PIK3CA*-mutant HR+/HER2- patients. With the combination's PDUFA date set for November 27, 2024, we are increasing its LOA by 5%.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 1003)
Citeline Analysis

Keytruda for HR+/HER2- Breast Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - w/Trodelvy
Market Group:	Oncology
Lead Company:	Merck & Co., Inc. (MRK)
Partner Companies:	DRI Capital
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	47% (3% Above Avg.)
Average Approval:	44%

	Treatment	Treatment
Treatment Description	SG + Pembrolizumab	SG
Number of Patients	52	52
Number of Evaluable Patients	52	52
median PFS at 9.2 months ***(Endpoint=Primary)***	8.4 Months (P=0.26)	6.2 Months
ORR at 9.2 months ***(Endpoint=Secondary)***	21.2 %	17.3 %
OS (Immature) ***(Endpoint=Secondary)***	16.9 Months (P=0.28)	17.1 Months

An abstract entitled "SACI-IO HR+: A randomized phase II trial of sacituzumab govitecan with or without pembrolizumab in patients with metastatic hormone receptor-positive/HER2-negative breast cancer" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

Eligible patients (pts) had unresectable locally advanced or metastatic HR+ (ER≥1% and/or PR≥1%), HER2- breast cancer treated with ≥1 prior endocrine therapy and 0-1 chemotherapy (CT) for MBC. Pts with brain metastases were eligible if locoregional therapy was completed and steroids discontinued ≥7 days before study therapy. Pts who received prior topoisomerase I inhibitor ADC, irinotecan or PD-1/L1 inhibitors were excluded. Pts were randomized 1:1 to Arm A [SG 10 mg/kg IV (D1, D8) + pembrolizumab 200 mg IV (D1), 21-day cycle] or Arm B (SG alone). For this preliminary analysis, data were locked January 12, 2024.

Endpoints

The primary endpoint was progression-free survival (PFS); secondary endpoints included PFS in PD-L1+ pts (22C3 CPS ≥1), overall survival (OS), objective response rate (ORR) and toxicity (NCI CTCAE v5.0). Baseline and on-treatment biopsies were performed for correlative analyses.

Results

Between March 2021 - January 2024, 110 pts enrolled; 104 pts (52 Arm A; 52 Arm B) started study therapy and were included in the analysis. Median age was 57 yrs (range: 27-81); 102 pts (98.1%) were female. 80 pts (76.9%) received prior CDK4/6 inhibitor for MBC; 58 (55.8%) had no prior CT, 46 (44.2%) had 1 prior line of CT for MBC.

At a median follow-up of 9.2 months (mo), median PFS was 8.4 mo in Arm A vs 6.2 mo in Arm B (HR 0.76, 95% CI 0.47-1.23, log-rank p=0.26); ORR 21.2% and 17.3%, respectively. OS data are immature with only 26 events to date; OS was 16.9 mo vs 17.1 mo (HR 0.65, 95% CI 0.30-1.41, log-rank p=0.28), respectively.

Most Common Adverse Events

The most frequent treatment-related toxicities (≥G2) in Arm A were neutropenia (67.3%), fatigue (36.5%), alopecia (36.5%), anemia (32.7%), leukopenia (26.9%), diarrhea (21.2%) and nausea (21.2%); in Arm B, neutropenia (59.6%), alopecia (38.5%), diarrhea (34.6%), nausea (32.7%), fatigue (32.7%) and anemia (21.2%).

Conclusion

Addition of pembrolizumab to SG showed a non-significant trend toward improved PFS in unselected HR+/HER2- MBC at this preliminary time point.

Comments

The antibody–drug conjugate (ADC) Trodelvy (sacituzumab govitecan) is composed of a Trop-2-directed monoclonal antibody coupled to SN-38 via a proprietary linker. Trodelvy as a monotherapy has shown proven efficacy in the heavily pre-treated HR+/HER2- space and is approved in this setting based on the results of the Phase III TROPICS-02 trial. The Phase II SACI-IO HR+ investigator-initiated trial explores the efficacy of Trodelvy in the second-line and beyond as a monotherapy or in combination with the immune checkpoint inhibitor (ICI) Keytruda (pembrolizumab) in HR+/HER2- patients who have progressed on at least one-line of endocrine therapy (ET). This represents an area of unmet need, as chemotherapy, the standard of care for patients who do not respond to endocrine therapy, is associated with poor outcomes.

In the breast cancer space, ADCs are being investigated in novel combinations to enhance their activity and overcome resistance mechanisms. The combination of an ADC and ICI is intriguing, as the synergy of these two drug classes is not well established in the HR/HER2- breast cancer space. Based on the Phase III KEYNOTE-756 trial, there is evidence that Keytruda is efficacious in HR+/HER2- breast cancer, albeit in the neoadjuvant setting, but there is no data to confirm its efficacy with an ADC. In fact, SACIO-HR+ is the first trial to report the efficacy of a Trop-2 ADC combined with an ICI in breast cancer. Unfortunately, the results of the SACI-IO HR+ trial do not highlight the combination to be hugely active. The addition of Keytruda to Troveldy showed a non-significant trend toward improved PFS, with a final mPFS of 8.1 months versus 6.2 months in the Trodelvy monotherapy arm. In the PD-L1 positive subgroup, the Trodelvy and Keytruda arm showed a more positive but not significant mPFS of 11.1 months versus 6.7 months in the Trodelvy alone arm, which could indicate the drug combination would be more effective in this biomarker restricted subgroup. OS data were not mature, but at a median follow up of 12.5 months, OS did not significantly differ between the arms, with 18.5 versus 18.0 months in the Trodelvy and Keytruda arm and Trodelvy arm, respectively.

The results from SACI-IO HR+ don't bode well for Trodelvy's ongoing Phase III ASCENT-07 trial, which is investigating the drug in chemo-naïve patients who have progressed on at least two endocrine therapies. The results could, however, be more promising in the lower-risk patient population. Furthermore, the positive PFS data from Enhertu's Phase III DESTINY-Breast06 trial, which is investigating Enhertu in the same setting as that of ASCENT-07, will translate into incremental competitive pressure on Trodelvy, as Enhertu also seeks to enter the second-line and beyond treatment paradigm of HR+/HER2- metastatic breast cancer.

While the results from SACI-IO HR+ are unlikely to change clinical practice, they provide an idea of the utility of Trodelvy in an earlier line HR+/HER2- setting and pave the way for future novel drug combinations. Investigators also noted that a failure of the trial was the inability to recruit a PD-L1 positive population and provided evidence for potential efficacy of this patient subgroup and the possibility for larger biomarker restricted trial in future.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract LBA1004)
Citeline Analysis

Trodelvy for HR+/HER2- Breast Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - +/- Pembrolizumab
Market Group:	Oncology
Lead Company:	Gilead Sciences, Inc. (GILD)
Partner Companies:	Royalty Pharma (RPRX)
Former Companies:	Immunomedics
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Treatment	Treatment
Treatment Description	SG + Pembrolizumab	SG
Number of Patients	52	52
Number of Evaluable Patients	52	52
median PFS at 9.2 months ***(Endpoint=Primary)***	8.4 Months (P=0.26)	6.2 Months
ORR at 9.2 months ***(Endpoint=Secondary)***	21.2 %	17.3 %
OS (Immature) ***(Endpoint=Secondary)***	16.9 Months (P=0.28)	17.1 Months

An abstract entitled "SACI-IO HR+: A randomized phase II trial of sacituzumab govitecan with or without pembrolizumab in patients with metastatic hormone receptor-positive/HER2-negative breast cancer" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

Eligible patients (pts) had unresectable locally advanced or metastatic HR+ (ER≥1% and/or PR≥1%), HER2- breast cancer treated with ≥1 prior endocrine therapy and 0-1 chemotherapy (CT) for MBC. Pts with brain metastases were eligible if locoregional therapy was completed and steroids discontinued ≥7 days before study therapy. Pts who received prior topoisomerase I inhibitor ADC, irinotecan or PD-1/L1 inhibitors were excluded. Pts were randomized 1:1 to Arm A [SG 10 mg/kg IV (D1, D8) + pembrolizumab 200 mg IV (D1), 21-day cycle] or Arm B (SG alone). For this preliminary analysis, data were locked January 12, 2024.

Endpoints

The primary endpoint was progression-free survival (PFS); secondary endpoints included PFS in PD-L1+ pts (22C3 CPS ≥1), overall survival (OS), objective response rate (ORR) and toxicity (NCI CTCAE v5.0). Baseline and on-treatment biopsies were performed for correlative analyses.

Results

Between March 2021 - January 2024, 110 pts enrolled; 104 pts (52 Arm A; 52 Arm B) started study therapy and were included in the analysis. Median age was 57 yrs (range: 27-81); 102 pts (98.1%) were female. 80 pts (76.9%) received prior CDK4/6 inhibitor for MBC; 58 (55.8%) had no prior CT, 46 (44.2%) had 1 prior line of CT for MBC.

At a median follow-up of 9.2 months (mo), median PFS was 8.4 mo in Arm A vs 6.2 mo in Arm B (HR 0.76, 95% CI 0.47-1.23, log-rank p=0.26); ORR 21.2% and 17.3%, respectively. OS data are immature with only 26 events to date; OS was 16.9 mo vs 17.1 mo (HR 0.65, 95% CI 0.30-1.41, log-rank p=0.28), respectively.

Most Common Adverse Events

The most frequent treatment-related toxicities (≥G2) in Arm A were neutropenia (67.3%), fatigue (36.5%), alopecia (36.5%), anemia (32.7%), leukopenia (26.9%), diarrhea (21.2%) and nausea (21.2%); in Arm B, neutropenia (59.6%), alopecia (38.5%), diarrhea (34.6%), nausea (32.7%), fatigue (32.7%) and anemia (21.2%).

Conclusion

Addition of pembrolizumab to SG showed a non-significant trend toward improved PFS in unselected HR+/HER2- MBC at this preliminary time point.

Comments

The antibody–drug conjugate (ADC) Trodelvy (sacituzumab govitecan) is composed of a Trop-2-directed monoclonal antibody coupled to SN-38 via a proprietary linker. Trodelvy as a monotherapy has shown proven efficacy in the heavily pre-treated HR+/HER2- space and is approved in this setting based on the results of the Phase III TROPICS-02 trial. The Phase II SACI-IO HR+ investigator-initiated trial explores the efficacy of Trodelvy in the second-line and beyond as a monotherapy or in combination with the immune checkpoint inhibitor (ICI) Keytruda (pembrolizumab) in HR+/HER2- patients who have progressed on at least one-line of endocrine therapy (ET). This represents an area of unmet need, as chemotherapy, the standard of care for patients who do not respond to endocrine therapy, is associated with poor outcomes.

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The results from SACI-IO HR+ don't bode well for Trodelvy's ongoing Phase III ASCENT-07 trial, which is investigating the drug in chemo-naïve patients who have progressed on at least two endocrine therapies. The results could, however, be more promising in the lower-risk patient population. Furthermore, the positive PFS data from Enhertu's Phase III DESTINY-Breast06 trial, which is investigating Enhertu in the same setting as that of ASCENT-07, will translate into incremental competitive pressure on Trodelvy, as Enhertu also seeks to enter the second-line and beyond treatment paradigm of HR+/HER2- metastatic breast cancer.

While the results from SACI-IO HR+ are unlikely to change clinical practice, they provide an idea of the utility of Trodelvy in an earlier line HR+/HER2- setting and pave the way for future novel drug combinations. Investigators also noted that a failure of the trial was the inability to recruit a PD-L1 positive population and provided evidence for potential efficacy of this patient subgroup and the possibility for larger biomarker restricted trial in future.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract LBA1004)
Citeline Analysis

Keytruda for Melanoma

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase II - KEYNOTE-942 (w/mRNA-4157)
Market Group:	Oncology
Lead Company:	Merck & Co., Inc. (MRK)
Partner Companies:	DRI Capital
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

Moderna and Merck announced results from a planned analysis from the Phase IIb randomized KEYNOTE-942/mRNA-4157-P201 study were presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. An abstract entitled, "Individualized neoantigen therapy mRNA-4157 (V940) plus pembrolizumab in resected melanoma: 3-year update from the mRNA-4157-P201 (KEYNOTE-942) trial," was presented on June 3, 2024.

Data from this study were last seen in December 2023.

Context

In the primary analysis of the Phase II mRNA-4157-P201 (KEYNOTE-942) trial (median planned follow-up, 23 mo), pts with completely resected high-risk stage IIIB–IV cutaneous melanoma receiving mRNA-4157 + pembrolizumab (pembro; combo) had prolonged recurrence-free survival (RFS) and distant metastasis-free survival (DMFS) vs pembro alone.

Design

KEYNOTE-942 is an ongoing randomized, open-label Phase IIb trial that enrolled 157 patients with high-risk stage III/IV melanoma. Following complete surgical resection, patients were assigned 2:1 (stratified by stage) to receive mRNA-4157 (V940) (1 mg every three weeks for nine doses) and KEYTRUDA (200 mg every three weeks up to 18 cycles [for approximately one year]) versus KEYTRUDA alone for approximately one year until disease recurrence or unacceptable toxicity. The KEYNOTE-942 trial is ongoing to collect additional translational data and an additional 100 patients are currently being enrolled.

Key eligibility criteria for the trial included: patients with resectable cutaneous melanoma metastatic to a lymph node and at high risk of recurrence, patients with complete resection within 13 weeks prior to the first dose of KEYTRUDA, patients were disease free at study entry (after surgery) with no loco-regional relapse or distant metastasis and no clinical evidence of brain metastases, patients had a formalin fixed paraffin embedded (FFPE) tumor sample available suitable for sequencing, Eastern Cooperative Oncology Group (ECOG) Performance Status 0 or 1 and patients with normal organ and marrow function reported at screening.

Endpoints

The primary endpoint is RFS, defined as the time from first dose of KEYTRUDA until the date of first recurrence (local, regional, or distant metastasis), a new primary melanoma, or death from any cause in the intention-to-treat population. Secondary endpoints include distant metastasis-free survival and safety, and exploratory endpoints include distribution of TMB expression in baseline tumor samples across study arms and their association with the primary RFS endpoint.

Results

With a median follow-up of approximately three years (34.9 months), adjuvant treatment with mRNA-4157 (V940) in combination with KEYTRUDA continued to demonstrate a clinically meaningful and durable improvement in recurrence-free survival (RFS), the primary endpoint of the study, reducing the risk of recurrence or death by 49% (HR [95% CI], 0.510 [0.288–0.906]; two-sided nominal p-value 0.019) compared with KEYTRUDA alone. mRNA-4157 (V940) in combination with KEYTRUDA also continued to demonstrate a meaningful improvement in

distant metastasis-free survival (DMFS), a key secondary endpoint of the study, compared with KEYTRUDA alone, reducing the risk of developing distant metastasis or death by 62% (HR [95% CI], 0.384 [0.172–0.858], two-sided nominal p-value 0.015). The 2.5-year RFS rate of mRNA-4157 (V940) in combination with KEYTRUDA was 74.8%, as compared to 55.6% for KEYTRUDA alone, with the benefit observed across exploratory subgroups.

Data from an exploratory subgroup analysis of the Phase IIb KEYNOTE-942/mRNA-4157-P201 study in patients with resected high-risk melanoma (stage III/IV) following complete resection showed that improvement in RFS was observed with mRNA-4157 (V940) in combination with KEYTRUDA compared to KEYTRUDA alone regardless of tumor mutational burden (TMB) or programmed death-ligand 1 (PD-L1) status.

The RFS benefit of mRNA-4157 (V940) in combination with KEYTRUDA compared to KEYTRUDA alone was maintained across both TMB high (HR [95% CI], 0.564 [0.253–1.258]), TMB non-high (0.571 [0.245–1.331]), PD-L1 positive (0.471 [0.226–0.979]), PD-L1 negative (0.147 [0.034–0.630]), and circulating tumor DNA (ctDNA) negative (0.207 [0.091–0.470]) subpopulations. ctDNA positive HR was not estimable due to the small sample size. There were no significant associations between individual human leukocyte antigen (HLA) alleles and RFS observed for mRNA-4157 (V940) in combination with KEYTRUDA.

The exploratory endpoint of overall survival (OS) favored mRNA-4157 (V940) in combination with KEYTRUDA compared to KEYTRUDA alone, with a 2.5-year OS rate of 96.0% vs. 90.2%, respectively (HR [95% CI], 0.425 [0.114–1.584]).

Most Common Adverse Events

The safety profile with mRNA-4157 (V940) in combination with KEYTRUDA in KEYNOTE-942/mRNA-4157-P201 remains consistent with the primary analysis. The most common adverse events attributed to mRNA-4157 (V940) in combination with KEYTRUDA were fatigue (60.6%), injection site pain (56.7%), and chills (49.0%). The majority of the adverse events attributed to mRNA-4157 (V940) were Grade 1-2, with fatigue being the most common Grade 3 event and no Grade 4-5 events. Immune-related adverse events occurred in 37.5% of patients receiving the combination and 36% receiving KEYTRUDA alone.

Conclusion

Per the abstract, the current analysis with ~3 y median follow-up showed durable and meaningful long-term RFS and DMFS benefit with mRNA-4157 + pembro vs pembro alone. A trend for improved OS with combo tx was also observed. HLA and translational subgroup results suggest mRNA-4157 + pembro may benefit a broader pt population vs pembro alone.

Comment

These three-year follow up data from the Phase III KEYNOTE-942 trial demonstrate mRNA-4175 addition to standard of care (SoC) therapy, Keytruda, to offer improved survival outcomes with less chance of disease relapse for high-risk stage III melanoma patients. Currently, most patients with Stage IIIB-IV resected melanoma will receive adjuvant PD-1 blockade, however, the results remain suboptimal and approximately half of treated patients go on to experience disease relapse with considerably worse prognosis. This means there is a high unmet need to improve the relapse-free survival which is currently afforded by adjuvant PD-1 blockade approaches. In these updated data the mRNA-4175 and Keytruda regimen reports nearly a 20% benefit in 2.5-year RFS rate (74.8% vs 55.6%) compared to Keytruda alone, suggesting the combination therapy has the potential to reduce disease relapse in this high-risk patient group and fulfil a critical unmet need. Though cross-trial comparisons can be misleading, the RFS data from KEYNOTE-942 further looks impressive when compared to the 13% RFS benefit seen at similar follow up in the Phase III CheckMate-238 trial, which investigated Opdivo compared to Yervoy as an adjuvant therapy in the same patient population. Considering this, the mRNA-4175 + Keytruda regimen looks to have the potential to become the new SoC. For now, we await to see if this RFS benefit can be replicated in the supportive Phase III V940-001 trial, which was initiated in July 2023.

In these three-year follow-up analyses we also see the first presentation of overall survival data. Whilst these data are still considerably immature with little events having occurred, the emerging trend looks to suggest that mRNA-4175 + Keytruda may also champion in this outcome as well. Currently, there are more survivors in the combination arm than control, with the 2.5-year OS rates reported at 96.0% vs 90.2%, respectively, and there is an expectation for this to deepen over time. Though the data is still too immature to show significance, these initial results undoubtedly merit further follow up. Maturity of the OS data is not expected for at least another two years.

The safety profile of the combination regimen is also promising with no potentiation of immune-related adverse events (Grade ≥3 immune-related AEs: 10.6% vs 14% in treatment vs control arm). This is a key safety outcome underlined by physicians and regulatory bodies alike, including the FDA. Other notable toxicities for this investigational regimen are the vaccine-related adverse events, however, with only 11.5% Grade ≥3 events reported, the combination looks to be relatively safe. Moreover, the presenter highlighted these vaccine-related toxicities to parallel those seen with the company's Covid-19 vaccine, suggesting that management of these toxicities may be relatively unproblematic, considering physician familiarity with vaccine-related AEs since the pandemic.

Though the adjuvant setting is currently dominated by PD-1 flagships Keytruda and Opdivo, alongside kinase inhibitor doublet Mekinist and Tafinlar, the space looks set to heat up for more competition. BMS's melanoma sensation Opdualag is also being investigated for adjuvant use in the Phase III RELATIVITY-098 trial, and whilst data is yet to be released, considering the dual blockade's success in the frontline setting hopes are high for its potential in earlier lines. Opdualag's rapid uptake in the first-line setting, represented by a 25% share capture in its first year to market, can largely be attributed to its comparable efficacy to the Opdivo + Yervoy regimen with the advantage of considerably more favorable safety and tolerability profiles. If RELATIVITY-098 were to prove successful in primary endpoint RFS, Opdualag may have the upper hand over the mRNA-4175 regimen in terms of safety as well, with no risk of vaccine-related adverse events. With both RELATIVITY-098 and V940-001 currently lacking data readouts, the race to potentially be the new SoC looks is starting to gear up. Whilst the mRNA-4175 regimen is armored with strong Phase II data, the RELATIVITY-098 trial looks to have the advantage of a head start, with patient enrolment already complete. For now, data from both these trials is eagerly awaited and anticipation to see which regimen can be the first to improve upon SoC single blockade is high.

Overall, these three-year follow up data from the Phase II KEYNOTE-942 trial prime the mRNA-4715 + Keytruda regimen as a promising candidate to improve upon SoC adjuvant therapy and bode well for a positive Phase III read-out.

Source:

Press Release 06/03/2024 (MRK)
American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract LBA9512)
Citeline Analysis

Tilsotolimod for Melanoma

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - ILLUMINATE-301 (w/Ipilimumab)
Market Group:	Oncology
Lead Company:	Aceragen, Inc. (ACGN)
Partner Companies:	N/A
Former Companies:	Idera Pharmaceuticals
Change to Likelihood of Approval:	0%
Likelihood of Approval:	0% (Same As Avg.)
Average Approval:	N/A

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Ipilimumab	Tilsotolimod + Ipilimumab	Tilsotolimod + Ipilimumab vs. Ipilimumab
Number of Patients	243	238	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Objective Response Rate *(Endpoint=Primary)*	8.6 %	8.8 %	N/A
Overall Survival *(Endpoint=Primary)*	10.0 Months	11.6 Months	N/A (P=0.7)

The abstract entitled "Phase III randomized trial evaluating tilsotolimod in combination with ipilimumab versus ipilimumab alone in patients with advanced refractory melanoma (ILLUMINATE 301)" was presented at the American Society of Clinical Oncology Annual Meeting on June 3, 2024.

Data from the study were last seen in March 2021.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

The Phase III ILLUMINATE-301 study evaluated tilsotolimod, a toll-like receptor 9 agonist, with or without ipilimumab in patients with anti-programmed death-1 (PD-1)-advanced refractory melanoma. Patients with unresectable Stage III–IV melanoma that progressed during or after anti-PD-1 therapy were randomized 1:1 to receive 24 weeks of tilsotolimod plus ipilimumab or 10 weeks of ipilimumab alone. Nine IT injections of tilsotolimod were administered to a single designated lesion over 24 weeks. Intravenous ipilimumab 3 mg/kg was administered every 3 weeks from Week 2 in the tilsotolimod arm and Week 1 in the ipilimumab arm.

Endpoints

The primary endpoint was efficacy measured using objective response rate (ORR; independent review) and overall survival (OS).

Results

A total of 481 patients received tilsotolimod plus ipilimumab (n=238) or ipilimumab alone (n=243). ORRs were 8.8% in the tilsotolimod arm and 8.6% in the ipilimumab arm, with disease control rates of 34.5% and 27.2%, respectively. Median OS was 11.6 months in the tilsotolimod arm and 10.0 months in the ipilimumab arm (hazard ratio (HR) 0.96 [95% confidence interval (CI) 0.77–1.19]; p=0.7).

Most Common Adverse Events

Grade ≥3 treatment-emergent adverse events occurred in 61.1% and 55.5% of patients in the tilsotolimod and ipilimumab arms, respectively.

Conclusion

Adding tilsotolimod to ipilimumab did not improve response or OS in patients with PD-1 refractory advanced melanoma.

Comment

More disappointing, though not unexpected, news for Aceragen's tilsotolimod, as the drug fails to meet significance on the overall survival outcome. These data from the Phase III ILLUMINATE-301 trial mark the final nail in the coffin for tilsotolimod's development in anti-PD-1 refractory advanced melanoma, following the trials previous failure to meet the co-primary endpoint of objective response rate in March, 2021. Though numerically longer, the median overall survival was only extended by 1.6 months in the combination treatment arm compared to the Yervoy arm, representing a non-significant difference with addition of Aceragen's toll-like receptor 9 agonist. Considering the little differentiation observed between the response data previously, expectations for a significant OS benefit were low and these results come as no surprise. Nevertheless, these results will be unwelcomed by Aceragen who hoped to continue discussions with regulatory authorities, if OS data had proved successful.

Even if the combination treatment were to demonstrate significance in OS compared to Yervoy alone, the safety data would have presented another hitch in the road for the regimen. The rate of Grade ≥3 treatment-emergent adverse events occurred in 61.1% in the tilsotolimod arm compared to 55.5% in the Yervoy arm. Though doublet regimens would anticipate increased toxicity, the lack of response benefit paired with these additional safety issues would likely cause for concern regardless of the OS outcome.

Overall, these results represent the end of the road for tilsotolimod's development in melanoma, and with no active trials underway in other indications, it seems prospects have dwindled for the agent.

Source:

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract LBA9516)
Citeline Analysis

Opdivo for Melanoma

Event Date:	06/02/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - NADINA (Neoadjuvant)
Market Group:	Oncology
Lead Company:	Bristol Myers Squibb Company (BMY)
Partner Companies:	Ono Pharmaceutical (4528:JP)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Treatment	Comparator
Treatment Description	Neoadjuvant ipilimumab 80mg + nivolumab 240mg	Adjuvant nivolumab 480mg
Number of Patients	212	211
Number of Evaluable Patients	N/A	N/A
12-month Event-Free Survival Rate ***(Endpoint=Primary)***	83.7 %	57.2 %
Event-Free Survival Rates in BRAFmut Melanoma Subgroup ***(Endpoint=Primary)***	83.5 %	52.1 %
Event-Free Survival in BRAFwt Subgroup ***(Endpoint=Primary)***	83.9 %	62.4 %

The abstract entitled, "Neoadjuvant nivolumab plus ipilimumab versus adjuvant nivolumab in macroscopic, resectable stage III melanoma: The phase 3 NADINA trial." was presented at the 2024 ASCO Conference and simultaneously published in an abstract entitled "Neoadjuvant Nivolumab and Ipilimumab in Resectable Stage III Melanoma" in the *New England Journal of Medicine* on June 2, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website.

Context

Standard of care (SOC) for resectable, macroscopic stage III melanoma is therapeutic lymph node dissection (TLND) followed by adjuvant (adj) therapy with nivolumab (NIVO), pembrolizumab (PEM) or, in BRAFmut melanoma, dabrafenib + trametinib (DAB/TRAM). The recent Phase II SWOG S1801 trial showed superior event-free survival (EFS) of neoadjuvant (neoadj) + adj PEM as compared to adj PEM (estimated 2y-EFS 72% vs 49%). Additional Phase II trials demonstrated safety and high efficacy (77-80% 2y-EFS) of neoadj ipilimumab (IPI) 1 mg/kg + nivolumab (NIVO) 3 mg/kg, providing the rationale for testing neoadj IPI + NIVO against SOC in a Phase III trial.

Design

In this investigator initiated, international Phase III trial, resectable, macroscopic, nodal stage III melanoma pts, naive to ICI and BRAFi/MEKi, were randomized to receive 2 cycles of neoadj IPI 80mg + NIVO 240mg (q3w) followed by TLND, and in case of not achieving a major pathologic response (MPR) adj DAB/TRAM (150mg BID/2mg QD; 46 wks) or 11 cycles of adj NIVO (480mg; q4w; if BRAFwt) versus TLND

followed by 12 cycles of adj NIVO (480mg; q4w).

Endpoints

The primary endpoint EFS is defined as time from randomization until progression, recurrence or death due to melanoma or treatment, and was assessed using a Cox regression model. An interim analysis using a 2-sided alpha of 0.1% (Haybittle-Peto stopping rule) was planned per protocol after completing recruitment.

Results

Between Aug 2021 and Dec 2023, 423 pts were randomly assigned; 212 pts to the neoadj arm and 211 to the adj arm. At data cutoff on January 12, 2024, with a median FU of 9.9 mos, significantly less events occurred in the neoadj arm vs the adj arm (28 vs 72), with HR 0.32 (99.9% CI 0.15-0.66, p<0.0001) and estimated 12-mo EFS rates of 83.7% (99.9% CI 73.8-94.8) vs 57.2% (99.9% CI 45.1-72.6) favoring the neoadj arm. In the subgroup of BRAFmut melanoma, estimated EFS rates were 83.5% and 52.1%, and in BRAFwt 83.9% and 62.4% for neoadj versus adj respectively. 58.0% of pts in the neoadj arm had an MPR, 8.0% a path partial-response (pPR), 26.4% a path non-response (pNR), 2.4% had progression before surgery and 5.2% were not reported (95% centrally reviewed). The 12-mo RFS rates according to path response were 95.1% for MPR, 76.1% for pPR and 57.0% for pNR.

Most Common Adverse Events

Systemic treatment related adverse events (AE) grade ≥3 were seen in 29.7% and 14.7% in the neoadj and adj arm; 1 pt died due to toxicity in adj arm (pneumonitis). Surgery related grade ≥3 AEs were reported in 14.6% and 14.4% respectively.

Conclusion

NADINA is the first Phase III trial that evaluates neoadj immunotherapy against SOC in melanoma, and is also the first Phase III trial in oncology evaluating a neoadj regimen consisting of immunotherapy alone. Neoadj IPI+NIVO followed by response-driven adj treatment results in statistically significant improved EFS compared to adj NIVO and should be considered a new SOC treatment in macroscopic stage III melanoma.

Comment

The NADINA trial represents the first Phase III head-to-head comparison of neoadjuvant and adjuvant therapy in melanoma patients and, with this top-line readout, underlines the potential benefit of bringing neoadjuvant treatment into the melanoma space. The current standard of care treatment for stage III resectable melanoma is surgery followed by adjuvant therapy, typically with a PD-1 inhibitor. However, many patients are still at risk of relapse and face the prospect of considerably worse prognosis upon disease progression. Stage III patients are a particularly high-risk subgroup, and reduction in disease relapse for stage III patients represents a crucial area of unmet need, especially considering that the five-year survival rate drops from approximately 70% to less than a third when patients progress from stage III to stage IV. With hopes to improve upon these sub-optimal long-term outcomes for melanoma patients, several initiatives have been undertaken to investigate whether neoadjuvant therapy may be the solution. In these top-line results from the Phase III NADINA trial, we see for the first time that neoadjuvant therapy looks to potentially offer a survival benefit compared to adjuvant therapy. The 12-month event-free survival (EFS) rate of 83.7% for the neoadjuvant treatment arm is impressive compared to 57.2% in the adjuvant arm. Importantly, this survival benefit looks to be observed irrespective of BRAF mutation status. These data indicate that neoadjuvant therapy may improve long-term outcomes for stage III patients compared to the current SoC regimen of adjuvant therapy. However, it should be noted that the survival benefit observed here could be a result of the increased potency of a dual blockade regimen compared to single blockade alone, and this could compound the conclusion that neoadjuvant therapy offers improved survival outcomes compared to adjuvant therapy. Nevertheless, if the dual blockade regimen continues to improve upon EFS compared to SoC adjuvant therapy then it is likely that we can expect to see neoadjuvant dual blockade move into the clinic.

Whilst the NADINA trial's primary endpoint is EFS, physicians will also be eager to see the outcome of secondary endpoint recurrence free survival (RFS), though this can likely be expected at considerably longer follow-up. If neoadjuvant therapy is to prove superior compared to adjuvant therapy in RFS then this would frame the regimen as a strong candidate to meet the overarching unmet need of reducing disease relapse for these high-risk patients. ASCO 2024 also saw the presentation of data from the Phase III PIVOTAL trial which is investigating cytokine therapy Nidlegy as a neoadjuvant treatment for patients with stage III resectable melanoma. In this study, which compares Nidlegy to surgery alone, the neoadjuvant regimen was demonstrated to significantly improve recurrence free survival by 10 months. The release of these data at ASCO 2024, primes Nidlegy to have the potential to become the new standard of care for these high-risk patients, and thus, the Opdivo + Yervoy regimen would do well to also prove successful on this important endpoint.

Whilst it looks as though Nidlegy is inching closer to snatch the crown as the first neoadjuvant therapy approved for melanoma, BMS' dual blockade regimen may not be left completely in the dust with the advantage of having clinical trial data against adjuvant therapy

opposed to surgery alone. Using adjuvant therapy as the comparator in the NADINA trial has set BMS's doublet therapy to potentially be the first regimen to prove superior to the current standard of care treatment, and this will be key in securing uptake with physicians. The lack of comparison to adjuvant therapy in the PIVOTAL trial, on the other hand, means it is unclear if neoadjuvant Nidlegy therapy offers a survival benefit compared to the current standard of care regimen and this may leave physicians to question if it is worth the risk of surgery delay. Nevertheless, despite the race to be the first neoadjuvant therapy approved for melanoma, it is unlikely that these regimens will directly compete. With the NADINA trial being conducted in Australia and the PIVOTAL trial underway in locations across Europe, it is likely that these regimens will launch in different geographic markets, and if the data continues to be positive, uptake can be expected for both regimens.

The safety profile of a neoadjuvant therapy regimen plays an essential role and whilst perhaps not alarmingly high, the rate of grade ≥3 Systemic treatment related adverse events seen with the Opdivo + Yervoy doublet may stir up some concern, with 15% higher occurrence compared to adjuvant therapy alone. Whilst increased toxicity would be expected with a dual blockade regimen compared to single blockade, when drawing comparison to the rate of grade 3 treatment emergent adverse events seen in PIVOTAL (14%), it could call into question whether dual blockade is safe enough to see use in the neoadjuvant setting. It is crucial that neoadjuvant treatment does not introduce toxicities which may delay or preclude curative resection, and thus immunotherapy regimens with high rates of immune adverse events, such as dual blockade, may not be the most appropriate candidates. More mature safety and efficacy data will be crucial to better discern the benefit/risk profile of this regimen and if it can win over physicians.

Source:

American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract LBA2)
New England Journal of Medicine 06/02/2024 (DOI: 10.1056/NEJMoa2402604)
Citeline Analysis

Yervoy for Melanoma

Event Date:	06/02/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - NADINA (Neoadjuvant)
Market Group:	Oncology
Lead Company:	Bristol Myers Squibb Company (BMY)
Partner Companies:	Ono Pharmaceutical (4528:JP)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Treatment	Comparator
Treatment Description	Neoadjuvant ipilimumab 80mg + nivolumab 240mg	Adjuvant nivolumab 480mg
Number of Patients	212	211
Number of Evaluable Patients	N/A	N/A
12-month Event-Free Survival Rate ***(Endpoint=Primary)***	83.7 %	57.2 %
Event-Free Survival Rates in BRAFmut Melanoma Subgroup ***(Endpoint=Primary)***	83.5 %	52.1 %
Event-Free Survival in BRAFwt Subgroup ***(Endpoint=Primary)***	83.9 %	62.4 %

The abstract entitled, "Neoadjuvant nivolumab plus ipilimumab versus adjuvant nivolumab in macroscopic, resectable stage III melanoma: The phase 3 NADINA trial." was presented at the 2024 ASCO Conference and simultaneously published in an abstract entitled "Neoadjuvant Nivolumab and Ipilimumab in Resectable Stage III Melanoma" in the *New England Journal of Medicine* on June 2, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website.

Context

Standard of care (SOC) for resectable, macroscopic stage III melanoma is therapeutic lymph node dissection (TLND) followed by adjuvant (adj) therapy with nivolumab (NIVO), pembrolizumab (PEM) or, in BRAFmut melanoma, dabrafenib + trametinib (DAB/TRAM). The recent Phase II SWOG S1801 trial showed superior event-free survival (EFS) of neoadjuvant (neoadj) + adj PEM as compared to adj PEM (estimated 2y-EFS 72% vs 49%). Additional Phase II trials demonstrated safety and high efficacy (77-80% 2y-EFS) of neoadj ipilimumab (IPI) 1 mg/kg + nivolumab (NIVO) 3 mg/kg, providing the rationale for testing neoadj IPI + NIVO against SOC in a Phase III trial.

Design

In this investigator initiated, international Phase III trial, resectable, macroscopic, nodal stage III melanoma pts, naive to ICI and BRAFi/MEKi, were randomized to receive 2 cycles of neoadj IPI 80mg + NIVO 240mg (q3w) followed by TLND, and in case of not achieving a major pathologic response (MPR) adj DAB/TRAM (150mg BID/2mg QD; 46 wks) or 11 cycles of adj NIVO (480mg; q4w; if BRAFwt) versus TLND

followed by 12 cycles of adj NIVO (480mg; q4w).

Endpoints

The primary endpoint EFS is defined as time from randomization until progression, recurrence or death due to melanoma or treatment, and was assessed using a Cox regression model. An interim analysis using a 2-sided alpha of 0.1% (Haybittle-Peto stopping rule) was planned per protocol after completing recruitment.

Results

Between Aug 2021 and Dec 2023, 423 pts were randomly assigned; 212 pts to the neoadj arm and 211 to the adj arm. At data cutoff on January 12, 2024, with a median FU of 9.9 mos, significantly less events occurred in the neoadj arm vs the adj arm (28 vs 72), with HR 0.32 (99.9% CI 0.15-0.66, p<0.0001) and estimated 12-mo EFS rates of 83.7% (99.9% CI 73.8-94.8) vs 57.2% (99.9% CI 45.1-72.6) favoring the neoadj arm. In the subgroup of BRAFmut melanoma, estimated EFS rates were 83.5% and 52.1%, and in BRAFwt 83.9% and 62.4% for neoadj versus adj respectively. 58.0% of pts in the neoadj arm had an MPR, 8.0% a path partial-response (pPR), 26.4% a path non-response (pNR), 2.4% had progression before surgery and 5.2% were not reported (95% centrally reviewed). The 12-mo RFS rates according to path response were 95.1% for MPR, 76.1% for pPR and 57.0% for pNR.

Most Common Adverse Events

Systemic treatment related adverse events (AE) grade ≥3 were seen in 29.7% and 14.7% in the neoadj and adj arm; 1 pt died due to toxicity in adj arm (pneumonitis). Surgery related grade ≥3 AEs were reported in 14.6% and 14.4% respectively.

Conclusion

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Source:

American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract LBA2)
New England Journal of Medicine 06/02/2024 (DOI: 10.1056/NEJMoa2402604)
Citeline Analysis

Nidlegy for Melanoma

Event Date:	05/31/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - PIVOTAL
Market Group:	Oncology
Lead Company:	Philogen S.p.A. (PHIL)
Partner Companies:	Sun Pharmaceutical Industries (SUNP)
Former Companies:	N/A
Change to Likelihood of Approval:	2%
Likelihood of Approval:	49% (5% Above Avg.)
Average Approval:	44%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Surgery	Nidlegy	Nidlegy vs Surgery
Number of Patients	N/A	N/A	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Recurrence-Free Survival (RFS) - HR per BICR assessment ***(Endpoint=Primary)***	N/A	N/A	0.59 (P=0.005)
Recurrence-Free Survival (RFS) - HR per Investigator Assessment ***(Endpoint=Primary)***	N/A	N/A	0.61 (P=0.018)
Median Recurrence-Free Survival (RFS) - per BICR	6.9 Months	16.7 Months	N/A
Distant Metastasis-Free Survival (DMFS) - HR	N/A	N/A	0.60 (P=0.029)
Complete Pathological Responses (pCR) After Surgery	N/A	21 %	N/A

Philogen and Sun Pharmaceutical announced primary results from the Nidlegy Phase III PIVOTAL trial of Nidlegy as a neoadjuvant intralesional therapy for fully resectable, locally advanced melanoma. The abstract entitled "Phase 3 study (PIVOTAL) of neoadjuvant intralesional daromun vs. immediate surgery in fully resectable melanoma with regional skin and/or nodal metastases" was presented on May 31, 2024.

Data from this study were last seen in October 2023.

Context

Philogen and Sun Pharma entered into a distribution, license and supply agreement in May 2023 for commercializing Nidlegy in Europe, Australia and New Zealand for the treatment of skin cancers. In October 2023, both companies announced that PIVOTAL met the primary endpoint of recurrence-free survival.

Design

PIVOTAL is an open-label, randomized, multicenter Phase III trial evaluating Nidlegy as a neoadjuvant intralesional therapy for fully resectable, locally advanced melanoma. The study was conducted at 22 sites in 4 European countries and enrolled a total of 256 patients randomized 1:1 to the treatment (neoadjuvant Nidlegy followed by surgery) and to the control arm (surgery). More than 90% of the enrolled patients had received previous treatments, including surgery, systemic therapy or radiotherapy.

Per the abstract, each weekly administration of Daromun (13 Mio IU of L19IL2 and 400 µg of L19TNF) was distributed among all injectable tumor lesions. Cutaneous melanoma pts with skin and/or LN metastases amenable to complete surgical resection were eligible. Any approved adjuvant treatment post-surgery during follow-up was equally allowed. Pts with uveal or mucosal melanoma, metastatic melanoma with unknown primary, or distant metastases at screening (ruled out by PET/CT) were not eligible.

Endpoints

The primary endpoint of the study was recurrence-free survival (RFS), assessed by investigators and confirmed by retrospective Blinded Independent Central Review (BICR) of PET/CT scans.

Results

The primary outcome analysis shows that the RFS HR between the treatment and the control arm is 0.59 [95% CI 0.41-0.86; log-rank p=0.005] as per BICR assessment and 0.61 [0.41-0.92; p=0.018] as per investigator assessment (power = 85%; two-sided α = 0.05). Median RFS was 16.7 months in the treatment and 6.9 months in the control arm as per BICR. Moreover, distant metastasis-free survival (DMFS) was significantly improved by the neoadjuvant treatment, with an HR between the two arms of 0.60 [0.37-0.95; p=0.029].

Per the abstract, from July 2016 to August 2023, 127 pts were randomized to the treatment and 129 to the control arm. Complete pathological responses (pCR) after surgery were recorded in 21% of treatment arm pts.

Most Common Adverse Events

The safety profile of Nidlegy was characterized mostly by low-grade, local adverse events (12.7% grade 3 TEAEs). No grade 3–4 immune-related adverse events and no drug-related deaths were recorded.

Per the abstract, the safety profile of Daromun was characterized mostly by low-grade, local adverse events (14% grade 3 TEAEs). Systemic AEs were limited and of low grade (no autoimmune TEAEs and no drug-related death recorded).

Conclusion

Collectively, the analysis of primary (RFS) and secondary (DMFS and safety) endpoints show that neoadjuvant Nidlegy is an effective therapeutic option for this patient population.

Comment

These results from the Phase III PIVOTAL study represent a first-time victory in the neoadjuvant space for melanoma and point to a lucrative horizon for Philogen's Nidlegy. The PIVOTAL trial investigated cytokine therapy Nidlegy as a neoadjuvant treatment for patients with resectable, locally advanced Stage III melanoma compared to surgery alone. Currently, there are no neoadjuvant therapies approved for melanoma, and while there are several adjuvant therapies available, these offer suboptimal long-term outcomes, with approximately half of all patients experiencing disease relapse post-resection. For patients who progress to metastatic disease, prognosis considerably worsens, rendering this an area of great unmet need, especially for the high-risk patient subgroup of Stage III resectable disease. In these results presented at ASCO 2024, Nidlegy looks to be the first neoadjuvant agent to offer a significant survival benefit compared to surgery alone in a Phase III trial, with a 10-month improvement in median recurrence-free survival (mRFS; 16.7 months vs. 6.9 months). Distant metastasis-free survival was also significantly improved by the neoadjuvant treatment, which also suggests that Nidlegy may be able to offer an improved prognosis for these high-risk patients.

Importantly, Nidlegy's safety profile looks promising, helping to swing the benefit/risk profile in favor of neoadjuvant use of the drug. Many concerns surrounding the application of neoadjuvant therapies center around whether the therapy could considerably delay or preclude surgery due to toxicity issues. For an agent to prove successful in this setting, it needs to demonstrate a toxicity profile that will not introduce a significant threat to the patient's potential to undergo resection. This is especially crucial in melanoma, whereby surgery is undertaken with curative intent. These data from PIVOTAL demonstrate Nidlegy's safety profile to be characterized by mostly low-grade, local adverse events, with only 14% grade 3 treatment-emergent adverse events (TEAEs) reported, supporting Nidlegy as a suitable low-toxicity regimen for patients preparing for surgery. These safety data are exceptionally impressive when considering the 90% reported rate of TEAEs seen with Opdivo + Yervoy in the Phase II OpACIN trial, which investigated the doublet regimen for neoadjuvant use in resectable Stage III patients (though it should be noted that this rate was improved upon dose revisions in the Phase II OpACIN-neo

trial).

Crucially, at this follow-up of PIVOTAL there were no autoimmune TEAEs, which will also prove advantageous to Nidlegy in winning favor with physicians. Immune adverse events are typically perceived as difficult to manage because they do not tend to resolve upon cessation of therapy, unlike many other treatment-related toxicities, and this could implicate surgery timings. No reports of immune TEAEs indicate Nidlegy to be a manageable therapy; however, autoimmune TEAEs can have delayed presentation, and this outcome may be liable to change at future follow-up.

Overall, these data demonstrate Nidlegy to have the potential to be the first neoadjuvant therapy to hit the melanoma market, and this news will undoubtedly be welcomed by biotech company Philogen, which is yet to launch any of its pipeline therapies. We now await data from the Phase III Neo-DREAM trial, and are raising the LOA by a further 2%.

Source:

Press Release 05/31/2024 (Philogen)
American Society of Clinical Oncology (ASCO) 05/31/2024 (Abstract LBA9501)
Citeline Analysis

Blenrep for Multiple Myeloma (MM)

Event Date:	06/02/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - DREAMM 8 (w/ Pd)
Market Group:	Oncology
Lead Company:	GSK plc (GSK)
Partner Companies:	Pfizer (PFE)
Former Companies:	Seagen (SGEN)
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	PVd	BPd	BPd vs PVd
Number of Patients	147	155	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Median PFS at 21.8 Months ***(Endpoint=Primary)***	12.7 Months	N/A	N/A (P<0.001)
12-Month PFS Rate ***(Endpoint=Primary)***	51 %	71 %	N/A
ORR ***(Endpoint=Secondary)***	72 %	77 %	N/A
Stringent Complete Response (sCR) ***(Endpoint=Secondary)***	3 %	9 %	N/A
Complete Response (CR) ***(Endpoint=Secondary)***	14 %	31 %	N/A
Very Good Partial Response (VGPR) ***(Endpoint=Secondary)***	22 %	24 %	N/A
Partial Response (PR) ***(Endpoint=Secondary)***	34 %	14 %	N/A
CR or Better Rate (sCR+CR) ***(Endpoint=Secondary)***	16 %	40 %	N/A
VGPR or Better Rate (sCR+CR+VGPR) ***(Endpoint=Secondary)***	38 %	64 %	N/A

MRD Negativity Rate In Patients with a sCR or CR ***(Endpoint=Secondary)***	4.8 %	23.9 %	N/A
Median Duration of Response ***(Endpoint=Secondary)***	17.5 Months	N/A	N/A

GSK announced results from an interim analysis of the Phase III DREAM-8 head-to-head trial evaluating belantamab mafodotin, in combination with pomalidomide plus dexamethasone (PomDex), versus a standard of care, bortezomib plus PomDex, as a second line and later treatment for relapsed or refractory multiple myeloma at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. An abstract entitled, "Results from the randomized phase 3 DREAMM-8 study of belantamab mafodotin plus pomalidomide and dexamethasone (BPd) vs pomalidomide plus bortezomib and dexamethasone (PVd) in relapsed/refractory multiple myeloma (RRMM)," was presented at the meeting on June 2, 2024.

Data from this study were last seen in March 2024.

Context

These data were simultaneously published in *The New England Journal of Medicine* in an article entitled, "Belantamab Mafodotin, Pomalidomide, and Dexamethasone in Multiple Myeloma."

Design

The DREAMM-8 Phase III clinical trial is a multi-center, open-label, randomized trial evaluating the efficacy and safety of belantamab mafodotin in combination with PomDex compared to a combination of bortezomib and PomDex in patients with relapsed/refractory multiple myeloma previously treated with at least one prior line of multiple myeloma therapy, including a lenalidomide-containing regimen, and who have documented disease progression during or after their most recent therapy. Compared to the patient population studied in the Phase III DREAMM-7 trial, patients in DREAMM-8 were more heavily pre-treated in that all had prior exposure to lenalidomide, 75% were refractory to lenalidomide, 25% had prior daratumumab exposure and of those most were daratumumab refractory.

A total of 302 participants were randomized at a 1:1 ratio to receive either belantamab mafodotin plus PomDex, or bortezomib plus PomDex.

Endpoints

The primary endpoint is PFS as per an independent review committee. Key secondary endpoints include OS, minimal residual disease negativity as assessed by next-generation sequencing, and duration of response. Other secondary endpoints include ORR, patient-reported quality of life outcomes, adverse events, eye exam findings, and laboratory investigations.

Results

On the primary endpoint of progression-free survival (PFS), a statistically significant and clinically meaningful improvement (hazard ratio [HR]: 0.52 [95% confidence interval (CI): 0.37-0.73], p-value<0.001) was observed with the belantamab mafodotin combination (n=155) compared to the bortezomib combination (n=147). At a median follow-up of 21.8 months, the median PFS was not yet reached (95% CI: 20.6-not yet reached [NR]) with the belantamab mafodotin combination compared to 12.7 months (95% CI: 9.1-18.5) in the bortezomib combination. At the end of one year, 71% (95% CI: 63-78) of patients in the belantamab mafodotin combination group compared to 51% (95% CI: 42-60) in the bortezomib combination group were alive and had not progressed. A benefit for belantamab mafodotin plus PomDex was observed across all pre-specified subgroups including those with poor prognostic features, such as patients who were refractory to lenalidomide and patients with high-risk cytogenetics.

A positive overall survival (OS) trend was observed but not statistically significant (HR: 0.77 [95% CI: 0.53-1.14]) at the interim analysis. OS follow-up continues and further analyses are planned. At the end of one year, 83% (95% CI: 76-88) of patients were alive in the belantamab mafodotin combination group versus 76% (95% CI: 68-82) in the bortezomib combination group.

Similar to the results seen in the DREAMM-7 phase III head-to-head trial, in DREAMM-8 the belantamab mafodotin combination also resulted in clinically meaningful improvements consistently across secondary efficacy endpoints, showing that the belantamab mafodotin combination resulted in deeper and more durable responses compared to the bortezomib combination. Key improvements included rate of complete response (CR) or better (more than twofold improvement); minimal residual disease (MRD) negativity rate (nearly fivefold improvement); and duration of response (median not yet reached with the belantamab mafodotin combination versus 17.5 months with the bortezomib combination).

Per the abstract, 155 pts were randomly assigned to belantamab mafodotin plus pomalidomide and dexamethasone (BPd) and 147 to pomalidomide plus bortezomib and dexamethasone (PVd). With a median (range) follow-up of 21.78 mo (0.03-39.23), median PFS (95% CI)

was not reached (NR; 20.6-NR) with BPd vs 12.7 mo (9.1-18.5) with PVd (HR, 0.52; 95% CI, 0.37-0.73; p<0.001). 12-month PFS rate (95% CI) was 71% (63-78%) with BPd vs 51% (42-60%) with PVd. ORR (95% CI) was 77% (70.0-83.7%) with BPd vs 72% (64.1-79.2%) with PVd; rate of complete response or better (95% CI) was 40% (32.2-48.2%) with BPd vs 16% (10.7-23.3%) with PVd. Median duration of response (95% CI) was NR (24.9-NR) with BPd vs 17.5 mo (12.1-26.4) with PVd. A positive trend favoring BPd was seen for OS (HR, 0.77; 95% CI, 0.53-1.14); follow up for OS is ongoing.

Most Common Adverse Events

The safety and tolerability profile of the belantamab mafodotin combination was broadly consistent with the known profile of the individual agents.

Grade 3 or higher non-ocular adverse events (AEs) of clinical interest in the belantamab mafodotin combination versus bortezomib combination arms, respectively, included neutropenia (57% vs 39%; 42 patients/100 person-years in both arms); thrombocytopenia (38% vs 29%; 28 vs 31 patients/100 person-years); and pneumonia (17% vs 8%; 13 vs 8 patients/100 person-years).

Eye-related side effects, a known risk of treatment with belantamab mafodotin, were generally reversible, manageable with dose modifications, and led to low (9%) treatment discontinuation rates. Grade 3 or higher ocular adverse events occurred in 43% of patients receiving the belantamab mafodotin combination (Grade 3: 42%; Grade 4: 1%). Most commonly reported grade 3 or higher ocular symptoms included blurred vision (Grade 3: 17%; Grade 4: 0), dry eye (Grade 3: 8%: Grade 4: 0), and foreign body sensation in the eyes (Grade 3: 6%; Grade 4: 0). Fifty-one patients (34%) with a best corrected visual acuity (BCVA) of 20/25 or better in at least one eye at baseline had a worsening in both eyes to 20/50 or worse. At the time of this analysis, the first occurrence of such events had improved in 92% of these patients, and resolved in 85%, with a median time to resolution of 57 days (range: 14-451 days).

Global health status quality of life (QOL), as measured by the EORTC-QLQ-C30 remained stable in both treatment arms over time, suggesting that treatment did not lead to any decline in overall health related QOL.

Per the abstract, adverse events (AEs) were reported in >99% and 96% of pts in the BPd and PVd arms, respectively. Of pts treated with BPd, 89% had ocular AEs (CTCAE grade 3/4, 43%) vs 30% (grade 3/4, 2%) in the PVd arm. AEs were generally manageable, and broadly consistent with known safety profile of individual agents.

Conclusion

Per the abstract, the DREAMM-8 study demonstrated a statistically significant and clinically meaningful PFS benefit with BPd vs PVd in RRMM with >1 prior LoT. BPd also led to deeper and more durable responses, showed a favorable OS trend, and had a manageable safety profile.

Comment

Following a negative confirmatory Phase III trial in November 2022, Blenrep was withdrawn from the US and EU markets. However, in a remarkable comeback Blenrep has since reported positive results in two additional Phase III trials (DREAMM-7 and DREAMM-8) and is expected to be approved for relapsed/refractory multiple myeloma in 2025. Numerical results for DREAMM-8, which compared Blenrep combined with Pomalyst and dexamethasone (dex) to bortezomib combined with Pomalyst and dex in second-line or later multiple myeloma, were presented at ASCO. The results impress with a statistically significant improvement in median PFS (not reached vs 12.7 months with a median follow-up of 21.8 months) and induction of deep responses as measured by the ≥CR rate (40% vs 16%) and by the MRD-negativity rate in patients with a ≥VGPR (32% vs 5%). Although the median PFS was not reached in the Blenrep arm, the 12-months PFS rate was 71% vs 51% in the comparator arm. The impressive results in DREAMM-8 are bolstered by the similarly impressive results in DREAMM-7 which compared Blenrep combined with bortezomib and dex to Darzalex combined with bortezomib and dex. DREAMM-7 also reported an improvement in median PFS (37 months vs 13 months) with improvements in ≥CR rate (35% vs 17%) and MRD-negativity rate in patients with a ≥VGPR (39% vs 17%). Dr Sagal Lonial, the discussant for the DREAMM-8 abstract, noted that the median PFS for DREAMM-7 was the longest median PFS ever reported for a bortezomib + dex backbone. He also noted that earlier trials had also shown long durations of response (DOR). The single arm DREAMM-2 trial reported a mDOR of 11 months for Blenrep monotherapy and while the DREAMM-3 trial failed to show superiority of Blenrep vs Pomalyst + dex on the primary endpoint of PFS, the Blenrep arm did show a longer DOR (not reached vs 8.5 months with a median follow-up of 11.5 months). Dr Lonial went on further to say that the long PFS and long DORs seen with Blenrep suggest that it is not simply acting as a standard antibody-drug conjugate but may be modulating the immune response in some way to induce these long duration responses.

DREAMM-7 and DREAMM-8 have both shown a trend for improvement in OS and with longer follow-up this trend may reach statistical significance.

The Blenrep payload is MMAF, a tubulin inhibitor associated with ocular toxicity. When Blenrep was first approved, it could only be

prescribed by physicians participating in a Risk Evaluation and Mitigation Strategy (REMS) program to manage the risk of ocular toxicity. In DREAMM-8, 83% of patients in the Blenrep arm had an ocular adverse event leading to dose interruption/delay compared to 1% of patients in the comparator arm. These ocular events were managed by dose holds (83%) and reduction in dose frequency (59%; most had dose frequency reduced from 1.9 mg/kg Q4W to 1.9 mg/kg Q8W, nine patients had dose reduced to 1.4 mg/kg Q8W) and led to a low rate of treatment discontinuation due to ocular events (9%). Dose interruptions due to any adverse events occurred in 91% of patients in the Blenrep arm compared to 75% of patients in the comparator arm. Discontinuation of treatment due to any adverse event occurred in 15% of patients in the Blenrep arm compared to 12% of patients in the comparator arm. Finally, fatal adverse events occurred in 11% of patients in each arm.

Delving deeper into the ocular toxicity, 34% of patients reported worsening of vision (20/50 or worse in both eyes) with only 1% reporting a severe worsening of vision (20/200 or worse in both eyes). For the 51 patients who reported worsening of vision, dose holds and/or reduced dosing frequency were implemented such that 47 patients (92%) achieved normal vision during the follow-up period. For the two patients with a severe worsening of vision, normal vision was restored in one of the two patients during follow-up.

In DREAMM-8, Blenrep was given Q4W (2.5 mg/kg for cycle 1 then 1.9 mg/kg for cycle 2) while in DREAMM-7 Blenrep was given Q3W at 2.5 mg/kg. Interestingly, both trials reported 34% of patients with worsening of vision (20/50 or worse) while the percentage of patients reporting severe worsening of vision (20/200 or worse) was higher in the DREAMM-7 trial than the DREAMM-8 trial (2% vs 1%). While ocular toxicity was managed by dose delays (83%) and/or reduced dose frequency (59%) in DREAMM-8, in DREAMM-7, ocular toxicity was managed by dose delays (78%) and/or dose reductions (44%). In both trials, 9% of patients discontinued due to any ocular event. An analysis of DREAMM-7 suggested that dose delays did not have an impact on PFS as 126 patients with ≥1 dose delay of ≥12 weeks had a median PFS of 37 months. Dr Lonial suggested that with Blenrep, less is more and that less frequent dosing may preserve efficacy while increasing tolerability. He also noted that the standard way of determinig dosing, looking at measures of PK and PD, may not be the optimal way to determine dosing for an agent that may be modulating the immune system. At this point, it is not yet clear if 1.9 mg/kg Q4W is the optimal dose. Lately, the FDA has been concerned that drugs have been approved prior to determination of the optimal dose. It is possible that the FDA will require a dose optimizing trial prior to approval.

Given the positive efficacy reported here, we expect that Blenrep will be approved and will become an option for relapsed/refractory multiple myeloma. The DREAMM-8 regimen of Blenrep + Pomalyst + dex would be useful for both lenalidomide refractory patients (common as early as second-line given many patient are receiving lenalidomide maintenance), bortezomib refractory patients (less common at second-line) and patients previously treated with an anti-CD38 antibody (increasingly more common at second-line with the rising popularity of Darzalex-based regimens for first-line patients). The main drawback for Blenrep remains its ocular toxicity as this has to be closely managed and the pros and cons discussed with the patient.

Carvykti has been recently approved for second-line or later patients and cross-trial comparisons suggest that is has better efficacy than either the DREAMM-8 or DREAMM-7 combinations with the FDA label for Carvykti reporting a ≥CR rate of 74% for this setting (median PFS has not been reached). However, Carvykti has to be custom manufactured for each patient and requires hospitalization in specialty centers able to manage the associated toxicities (cytokine release syndrome and neurotoxicity). The bispecific antibodies Tecvayli and Elrexfio offer an off-the-shelf option but are currently approved only for later line disease (fifth-line or later in the US, fourth-line or later in the EU). Phase III trials are evaluating these bispecifics for second-line or later patients but we are not expecting approval in this setting until 2026. However, even once the bispecifics are approved for this earlier setting, they will also likely require hospitalization and treatment at specialized centers. As such, we expect community doctors to favor Blenrep over CAR-T and bispecifics as they learn to manage the ocular toxicity. For now, we await regulatory submissions for Blenrep in the US, EU, and Japan.

Source:

Business Wire 06/02/2024 (GSK)
American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract LBA105)
New England Journal of Medicine 06/02/2024 (DOI: 10.1056/NEJMoa2403407)
Citeline Analysis

Opdivo for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - CheckMate-77T (Neoadjuvant)
Market Group:	Oncology
Lead Company:	Bristol Myers Squibb Company (BMY)
Partner Companies:	Ono Pharmaceutical (4528:JP)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

Bristol Myers Squibb announced results from the CheckMate-77T study evaluating the perioperative regimen of neoadjuvant Opdivo with chemotherapy followed by surgery and adjuvant Opdivo in patients with stage III resectable NSCLC was presented in an oral presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. An abstract entitled "Clinical outcomes with perioperative nivolumab (NIVO) by nodal status among patients (pts) with stage III resectable NSCLC: Results from the phase 3 CheckMate 77T study" was presented on June 3, 2024.

Data from this study were last seen in May 2024.

Design
CheckMate -77T is a Phase III randomized, double-blind, placebo-controlled, multi-center trial evaluating neoadjuvant Opdivo with chemotherapy followed by surgery and adjuvant Opdivo versus neoadjuvant placebo plus chemotherapy followed by surgery and adjuvant placebo in 461 patients with resectable stage IIA to IIIB NSCLC.

Per the abstract, adults with resectable stg IIA–IIIB (N2; AJCC v8) NSCLC were randomized to neoadj NIVO 360 mg Q3W + chemo (4 cycles [cyc]) followed by adj NIVO 480 mg Q4W (13 cyc) or neoadj PBO Q3W + chemo (4 cyc) followed by adj PBO Q4W (13 cyc).

Endpoints
The primary endpoint of the trial is EFS. Secondary endpoints include OS, pathologic complete response and major pathologic response.

Results
In the analysis, the perioperative Opdivo regimen improved median event-free survival (EFS) regardless of nodal status, including in the N2 subgroup (30.2 vs. 10.0 months; HR, 0.46; 95% CI, 0.30–0.70) and non-N2 subgroup (NR vs. 17.0 months; HR, 0.60; 95% CI, 0.33-1.08) versus neoadjuvant chemotherapy and placebo followed by surgery and adjuvant placebo. One-year EFS rates were higher in both subgroups with the perioperative Opdivo regimen (N2 70% vs. 45%, and non-N2 74% vs. 62%, respectively). Surgical feasibility was similar between patients with N2 and non-N2 disease and was also similar between the Opdivo and placebo arms (77% vs. 73% among patients with N2 status; 82% vs. 79% among patients with non-N2). After surgery, a higher proportion of patients in the Opdivo arm had a pathologic complete response compared with placebo in both N2 (28.6% vs. 7.6%) and non-N2 (31.1% vs. 6.7%) subgroups.

Most Common Adverse Events
Grade 3–4 treatment-related adverse events (TRAEs) occurred in 34% and 26% in patients with N2 disease and 29% and 21% of patients with non-N2 disease with the perioperative Opdivo regimen and placebo regimen, respectively.

Conclusion
These data represent a comprehensive analysis by nodal status among patients with stage III resectable NSCLC from a global Phase III study of perioperative immunotherapy.

Comment:

Encouraging results in terms of event-free survival (EFS) hazard ratio (HR) from this sub analysis by nodal status trial support perioperative Opdivo as a potential new treatment for resectable NSCLC, including those with poor prognosis such as stage III N2. It also reinforces the efficacy outcomes demonstrated by the primary results from CheckMate-77T trial which led to the regulatory filing for the Opdivo-based regimen in this setting by the FDA and EMA in February 2024. Also, four-year survival data from the Phase III CheckMate -816 study that was presented at ASCO 2024 demonstrated an impressive median EFS of 43.8 months. However, it should be noted that these outcomes are comparable to those demonstrated by Keytruda in KEYNOTE-671.

Keytruda became the initial therapy approved for perioperative use in October 2023 following favorable overall survival (OS) data. Notably, while OS was not the primary focus of the CheckMate-77T trial and the trial group was relatively small, Keytruda's approval highlights its potential impact in this setting. In addition, findings from the Phase III KEYNOTE-671 trial evaluating the Health-Related Quality of Life (HRQoL) outcomes of perioperative Keytruda, also presented at ASCO 2024, displayed marked enhancements in efficacy. These findings support integrating perioperative Keytruda as the standard of care and a strong competitor for Opdivo in this setting, once the latter is approved. Additionally, Keytruda enjoys a first-to-market advantage and familiarity among physicians in this setting.

Source:

Business Wire 06/03/2024 (BMY)
American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract LBA8007)

Telisotuzumab Vedotin for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	06/02/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase II - LUMINOSITY
Market Group:	Oncology
Lead Company:	AbbVie Inc. (ABBV)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	3%
Likelihood of Approval:	52% (8% Above Avg.)
Average Approval:	44%

AbbVie announced data from the primary analysis of the Phase II LUMINOSITY non-small cell lung cancer (NSCLC) trial evaluating telisotuzumab vedotin at the American Society of Clinical Oncology (ASCO) Annual Meeting. The abstract entitled "Telisotuzumab vedotin monotherapy in patients with previously treated c-Met–overexpressing non-squamous EGFR wildtype advanced NSCLC: Primary analysis of the LUMINOSITY trial" was presented at the meeting on June 2, 2024.

Data from this study were last seen in November 2023.

Context
Per the abstract, the researchers report on the primary analysis for pts with c-Met OE NSQ EGFRWT NSCLC.

Design
Per the abstract, this Phase II, non-randomized, multicenter study enrolled pts with locally advanced/metastatic c-Met OE NSCLC, ≤2 prior lines of therapy (chemotherapy [CTx] + immunotherapy [IO] or sequential CTx + IO), and ≤1 line of chemotherapy. c-Met OE (Ventana MET [SP44] clinical trial assay [CTA]) was defined as ≥25% tumor cells with 3+ staining (high: ≥50% 3+; intermediate [int]: 25 to <50% 3+). Teliso-V was dosed at 1.9 mg/kg IV Q2W. The Phase II LUMINOSITY trial aimed to identify the c-Met–overexpressing (OE) NSCLC population best suited to Teliso-V and expand selected group(s) for further evaluation of efficacy.

Endpoints
Per the abstract, primary endpoint was overall response rate (ORR) by independent central review per RECIST v1.1.

Results
Per the abstract, 172 pts with NSQ EGFR WT NSCLC received ≥1 dose of Teliso-V and comprised the safety population; 161 (c-Met high, 78; c-Met int, 83) were included in baseline and efficacy analyses. Median age was 64 yrs (range 33–83), 69% were male, and 70% had ECOG PS 1. 97.5% had prior platinum and 82.0% had prior immune checkpoint inhibitor. ORR was 34.6% (c-Met high), 22.9% (c-Met int), 28.6% (overall). Median DOR was 9.0 mo (c-Met high), 7.2 mo (c-Met int), 8.3 mo (overall).

Most Common Adverse Events
Per the abstract, most common any-grade treatment-related AEs (TRAEs) were peripheral sensory neuropathy (30%), peripheral edema (16%), and fatigue (14%). Grade 5 TRAEs occurred in 2 pts (interstitial lung disease, respiratory failure).

Conclusion
Per the abstract, Teliso-V has shown compelling and durable responses in pts with c-Met OE NSQ EGFR WT NSCLC, especially in pts with c-Met high. Teliso-V had an acceptable safety profile that was clinically manageable, which is consistent with previous data.

Comment:

AbbVie's telisotuzumab vedotin (Teliso-V) is an antibody-drug conjugate (ADC) targeting c-MET, currently being developed for the treatment of advanced or metastatic EGFR wild-type, non-squamous NSCLC patients who exhibit high levels of c-MET overexpression, which is seen in approximately 50% of NSCLC patients. Teliso-V has received breakthrough therapy designation from the FDA, an innovation passport from the UK's Medicines and Healthcare products Regulatory Agency, and the Sakigake designation from Japan's Ministry of Health, Labour and Welfare. Unlike other c-MET targeting drugs such as Johnson's Rybrevant and AstraZeneca's savolitinib, Teliso-V is specifically aimed at *EGFR* wild-type NSCLC.

The final results presented at ASCO 2024 are consistent with the top-line results published in November 2023. These results fall short of an earlier 2021 analysis, where Teliso-V demonstrated an ORR of 53.8% in c-MET high patients and 25.0% in c-MET intermediate patients. However, Teliso-V's safety profile remains a significant concern. In 2021, it had resulted in the death of three patients: two with squamous NSCLC and one with non-squamous *EGFR* wild-type NSCLC. Moreover, in the Phase II Lung-MAP S1400K trial, three (13%) patients had experienced Grade 5 adverse events, including pneumonitis and bronchopulmonary hemorrhage.

If Teliso-V can demonstrate comparable or superior efficacy and safety data in the ongoing global Phase III TeliMET NSCLC-01 study compared to docetaxel in c-MET-positive patients whose disease has progressed after platinum-based therapy, it is highly likely to receive regulatory approval. This is due to the high unmet need in this patient population, which currently lacks approved therapies.

Based on these results, we are raising the LOA of Teliso-V by 3%.

Source:

PR Newswire 05/28/2024 (ABBV)
American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract 103)
Citeline Analysis

Tagrisso for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	06/02/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - LAURA
Market Group:	Oncology
Lead Company:	AstraZeneca PLC (AZN)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Treatment	Placebo
Treatment Description	Tagrisso	Placebo
Number of Patients	143	73
Number of Evaluable Patients	N/A	N/A
Median PFS ***(Endpoint=Primary)***	39.1 Months	5.6 Months

The abstract entitled, "Osimertinib (osi) after definitive chemoradiotherapy (CRT) in patients (pts) with unresectable stage (stg) III epidermal growth factor receptor-mutated (EGFRm) NSCLC: Primary results of the phase 3 LAURA study" was presented at the 2024 ASCO Conference on June 2, 2024.

Data from this study were last seen in February 2024.

Context

Tagrisso is approved as monotherapy in more than 100 countries including in the US, EU, China and Japan. Approved indications include for 1st-line treatment of patients with locally advanced or metastatic EGFRm NSCLC, locally advanced or metastatic EGFR T790M mutation-positive NSCLC, and adjuvant treatment of early-stage EGFRm NSCLC.*Tagrisso* with the addition of chemotherapy is also approved in the US and several other countries for 1st-line treatment of patients with locally advanced or metastatic EGFRm NSCLC.

Design

Per the abstract, eligible pts: aged ≥18 years (≥20 in Japan), WHO PS 0/1, unresectable stg III EGFRm (Ex19del/L858R) NSCLC, had received definitive platinum-based cCRT/sequential CRT (sCRT) with no progression. Pts were stratified (cCRT vs sCRT; stg IIIA vs IIIB/IIIC; Chinese vs non-Chinese) and randomized 2:1 to receive osi 80 mg or PBO QD until progression (blinded independent central review [BICR]-confirmed)/discontinuation. Imaging, including brain MRI, was mandated at baseline, every 8 wks to wk 48, then every 12 wks, until progression by BICR. Open-label osi was offered after progression by BICR.

Endpoints

Primary endpoint: progression-free survival (PFS; RECIST v1.1) assessed by BICR. Secondary endpoints included overall survival (OS) and safety. Data cut-off: January 5, 2024.

Results

Results showed *Tagrisso* reduced the risk of disease progression or death by 84% compared to placebo (hazard ratio [HR] 0.16; 95% confidence interval [CI] 0.10-0.24; p<0.001) as assessed by blinded independent central review (BICR). Median PFS was 39.1 months in patients treated with *Tagrisso* versus 5.6 months for placebo. A clinically meaningful PFS benefit was observed across all prespecified subgroups including sex, race, type of EGFR mutation, age, smoking history, and prior CRT.

Overall survival (OS) data showed a favourable trend for *Tagrisso*, although data were not mature at the time of this analysis. The trial will continue to assess OS as a secondary endpoint.

Most Common Adverse Events

Safety results and discontinuation rates due to adverse events (AEs) were as expected and no new safety concerns were identified. Grade 3 or higher AEs from all causes occurred in 35% of patients in the *Tagrisso* arm versus 12% in the placebo arm.

Conclusion

Results from the LAURA Phase III trial showed AstraZeneca's *Tagrisso* (osimertinib) demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) for patients with unresectable, Stage III epidermal growth factor receptor-mutated (EGFRm) non-small cell lung cancer (NSCLC) whose tumours have exon 19 deletions or exon 21 (L858R) mutations, after chemoradiotherapy (CRT) compared to placebo after CRT.

Comment:

The practice-changing data in terms of progression-free survival (PFS) benefit demonstrated by Tagrisso mark a significant advancement for patients with unresectable, stage III EGFRm NSCLC with exon 19 deletions or exon 21 (L858R) mutations. Approximately 30% of NSCLC patients are diagnosed with stage III disease, predominantly with unresectable tumors. Of these, around 15% have EGFRm unresectable stage III disease, which represents ~70,000 patients across the world. The established global standard of care (SoC) in this setting is chemoradiotherapy, which yields modest outcomes.

The potential approval of Tagrisso in this setting would help defend its revenue against increasing competition in the early-line treatment space. This is particularly crucial in light of the robust outcomes demonstrated by the combination of subcutaneous (SQ) Rybrevant with lazertinib in the PALOMA-3 trial. Additionally, updated results from the CHRYSALIS-2 trial and new data from the MARIPOSA subgroup analysis have also shown the benefit of first-line treatment with Rybrevant combined with lazertinib, posing a significant threat to Tagrisso's dominance in the first-line setting.

Source:

Press Release 06/02/2024 (AZN)
American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract LBA4)

Krazati for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - KRYSTAL-12
Market Group:	Oncology
Lead Company:	Bristol Myers Squibb Company (BMY)
Partner Companies:	Zai Lab (ZLAB)
Former Companies:	Mirati Therapeutics
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Docetaxel	Krazati	Krazati vs. Docetaxel
Number of Patients	152	301	453
Number of Evaluable Patients	N/A	N/A	N/A
Median Progression-Free Survival (PFS) ***(Endpoint=Primary)***	3.8 Months	5.5 Months	N/A
PFS by BICR Hazard Ratio ***(Endpoint=Primary)***	N/A	N/A	0.58 (P<0.0001)
Overall Response Rate (ORR) ***(Endpoint=Secondary)***	9 %	32 %	N/A (P<0.0001)
Median Duration of Response ***(Endpoint=Secondary)***	5.36 Months	8.31 Months	N/A

Bristol Myers Squibb announced results from the Phase III KRYSTAL-12 study evaluating KRAZATI (adagrasib) compared to standard of care chemotherapy in patients with locally advanced or metastatic *KRAS*^{G12C}-mutated non-small cell lung cancer (NSCLC) who had previously received platinum-based chemotherapy, concurrently or sequentially with anti-PD-(L)1 therapy. The abstract entitled "KRYSTAL-12: Phase 3 Study of Adagrasib versus Docetaxel in Patients with Previously Treated Advanced/Metastatic Non-Small Cell Lung Cancer (NSCLC) Harboring a KRASG12C Mutation" was presented at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2024.

Data from this study were last seen in March 2024.

Context

The KRYSTAL-12 study remains ongoing to assess the additional key secondary endpoint of overall survival.

Design

Per the abstract, KRYSTAL-12 is a randomized, open-label Phase III trial of ADA compared with docetaxel (DOCE) in pts with *KRAS*^{G12C}-mutated locally advanced or metastatic NSCLC who had previously received a platinum-based chemotherapy, concurrently or sequentially with anti-PD-(L)1 therapy. Pts with *KRAS*^{G12C}-mutated locally advanced or metastatic NSCLC, previously treated with

platinum-based chemotherapy and anti-PD-(L)1 therapy, were randomized 2:1 (stratified by region [non-Asia Pacific vs Asia Pacific] and sequential vs concurrent chemoimmunotherapy) to receive ADA (600 mg BID orally; tablet formulation) or DOCE (75 mg/m^2 Q3W IV), with the ability to crossover to ADA upon disease progression (assessed by real-time blinded independent central review [BICR]). No washout period was required between prior anti-PD-(L)1 therapy and study treatment.

Endpoints

The primary endpoint of the study is progression-free survival (PFS) as assessed by Blinded Independent Central Review (BICR). Secondary endpoints included overall survival (OS), overall response rate (ORR), duration of response (DOR), and safety.

Results

At a median follow-up of 9.4 months, KRAZATI demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS), the study's primary endpoint, as assessed by Blinded Independent Central Review (BICR) compared to docetaxel (HR: 0.58; [95% CI, 0.45-0.76]; P <0.0001). Median PFS was 5.5 months for *KRAZATI* compared to 3.8 months for docetaxel. Overall response rate (ORR) as assessed by BICR was also significantly higher with KRAZATI compared to docetaxel (32% vs 9%; odds ratio, 4.68; P < 0.0001). The median duration of response (mDOR) was 8.31 months (95% CI, 6.05–10.35) versus 5.36 months (95% CI, 2.86–8.54), respectively.

KRAZATI demonstrated intracranial response among patients with central nervous system (CNS) metastases at baseline, with a response rate per BICR that was more than double that observed with docetaxel (24% with *KRAZATI* vs. 11% with docetaxel).

Per the abstract, in total, 301 pts were randomized to ADA and 152 to DOCE. Baseline characteristics were generally similar between treatment arms. With a median follow-up of 9.4 mo (data cutoff December 31, 2023), the primary endpoint of PFS was significantly improved with ADA over DOCE (HR 0.58 [95% CI, 0.45–0.76]; p<0.0001; median PFS 5.49 vs 3.84 mo). ORR by BICR was also significantly higher with ADA compared with DOCE (31.9% [95% CI, 26.7–37.5] vs 9.2% [95% CI, 5.1–15.0]; odds ratio 4.68 [95% CI, 2.56–8.56]; p<0.0001); median DOR was 8.31 (95% CI, 6.05–10.35) vs 5.36 (95% CI, 2.86–8.54) mo, respectively.

Most Common Adverse Events

No new safety signals were identified for *KRAZATI*, and the safety data were consistent with the known safety profile. Treatment-related adverse events (TRAEs) of any grade were reported in 94% of patients treated with *KRAZATI* and 86.4% with docetaxel. Grade ≥3 TRAEs occurred in 47% and 46% of patients, respectively.

Per the abstract, treatment-related adverse events (TRAEs) were reported in 94.0% of pts treated with ADA and 86.4% with DOCE; grade ≥3 TRAEs occurred in 47.0% and 45.7% of pts, respectively. TRAEs led to discontinuation of ADA in 7.7% of pts and DOCE in 14.3%.

Conclusion

In the Phase III KRYSTAL-12 trial, ADA demonstrated a statistically significant and clinically meaningful improvement in PFS and ORR over DOCE in pts with previously treated *KRAS*^{G12C}-mutated NSCLC. Safety profile of ADA was consistent with previous reports and with no new safety signals. These results further support ADA as an efficacious treatment option for pts with previously treated *KRAS*^{G12C}-mutated locally advanced or metastatic NSCLC.

Comment:

In April 2024, interim results from the KRYSTAL-12 demonstrated positive outcomes in terms of progression-free survival (PFS) and objective response rate (ORR). The final data from the KRYSTAL-12 trial are now available and showcase a statistically significant and clinically meaningful improvement in mPFS of 1.6 months and overall response rate (ORR) of 22.7% over docetaxel, indicating that Krazati may emerge as the preferred option for patients with KRAS G12C-mutated NSCLC in the second-line or subsequent treatment stages. However, BMY has not yet confirmed if they will seek full approval based solely on PFS data, stating that the results will be discussed with the FDA and the EMA. Additionally, there is still scepticism about Krazati's OS benefits, especially given the lack of full data disclosure. Moreover, in the CodeBreak trial, cross-over from docetaxel control group was allowed, hampering the ability of the study to demonstrate OS benefit compared to docetaxel in the target population. Thus, the FDA had commented on the unlikeliness of the trial to detect statistical significance on OS.

Amgen's Lumakras is the major competitor of Krazati in this setting. Both Lumakras and Krazati received accelerated approvals from the FDA as targeted therapies for patients with KRASG12C-mutated NSCLC who have undergone at least one prior systemic therapy, in 2021 and 2022, respectively. It is to be further highlighted that in the Lumakras confirmatory study (CodeBreak 200), the primary PFS endpoint was statistically significant, but the FDA deemed it lacked clinical significance, with only a 1.1-month benefit observed at the median and thus issued a complete response letter, requiring Amgen to conduct another confirmatory trial by February 2028. Moreover,

the FDA Advisory Committee had also highlighted some concerns regarding the trial design.

The KRYSTAL-12 study employed a two-to-one randomization approach and mandated centrally confirmed disease progression in the control arm before allowing crossover, thereby addressing one of the concerns identified by regulators in the CodeBreak200. In addition, the KRYSTAL-12 study has PFS as the primary endpoint, with ORR and OS as secondary endpoints, in contrast with the CodeBreak 200 trial, which had solely focused on PFS as the endpoint, prompting the necessity for another Phase III confirmatory trial.

At ASCO 2024, Amgen has also reported robust interim efficacy and safety data from the international CodeBreaK 101 phase 1b trial investigating Lumakras in combination with platinum-based chemotherapy, thereby supporting the evaluation of this regimen in the ongoing CodeBreaK 202 phase III trial in treatment naïve, PD-L1 negative, KRAS G12C-mutated advanced NSCLC.

The positive results from the KRYSTAL-12 trial are encouraging and demonstrate that Krazati is a viable drug, offering strong competition to Lumakras.

Source:

Business Wire 06/01/2024 (BMY)
American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract LBA8509)
Citeline Analysis

IBI-351 for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase Ib/II - w/Cetuximab (Europe)
Market Group:	Oncology
Lead Company:	GenFleet Therapeutics
Partner Companies:	Innovent Biologics (1801)
Former Companies:	N/A
Change to Likelihood of Approval:	1%
Likelihood of Approval:	1% (1% Above Avg.)
Average Approval:	N/A

GenFleet Therapeutics announced the Phase II trial data of KROCUS study of fulzerasib (GFH925) in combination with cetuximab for first-line non-small cell lung cancer (NSCLC) treatment was presented in a late breaking presentation entitled "KROCUS: A phase II study investigating the efficacy and safety of fulzerasib (GFH925) in combination with cetuximab in patients with previously untreated advanced KRAS G12C mutated NSCLC" at the 2024 American Society of Clinical Oncology (ASCO) annual meeting on June 1, 2024.

Context

The new drug application for fulzerasib monotherapy in treating advanced KRAS G12C-mutant NSCLC has been accepted and granted priority review designation by China's National Medical Products Administration (NMPA). Based on the data presented at 2023 ESMO Asia, the registrational Phase II study of GFH925 monotherapy for NSCLC showed an ORR of 46.6% and a DCR of 90.5%; the median progression-free survival (mPFS) was 8.3 months. In addition, fulzerasib monotherapy received two breakthrough designations for advanced G12C-mutant NSCLC and metastatic colorectal cancer (CRC) patients.

Design

The KROCUS study, is a European multi-center Phase Ib/II study initiated in March 2023 and sets its objectives to evaluate the safety/tolerance, efficacy and the pharmacokinetic characteristics of the combination in advanced NSCLC patients harboring KRAS G12C mutation.

Endpoints

Per the abstract, the primary objective was to evaluate the efficacy of fulzerasib in combination with cetuximab. Secondary objectives included safety/tolerability, pharmacokinetics and biomarkers.

Results

As of April19, 2024, a total of 40 subjects were enrolled and 33 of them received at least one available post-treatment tumor assessment: the objective response rate (ORR) reached 81.8% and the disease control rate (DCR) reached 100%. The post-treatment evaluation revealed that most patients (27/33) exhibited tumor response: one patient achieved complete response; the other two achieved partial response with a shrinkage in their tumor size by 100%.

A total of 40 treatment naïve advanced KRAS G12C positive NSCLC patients were treated with GFH925 in combination with cetuximab (fulzerasib 600mg BID + cetuximab 500 mg/m^2 Q2W) as of April 19, 2024. Most patients (95%) were diagnosed with stage IV disease and 13 (32.5%) patients with brain metastases.

As of cutoff date, of the 33 patients who received at least one post-treatment tumor assessment, ORR among patients with brain metastasis was 70%. The median duration of response (DoR) was not reached yet and 88% of patients were still on treatment with a median follow-up of 5.1 months.

Most Common Adverse Events

As of cutoff date, the combination therapy was well tolerated. Treatment-related adverse events (TRAEs) occurred in 87.5% of subjects and the majority of the TRAEs were grade 1-2. About 17.5% of subjects reported grade 3 TRAEs. There were no grade 4-5 TRAEs. No new safety

signals were identified compared with fulzerasib or cetuximab as single agent.

Per the abstract, the overall safety profile of the combination was favorable. Treatment-related adverse events (TRAEs) of any grade occurred in 21 (77.8%) pts. 5 pts (18.5%) experienced G3 TRAEs and no G4 or 5 TRAEs. Three pts (11.1%) had dose reduction/interruption with fulzerasib due to TRAEs but no pts discontinued treatment while one pt (3.7%) had dose reduction/interruption and three (11.1%) discontinued cetuximab due to TRAEs.

Conclusion

The combination therapy demonstrated a favorable safety/tolerability profile, with both treatment-related adverse events (TRAEs) and TRAEs above grade 3 occurring at a lower rate than those in the fulzerasib monotherapy study in second line and above NSCLC.

Comment:

Encouraging results regarding objective response rate (ORR) and disease control rate (DCR) indicate the potential efficacy of fulzerasib (GFH925) combined with cetuximab as a first-line therapy for patients with advanced KRAS G12C mutated NSCLC. While immunotherapy (IO) serves as the current standard of care (SoC) for treating KRAS-mutant NSCLC in the first-line setting, outcomes remain less than optimal. Given the modest activity of KRAS G12C inhibitors as monotherapy, there is a growing interest in exploring combination strategies to improve clinical outcomes in this context. Combining KRAS G12 inhibitors with EGFR antibodies has shown effectiveness in treating metastatic colorectal cancer with KRAS G12C mutations. Additionally, the combination of fulzerasib and cetuximab has exhibited anti-tumor effects in preclinical models of both NSCLC and pancreatic cancers, laying the groundwork for the KROCUS trial.

It's noteworthy to emphasize that KROCUS constitutes an exploratory phase II trial, relying on a limited patient cohort for its results. Despite the trial's notable ORR, attention must be given to addressing toxicity concerns, particularly regarding skin and low-grade hepatotoxicity. Moreover, the treatment protocol differs from the established standard of care by excluding immunotherapy or chemotherapy. Determining the patient subgroup that would derive the greatest benefit from this regimen remains uncertain. Further randomized studies are warranted to provide clarity on these matters.

Therefore, while combination strategies appear promising, the selection of the treatment line and the appropriate patient subset will be essential for achieving commercial success.

Based on these results, we are raising fulzerasib LOA by 1%.

Source:

PR Newswire 06/01/2024 (GenFleet)
American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract LBA8511)
Citeline Analysis

Olomorasib for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase I/II - w/KRAS G12C-Mutant Tumors
Market Group:	Oncology
Lead Company:	Eli Lilly and Company (LLY)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	49% (5% Above Avg.)
Average Approval:	44%

Eli Lilly announced updated data from the Phase II clinical trial evaluating olomorasib in patients with *KRAS* G12C-mutant advanced solid tumors and in combination with KEYTRUDA (pembrolizumab) in patients with KRAS G12C-mutant advanced non-small cell lung cancer (NSCLC) was presented in an oral presentation entitled "Efficacy and safety of olomorasib (LY3537982), a second-generation KRAS G12C inhibitor (G12Ci), in combination with pembrolizumab in patients with KRAS G12C-mutant advanced NSCLC" at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data from this study was last seen in May 2024.

Context

The SUNRAY-01 trial, a global, registrational study investigating olomorasib in combination with pembrolizumab or pembrolizumab plus chemotherapy in first-line NSCLC, is enrolling.

Methods

LOXO-RAS-20001 is an open-label, multicenter, Phase I/II study evaluating the safety, tolerability and preliminary efficacy of olomorasib in patients with KRAS G12C-mutant advanced solid tumors. The study includes a Phase Ia dose escalation phase of olomorasib monotherapy in KRAS G12C-mutant solid tumors and a Phase Ib dose expansion and optimization phase which are evaluating olomorasib as a monotherapy and in combination with other treatments.

Results

Results presented at ASCO utilized a cutoff date of March 18, 2024. Efficacy results are based on investigator response assessments, and objective response rates (ORR) include responses that are confirmed, as well as those pending confirmation and ongoing.

An oral presentation detailed updated data for olomorasib in combination with pembrolizumab in patients with KRAS G12C-mutant advanced NSCLC, studying the two doses (50mg and 100mg BID) under ongoing investigation in first-line NSCLC. This dataset consisted of 64 patients, including patients with first-line metastatic disease and those previously treated (prior KRAS G12C inhibitor, chemotherapy, and/or immunotherapy). Patients received a median of two prior lines of therapy (range: 0-8). In patients with first-line metastatic NSCLC, across a range of PD-L1 levels, the ORR for olomorasib in combination with pembrolizumab was 77% (13/17) and median PFS was not reached with follow-up ongoing.

Most Common Adverse Events

The most common TRAEs of any grade were diarrhea (23%), increased ALT (20%), pruritus (19%), increased AST (16%), and fatigue (16%). TRAEs led to discontinuation of olomorasib only in 3% of patients (2/64), pembrolizumab only in 11% of patients (7/64) and both drugs in 5% of patients (3/64)

Conclusions

Data demonstrated monotherapy activity with olomorasib across a range of KRAS G12C-mutant solid tumors, including non-small cell lung

cancer, and a tolerability profile in combination with pembrolizumab that is well-suited to first-line lung cancer development.

Comment:

Eli Lilly's olomorasib is an oral and highly selective second-generation KRAS G12C protein inhibitor. It is currently being evaluated in combination with Keytruda, with or without chemotherapy, in the Phase III SUNRAY-01 study. While olomorasib is entering a market already occupied by Lumakras and Krazati, it is unique through its targeting of the more lucrative first-line treatment setting, unlike its competitors, which are approved for second-line use. Immunotherapy (IO) is the current standard of care (SoC) for first-line treatment of KRAS-mutant NSCLC, but outcomes remain suboptimal. Additionally, the modest activity of KRAS G12C inhibitors has led to the exploration of combination strategies to enhance clinical benefits in this setting.

It is important to highlight that both Lumakras and Krazati have faced challenges in demonstrating effectiveness when combined with standard PD-1 inhibitors, primarily due to toxicity issues, particularly hepatotoxicity. In the olomorasib + Keytruda data presented at ASCO 2024, all grade 3 ALT/AST elevations were resolved through dose modifications or corticosteroids, and none of the patients discontinued treatment due to ALT/AST elevation. Nonetheless, the olomorasib+ Keytruda combination led to a 5% discontinuation rate, a slightly higher value than that seen in the KRYSTAL-7 trial for Krazati + Keytruda, although cross-trial comparisons can be fraught with errors.

Therefore, if the olomorasib and Keytruda regimen demonstrates favorable efficacy and safety results in the SUNRAY-01 trial, it will offer new hope for the first-line treatment of metastatic KRAS-mutant NSCLC patients.

Based on these results, we are raising the LOA of olomorasib by 5%.

Source:

PR Newswire 06/01/2024 (LLY)
American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 8510)
Citeline Analysis

Ivonescimab for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	05/31/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - HARMONi
Market Group:	Oncology
Lead Company:	Summit Therapeutics plc (SMMT)
Partner Companies:	Akeso
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	49% (5% Above Avg.)
Average Approval:	44%

	Placebo	Treatment	Difference Between Treatment and Placebo
Treatment Description	Placebo plus Chemotherapy	Ivonescimab plus Chemotherapy	Treatment vs. Placebo
Number of Patients	322	322	N/A
Number of Evaluable Patients	161	161	N/A
Median Follow-Up	7.89 Months	7.89 Months	N/A
Median Progression-Free Survival (PFS) ***(Endpoint=Primary)***	4.80 Months	7.06 Months	N/A (P<0.0001)
Overall Response Rate (ORR)	35.4 %	50.6 %	N/A

Akeso announced the data from the Phase III HARMONi-A study of ivonescimab combined with chemotherapy in patients with EGFR-mutant non-squamous non-small cell lung cancer at the American Society of Clinical Oncology Annual Meeting. Abstracts entitled "Ivonescimab combined with chemotherapy in patients with EGFR-mutant non-squamous non-small cell lung cancer who progressed on EGFR tyrosine-kinase inhibitor treatment (HARMONi-A): A randomized, double-blind, multi-center, phase 3 trial" and "Ivonescimab Plus Chemotherapy in Non-Small Cell Lung Cancer With EGFR Variant: A Randomized Clinical Trial" were presented at the meeting and simultaneously published in the *Journal of the American Medical Association* on May 31, 2024.

Design

Per the abstract, patients were randomized 1:1 to receive ivonescimab (20 mg/kg) plus pemetrexed (500 mg/m2) and carboplatin (AUC 5) or placebo plus chemotherapy once every 3 weeks for four cycles, with stratification according to the third-generation EGFR TKI (received vs not received) and brain metastases (presence vs absence), followed by maintenance therapy of ivonescimab and pemetrexed or placebo and pemetrexed.

Endpoints

The primary endpoint was progression-free survival (PFS) in the intention-to-treat (ITT) population assessed by independent radiographic review committee (IRRC) per RECIST v1.1. Here we report the results of the first planned interim analysis.

Results

PFS, the primary endpoint of the study, was significantly improved in the ivonescimab plus chemotherapy arm (HR 0.46; 95% CI: 0.34 – 0.62; p<0.001), representing a 54% reduction in the risk of disease progression compared to chemotherapy. Median PFS for ivonescimab plus chemotherapy was 7.1 months (95% CI: 5.9 – 8.7), as compared to 4.8 months (95% CI: 4.2 – 5.6) for placebo plus chemotherapy. In addition, for the subgroup of patients receiving a 3 rd generation TKI (e.g., osimertinib or other locally approved 3rd generation TKIs), patients experienced a reduced risk of disease progression of 52% (HR: 0.48; 95% CI: 0.35 – 0.66). The PFS benefit was demonstrated across all clinical subgroups.

While not yet mature, overall survival (OS) analyses performed on request of the NMPA trended positively for ivonescimab plus chemotherapy vs. chemotherapy alone: after 10.2 months of median follow-up, the hazard ratio (HR) was 0.72 (95% CI: 0.48 – 1.09). An additional analysis performed after approximately 17.6 months of median follow-up showed a hazard ratio of 0.80 (95% CI: 0.59 – 1.08). Both overall survival curves appear to demonstrate clear separation between the two arms of the trial and show a trend in improvement of survival towards ivonescimab plus chemotherapy.

Overall response rate (ORR) was 50.6% (95% CI: 42.6% – 58.6%) for those receiving ivonescimab plus chemotherapy vs. 35.4% (95% CI: 28.0% - 43.3%) for those receiving chemotherapy alone. Ivonescimab plus chemotherapy usage resulted in a disease control rate (DCR) – those who either responded or were considered to have stable disease under RECIST 1.1 criteria – of 93.1% (95% CI: 88.0% - 96.5%) vs. 83.2% (95% CI: 76.5% - 88.6%) for those receiving placebo plus chemotherapy.

Per the abstract, 322 patients were randomized (161 to the ivonescimab plus chemotherapy arm, 161 to the placebo plus chemotherapy arm). 86.3% versus 85.1% of patients had received 3rd generation EGFR TKI treatment, 21.7% versus 23.0% of patients had brain metastases. As of March 10, 2023, median follow-up time was 7.89 months. The prespecified subgroup analysis showed PFS benefit favoring patients receiving ivonescimab over placebo across almost all subgroups, including those with brain metastases (HR 0.40, 0.22-0.73), those with EGFR mutation of deletion 19 (HR 0.48, 0.32-0.73), and those who were T790M mutation positive (HR 0.22, 0.09-0.54).

Most Common Adverse Events

Ivonescimab demonstrated an acceptable and manageable safety profile. The most common treatment-related adverse events (TRAEs), both all grades and Grade 3 or higher, were hematological, laboratory count-based events: white blood cell count decreases, anemia, neutrophil count decreases, and platelet count decreases. There were nine patients (5.6%) who discontinued ivonescimab due to TRAEs compared to four patients (2.5%) who discontinued placebo due to TRAEs. Grade 3 or higher immune-related adverse events occurred in 6.2% of patients receiving ivonescimab plus chemotherapy and 2.5% of patients receiving placebo plus chemotherapy. Grade 3 or higher VEGF-related adverse events between the two arms were similar (3.1% vs. 2.5%, respectively); there were no Grade 3 bleeding or arterial thrombotic events in the ivonescimab plus chemotherapy arm. No TRAEs resulted in the death of a patient in either arm in this Phase III study.

Per the abstract, Grade ≥3 TEAEs occurred in 99 (61.5%) patients versus 79 (49.1%) patients, the most common grade ≥3 TEAEs were chemotherapy-related adverse events.

Conclusions

Per the abstract, Ivonescimab plus chemotherapy significantly improved PFS while maintaining a manageable safety profile in patients who had failed previous EGFR TKI treatments.

Comment

Ivonescimab (SMT112) is a bispecific antibody that targets both PD-1 and VEGF. VEGF is crucial for tumor angiogenesis, modulating the tumor microenvironment and affecting various immune cell populations, especially myeloid cells. Combining immune checkpoint inhibitors and anti-angiogenic agents has demonstrated synergistic antitumor effects in both preclinical and clinical studies, consistent with the proposed effects of anti-angiogenesis and immune checkpoint blockade on the tumor microenvironment. Ivonescimab's tetravalent structure is designed to form large complexes with dimeric VEGF, resulting in high avidity to PD-1, enhanced function, and potent antitumor activity in preclinical studies.

Encouraging results in terms of PFS from the HARMONi-A study evaluating ivonescimab combined with chemotherapy indicate its potential application in non-squamous *EGFR*-mutated NSCLC patients who have progressed after treatment with a third-generation EGFR tyrosine kinase inhibitor (TKI). Data indicate that this regimen could be an alternative treatment option for patients failing the FLAURA (Tagrisso) and MARIPOSA (Rybrevant + lazertinib) regimens. The ivonescimab + chemotherapy combination was approved in China in May 2024 for *EGFR*-mutated NSCLC patients who progress after EGFR TKI treatment. Additionally, ivonescimab has also demonstrated a clinically meaningful benefit over Keytruda in the Phase III HARMONi-2 trial in first-line treatment of PD-L1-positive NSCLC patients. However, it is important to note that HARMONi-2 recruited only Chinese patients, and the results would need to be

replicated in a Western population for an FDA regulatory success, which in turn would undoubtedly lead to substantial commercial returns.

The success of the HARMONi-A trial has revitalized interest in the bispecific treatment approach, although it remains unclear whether the observed benefits are due to VEGF inhibition alone or the combination of VEGF and PD-1 inhibition. Akeso's ivonescimab and Biotheus/BioNTech's PM8002 are the only two advanced bispecific antibodies targeting both VEGF-A and PD-(L)1. Biotheus has also presented clinical data for PM8002 in three indications – NSCLC, as well as cervical and platinum-resistant/recurrent ovarian cancer – through posters at ASCO 2024. PM8002 is being evaluated in various patient cohorts, including those with previously untreated advanced non-squamous NSCLC (EGFR/ALK wild-type and PD-L1+), advanced non-squamous NSCLC patients with EGFR mutations who have failed prior EGFR TKI treatment, and EGFR/ALK wild-type patients who have failed anti-PD-(L)1 therapy and platinum-based chemotherapy regimens. The median PFS observed in all cohorts ranged from five to 10 months.

If either company can identify the optimal setting to demonstrate superior efficacy and safety for ivonescimab or PM8002, the market potential could be substantial.

Based on these results, we are raising ivonescimab's LOA by 5%.

Source:

PR Newswire 05/31/2024 (Akeso)
American Society of Clinical Oncology (ASCO) 05/31/2024 (Abstract 8508)
Journal Abstract 05/31/2024 (*JAMA*; DOI: 10.1001/jama.2024.10613)

Lorbrena for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	05/31/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - CROWN (vs. Crizotinib)
Market Group:	Oncology
Lead Company:	Pfizer Inc. (PFE)
Partner Companies:	CStone Pharmaceuticals (2616)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

Pfizer announced longer-term follow-up results from the Phase III CROWN trial evaluating LORBRENA (lorlatinib, a third-generation ALK inhibitor, available in Europe under the brand name LORVIQUA) versus XALKORI (crizotinib) in people with previously untreated, anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). The abstract entitled "Lorlatinib vs crizotinib in treatment-naïve patients with advanced *ALK*+ non-small cell lung cancer: 5-year progression-free survival and safety from the CROWN study" was presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting on May 31, 2024. The article entitled "Lorlatinib Versus Crizotinib in Patients With Advanced *ALK*-Positive Non–Small Cell Lung Cancer: 5-Year Outcomes From the Phase III CROWN Study" has been simultaneously published in the *Journal of Clinical Oncology* on May 31, 2024.

Data from the study were last seen in June 2023.

Design

CROWN is a Phase III, randomized, open-label, parallel 2-arm trial in which 296 people with previously untreated ALK-positive advanced NSCLC were randomized 1:1 to receive LORBRENA monotherapy (n=149) or XALKORI monotherapy (n=147). Given that median PFS was not reached after three years of follow-up, an unplanned post-hoc analysis was executed with the intent to further quantify long-term outcomes based on investigator tumor assessment from this study at a clinically meaningful landmark follow-up of five years.

Endpoints

The primary endpoint of the CROWN trial is PFS based on Blinded Independent Central Review (BICR). Secondary endpoints include PFS based on investigator's assessment, overall survival (OS), objective response rate (ORR), intracranial objective response (IOR), and safety.

Results

After five years of median follow-up, median progression-free survival (PFS) based on investigator assessment was not reached with LORBRENA, with an observed Hazard Ratio (HR) of 0.19 (95% Confidence Interval [CI], 0.13-0.27), representing an 81% reduction in the rate of disease progression or death compared to XALKORI. Further, 60% of patients treated with LORBRENA (95% CI, 51-68) were alive without disease progression after five years compared to 8% (3-14) in the XALKORI treatment arm.

In this updated analysis, LORBRENA showed a 94% reduction in the risk of developing intracranial (IC) progression (HR, 0.06; 95% CI, 0.03-0.12). The median time to IC progression was not reached (95% CI, NR-NR) with LORBRENA and was 16.4 months (12.7-21.9) with XALKORI. In people without brain metastases at baseline receiving LORBRENA, only 4 of 114 developed brain metastases within the first 16 months of treatment, compared to 39 of 109 patients who received XALKORI. At the time of analysis, 50% of patients in the CROWN trial were still receiving LORBRENA compared to 5% of patients receiving XALKORI.

Most Common Adverse Events

The safety profiles of LORBRENA and XALKORI in the five-year follow-up were consistent with previous findings, with no new safety signals reported for LORBRENA. In this analysis, the most frequent (≥20%) adverse events (AEs) reported in patients treated with LORBRENA were consistent with the 2020 analysis of the CROWN trial, which included edema, weight gain, peripheral neuropathy, cognitive effects, mood

effects, diarrhea, dyspnea, arthralgia, hypertension, headache, cough, pyrexia, hypercholesterolemia, and hypertriglyceridemia. Grade 3/4 AEs occurred in 77% of patients with LORBRENA and in 57% of patients with XALKORI. Treatment-related AEs led to permanent treatment discontinuation in 5% and 6% of patients in the LORBRENA and XALKORI arms, respectively.

Conclusion

Per the abstract, after five years of follow-up, the median PFS in the lorlatinib arm has yet to be reached. Coupled with prolonged IC efficacy and absence of new safety signals, these results indicate an improvement in outcomes for pts with advanced *ALK*+ NSCLC.

Comment

NSCLC accounts for approximately 80–85% of lung cancers, with ALK-positive tumors occurring in about 3–5% of NSCLC cases. Patients with ALK-positive NSCLC are typically young, otherwise healthy individuals who are either never-smokers or light smokers. The median age of ALK-positive NSCLC patients is 52 years, and most patients report <10 cigarette packs smoked per year. Patients with ALK-positive NSCLC often receive their diagnosis at an advanced stage, typically stage 4, with metastases already present. Within two years of initial diagnosis, about 25–40% of patients with ALK-positive advanced NSCLC experience the development of brain metastases. Pfizer specifically designed and developed Lorbrena to target tumor mutations that induce resistance to other ALK inhibitors and to effectively cross the blood-brain barrier.

The impressive long-term findings from the Phase III CROWN trial highlight Lorbrena's potential to establish itself as the favored initial therapy for ALK-positive advanced NSCLC patients. The trial demonstrated that 60% of patients treated with Lorbrena were alive without disease progression after five years, nearly doubling the PFS seen with Alecensa treatment, which had a median PFS of 34.8 months in the ALEX trial. Moreover, Lorbrena's reported impact on brain metastases is far superior to that of Alecensa. However, Lorbrena showcases central nervous system (CNS) side effects, including cognitive function changes, seizures, psychotic effects, and impacts on speech and sleep, which significantly affect the patient's quality of life. In comparison, Alecensa led to anemia, myalgia, increased blood bilirubin, increased weight, musculoskeletal pain, and photosensitivity reactions in the ALEX trial. Thus, with robust efficacy data demonstrated by both drugs, the clear differentiators in choosing the first-line treatment option would be the intracranial benefit and their respective side-effect profiles. With such unprecedented efficacy seen in CROWN, prescribing physicians will have to carefully weigh the efficacy against the risk of severe adverse events in order to choose between Lorbrena and Alecensa for their first-line ALK-positive NSCLC patients.

The lack of approved targeted drugs post-Lorbrena failure may also make clinicians hesitant to use it in the front-line setting, as they aim to preserve treatment options for younger patients. Lorbrena is effective against many single-resistance mutations that commonly occur during progression on Alecensa, making an even stronger case for its use in the second-line setting. Given the lower quality of life and its activity for resistance mutations, physicians may prefer using Lorbrena in the second line after progression on Alecensa.

Currently, three second-generation tyrosine kinase inhibitors (TKIs) – Alecensa, Alunbrig, and Zykadia – along with one third-generation TKI – Lorbrena – are approved for front-line therapy of patients with ALK-positive NSCLC. Alecensa has established itself as the preferred first-line treatment due to its robust efficacy, extensive data in the front-line setting, physician familiarity, and manageability of resistance mutations. Lorbrena, on the other hand, is favored as the second-line treatment option because of its effectiveness against most known ALK inhibitor resistance mutations, including G1202R, which is the most common resistance mutation after Alecensa failure. Additionally, Lorbrena demonstrates superior efficacy compared to other second-generation TKIs in the second-line setting.

With significant chances of changing the current treatment paradigm, Lorbrena now has the not insignificant task of convincing prescribing physicians to switch from the current standard of care.

Source:

Business Wire 05/31/2024 (PFE)
American Society of Clinical Oncology (ASCO) 05/31/2024 (Abstract LBA8503)
Journal Article 05/31/2024 (*Journal of Clinical Oncology*, DOI: 10.1200/JCO.24.00581)
Citeline Analysis

Lazertinib for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	05/31/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - PALOMA-3
Market Group:	Oncology
Lead Company:	Genosco, Inc.
Partner Companies:	Johnson & Johnson (JNJ) Yuhan (000100)
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	49% (5% Above Avg.)
Average Approval:	44%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Amivantamab (IV) + lazertinib	Amivantamab (SC) + lazertinib	Amivantamab (IV) + lazertinib vs. Amivantamab (SC) + lazertinib
Number of Patients	N/A	N/A	N/A
Number of Evaluable Patients	212	206	418
Overall Response Rate	33 %	30 %	N/A (P=0.001)
Median Duration of Response (DOR)	8.3 Months	11.2 Months	N/A
Progression-Free Survival (PFS) ***(Endpoint=Secondary)***	4.3 Months	6.1 Months	N/A
Hazard Ratio Progression-Free Survival (PFS) ***(Endpoint=Secondary)***	N/A	N/A	0.84 (P=0.20)
Hazard Ratio Overall Survival ***(Endpoint=Secondary)***	N/A	N/A	0.62 (P=0.02)

Johnson & Johnson announced first data from the Phase III PALOMA-3 study evaluating subcutaneous (SC) amivantamab combined with lazertinib in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion (ex19del) or L858R mutations. These data were presented in an abstract entitled "Subcutaneous amivantamab vs intravenous amivantamab, both in combination with lazertinib, in refractory *EGFR*-mutated, advanced non-small cell lung cancer (NSCLC): Primary results, including overall survival (OS), from the global, phase 3, randomized controlled PALOMA-3 trial" at the 2024 American Society of

Clinical Oncology (ASCO) Annual Meeting on May 31, 2024.

Context

The company announced the submission of an application for the extension of the RYBREVANT marketing authorization (line extension) to the European Medicines Agency (EMA) seeking approval of SC amivantamab in combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR ex19del or L858R mutations and as monotherapy in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy based on the PALOMA-3 data. Johnson & Johnson will submit regulatory applications seeking the approval of SC amivantamab in other markets, including the United States.

Design

PALOMA-3, which enrolled 418 patients, is a randomized, open-label Phase III study evaluating the pharmacokinetics (PK), efficacy and safety of subcutaneous amivantamab (administered via manual injection) combined with lazertinib compared to IV amivantamab and lazertinib in patients with EGFR-mutated advanced or metastatic NSCLC after progression on osimertinib and chemotherapy.

Per the abstract, SC ami at 1600 mg (2240 mg, ≥80 kg) was manually injected weekly for the first 4 weeks, then every 2 weeks; IV ami was given at the approved dose of 1050 mg (1400 mg, ≥80 kg). Laz was orally dosed at 240 mg daily.

Endpoints

The co-primary PK endpoints of the study were trough concentration (C_{trough} on Cycle [C] 2 Day [D] 1 or C4D1) and C2 area under the curve (AUCD1-D15). Key secondary endpoints were objective response rate and progression-free survival. Overall survival was a predefined exploratory endpoint. Prophylactic anticoagulation was recommended for the first four months of treatment.

Results

Results showed SC amivantamab was non-inferior to IV amivantamab, meeting both co-primary pharmacokinetic (PK) efficacy endpoints as measured by amivantamab levels in the blood (C_{trough} and area under the serum concentration time curve from day 1 to 15).

At a median follow-up of seven months, the overall response rate was 30 percent (95 percent confidence interval [CI], 24–37) in the subcutaneous arm and 33 percent (95 percent CI, 26–39) for IV (relative risk, 0.92; 95 percent CI, 0.70-1.23; *P*=0.001), meeting the noninferiority criteria. SC amivantamab also demonstrated longer duration of response (DoR), progression-free survival (PFS) and significant improvement in overall survival (OS) compared to IV administration during this time. Specifically, median DoR was numerically longer for SC amivantamab combined with lazertinib compared to IV (median, 11.2 vs 8.3 months among confirmed responders) as was PFS (median, 6.1 vs 4.3 months; hazard ratio [HR], 0.84; 95 percent CI, 0.64–1.10; *P*=0.20). A prespecified exploratory endpoint showed patients treated with SC amivantamab had significantly longer OS compared with IV (HR, 0.62; 95 percent CI, 0.42–0.92; nominal *P*=0.02). At 12 months, 65 percent of patients who received SC amivantamab combined with lazertinib were alive compared with 51 percent of those treated with the IV regimen. It is theorized that the efficacy seen with SC amivantamab may be linked to SC absorption via the lymphatic system, potentially enhancing immune-mediated activity.

Administration time was substantially shorter for SC amivantamab (median less than approximately five minutes) compared to IV administration (up to five hours), with significantly more patients reporting convenience with the SC administration (85 percent with SC amivantamab vs 35 percent with IV administration at end of treatment; *P*<0.001).

Per the abstract, Geometric mean ratios (GMRs) comparing SC ami+laz vs IV for C_{trough} were 1.15 (90% CI, 1.04–1.26) for C2D1 and 1.43 (90% CI, 1.27–1.61) for C4D1. GMR for C2 AUC_{D1-D15} was 1.03 (90% CI, 0.98–1.09).

Most Common Adverse Events

The overall safety profile of SC amivantamab is consistent with the known profile of IV administration. The most common all-grade adverse events (≥ 20 percent) for SC amivantamab compared to IV were paronychia (54 percent vs 51 percent), hypoalbuminemia (47 percent vs 37 percent) and rash (46 percent vs 43 percent), respectively. No Grade 4 or 5 IRRs were reported. The rate of IRRs for patients treated with SC amivantamab combined with lazertinib was shown to be approximately five-fold lower than that observed with the IV formulation (13 percent vs 66 percent, respectively). Prophylactic anticoagulation was used in most patients in the study and was found to be safe and effective in reducing the rate of venous thromboembolic events (VTE). Patients receiving prophylactic anticoagulation had lower rates of VTE (10 percent) than those without prophylaxis (21 percent). Furthermore, VTE incidence was lower in the SC arm compared to the IV arm (9 percent vs 14 percent, respectively) regardless of anticoagulation use. Severe bleeding risk was low and similar among patients receiving anticoagulants in the SC (2 percent) and IV (1 percent) arms.

Conclusion

Study results showed non-inferior efficacy and pharmacokinetics for SC amivantamab combined with lazertinib compared to intravenous (IV) administration, the currently approved formulation of RYBREVANT (amivantamab-vmjw). Administration time for SC amivantamab was reduced

to approximately five minutes from five hours (across two days) and showed a five-fold reduction in infusion-related reactions (IRRs).

Comment

In May 2023, topline results from the PALOMA-3 trial showed that subcutaneous (SC) Rybrevant (given in combination with lazertinib) was well tolerated, improved the time and ease of administration, and meaningfully reduced infusion-related reactions (IRRs). The final data from the PALOMA-3 trial are now available. Impressive outcomes in terms of shorter infusion times, lower rates of IRRs and venous thromboembolism, with pharmacokinetics and efficacy comparable to the current intravenous (IV) administration indicate the potential of SC Rybrevant in improving the treatment experience for patients with EGFR exon 19 deletion or L858R mutations. It is further notable that PFS was extended and an OS benefit was observed with SC Rybrevant.

The first-line treatment landscape for *EGFR*-mutated NSCLC, which is currently dominated by AstraZeneca's Tagrisso, was disrupted by the pivotal MARIPOSA study results. These results indicated a new treatment option, namely Rybrevant + lazertinib, as the primary endpoint of PFS was shown to be superior to that for Tagrisso, and interim OS data trended in favor of the combination. However, there was significant debate regarding the regimen's toxicity profile, including severe infusion reactions associated with IV Rybrevant, compared to the orally available and relatively safe current standard of care Tagrisso. Therefore, from a quality of life perspective, Tagrisso monotherapy remained the preferred first-line standard of care. Additionally, the FLAURA2 trial results suggested that Tagrisso combined with chemotherapy could be a game changer in first-line *EGFR*-mutated NSCLC, as the median PFS significantly improved to 25.5 months compared to 16.7 months for Tagrisso monotherapy. However, in March 2024, further exploratory analysis of the MARIPOSA study confirmed that Rybrevant + lazertinib remained effective in *EGFR*-mutated NSCLC patients despite toxicity-related dose interruptions. Johnson & Johnson received priority review from the FDA for this combination in February 2024 for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or L858R substitution mutations. Consequently, the standard of care for first-line *EGFR*-mutated NSCLC remains uncertain. The updated results from the CHRYSALIS-2 trial and new data from the MARIPOSA subgroup analysis study have also been made public at ASCO 2024. Both studies have demonstrated the benefit of first-line treatment with Rybrevant + lazertinib.

The favorable results of the PALOMA trials, combined with the CHRYSALIS-2 and MARIPOSA subgroup trials, are already generating significant attention. The SC option for Rybrevant could potentially revolutionize the treatment paradigm for *EGFR*-mutated NSCLC, positioning the SC Rybrevant + lazertinib combination as the new standard of care.

Based on these results, we are raising SC Rybrevant's LOA by 5%.

Source:

PR Newswire 05/31/2024 (JNJ)
Globe Newswire 05/31/2024 (JNJ)
American Society of Clinical Oncology (ASCO) 05/31/2024 (Abstract LBA8505)
Citeline Analysis

Trodelvy for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	05/31/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - EVOKE-01
Market Group:	Oncology
Lead Company:	Gilead Sciences, Inc. (GILD)
Partner Companies:	Royalty Pharma (RPRX)
Former Companies:	Immunomedics
Change to Likelihood of Approval:	-5%
Likelihood of Approval:	41% (3% Below Avg.)
Average Approval:	44%

Gilead Sciences announced detailed results from the Phase III EVOKE-01 study that will be presented during an oral session at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. An abstract entitled, "Sacituzumab govitecan (SG) vs docetaxel (doc) in patients (pts) with metastatic non-small cell lung cancer (mNSCLC) previously treated with platinum (PT)-based chemotherapy (chemo) and PD(L)-1 inhibitors (IO): Primary results from the phase 3 EVOKE-01 study" was presented on May 31, 2024.

Data from this study were last seen in January 2024.

Context

The results were also published simultaneously in the *Journal of Clinical Oncology*. The company previously announced that the study did not meet the primary endpoint of overall survival (OS) in previously treated metastatic non-small cell lung cancer (NSCLC).

Design

The EVOKE-01 study is a global, multicenter, open-label Phase III study randomized 1:1 to evaluate Trodelvy vs. docetaxel in patients with advanced or metastatic NSCLC that has progressed on or after platinum-based chemotherapy and checkpoint inhibitor therapy. The study enrolled 603 participants.

Per the abstract, pts with mNSCLC with disease progression after PT-based chemo and IO were randomized 1:1 (stratified by histology, best response to last prior IO, and prior treatment for actionable genomic alterations [yes/no]) to receive SG (10 mg/kg IV, days 1 and 8) or doc (75 mg/m^2 IV, day 1) in 21-day cycles until progression or unacceptable toxicity.

Endpoints

The primary endpoint is overall survival (OS). Key secondary endpoints include progression-free survival (PFS), objective response rate (ORR), duration of response (DoR) and disease control rate (DCR) as assessed by investigator per Response Evaluation Criteria in Solid Tumors (RECIST 1.1) and safety. Additional efficacy measures include time to first deterioration in shortness of breath domain as measured by NSCLC Symptom Assessment Questionnaire (NSCLC-SAQ) Score and time to first deterioration NSCLC-SAQ Total Score.

Results

EVOKE-01, evaluating Trodelvy (sacituzumab govitecan-hziy; SG) vs. docetaxel, showed a 16% reduction in the risk of death (median OS: 11.1 vs. 9.8 months; HR: 0.84; 95% CI: 0.68-1.04; 1-sided p=0.0534) in patients with metastatic or advanced NSCLC that had progressed on or after platinum-based chemotherapy and anti-PD-(L)1-therapy. This numerical improvement in OS was observed consistently across both squamous and non-squamous histology. In patients with high unmet medical need whose tumors did not respond to last anti-PD-(L)1-containing treatment, a meaningful OS improvement of 3.5 months was seen when treated with Trodelvy vs. docetaxel (mOS: 11.8 vs. 8.3 months; HR: 0.75; 95% CI: 0.58-0.97). This subgroup represents approximately 2/3 of the study population. This prespecified subgroup analysis was not alpha-controlled for formal statistical testing.

For the subgroup of patients whose mNSCLC was responsive to last anti-PD-(L)1-containing treatment, median OS was 9.6 vs. 10.6 months

when treated with Trodelvy vs. docetaxel (HR: 1.09; 95% CI: 0.76-1.56). In the overall study population, numerically more patients were alive at 12 months when treated with Trodelvy compared to docetaxel (46.6% vs. 36.7%).

Most Common Adverse Events

In the study, Grade ≥3 adverse events (AEs) were lower among patients receiving Trodelvy (66.6%) vs. docetaxel (75.7%), and AEs leading to discontinuation were lower with Trodelvy (9.8%) vs. docetaxel (16.7%). The most common AEs of any grade for Trodelvy were fatigue (57%), diarrhea (53%), and alopecia (43%), and for docetaxel were fatigue (56%), neutropenia (43%), and diarrhea (34%). Patients treated with docetaxel had a greater incidence of neutropenia of any grade compared with Trodelvy (43% vs. 38%, respectively), while patients treated with Trodelvy experienced more diarrhea of any grade vs. docetaxel (53% vs. 34%, respectively). The safety profile for Trodelvy was consistent with prior studies, with no new safety signals identified in this patient population.

Conclusion

Per the abstract, although statistical significance was not met, SG showed numerical improvement in OS vs doc. Results were consistent across all major subgroups including histology. Clinically meaningful improvement in OS was noted in pts without response to prior IO. SG was better tolerated than doc; observed safety was consistent with the known profile.

Comment

Following the initial announcement in January 2024 that Trodelvy failed to meet the OS primary endpoint, numerical data from the EVOKE-01 trial are now available. This setback terminates the chances of Trodelvy claiming a position as a monotherapy in patients with metastatic or advanced NSCLC who have progressed on or after platinum-based chemotherapy and checkpoint inhibitor therapy. However, Trodelvy did demonstrate a 16% reduction in the risk of death compared to docetaxel. Also, subgroup analysis revealed a significant OS improvement of 3.5 months in patients whose tumors were unresponsive to anti-PD-(L)1 therapy, which accounted for 60% of the EVOKE-01 study's participants.

However, with EVOKE-01 failing to demonstrate an OS improvement, Gilead's hopes for Trodelvy in NSCLC now rest on the two combinations being evaluated in the EVOKE-02 (Trodelvy in combination with Keytruda with/without platinum chemotherapy) and EVOKE-03 (Trodelvy in combination with Keytruda) trials. Longer-term results from Cohort A of the Phase II EVOKE-02 study in first-line metastatic PD-L1 ≥50% NSCLC have also been made public at ASCO 2024. The combination of Trodelvy and Keytruda has demonstrated promising activity, with the primary endpoint of objective response rate reported as 67% and a median PFS of 13.1 months. These results, however, come from a relatively small patient sample size. By adding its antibody-drug conjugate to Keytruda in the first-line setting, Gilead hopes that Trodelvy will demonstrate superior efficacy over Keytruda alone, but after the results seen in the EVOKE-01 trial, Keytruda remains a high bar to overcome. Additionally, in EVOKE-01, grade ≥3 treatment-emergent adverse event incidence was 66.6%, while 9.8% of patients discontinued the study. Thus, with Trodelvy associated with two black box warnings for severe diarrhea and neutropenia, and Keytruda leading to only 9.5% of patients experiencing a grade 3/5 adverse event in the KEYNOTE-001 trial, the safety profiles of the two drugs may serve as important differentiators should the efficacy of the combination match that of Keytruda monotherapy. Also, unless superior data can be seen over Keytruda in late-phase trials, it will be difficult to displace a less toxic and cheaper single-agent regimen.

A huge unmet need remains for therapies for NSCLC patients previously treated with platinum-based chemotherapy and an approved targeted therapy or PD-1/PD-L1 inhibitors, with many patients progressing on immune checkpoint inhibitors and quickly running out of therapeutic options. As such, Trodelvy's failure is disappointing, leaving a large commercial opportunity still untapped.

Based on these results, we are decreasing Trodelvy's LOA in NSCLC by 5%.

Source:

Business Wire 05/31/2024 (GILD)
American Society of Clinical Oncology (ASCO) 05/31/2024 (Abstract LBA8500)
Journal Article 05/31/2024 (DOI: 10.1200/JCO.24.00733)
Citeline Analysis

Amivantamab SC for Non-Small Cell Lung Cancer (NSCLC)

Event Date:	05/31/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - PALOMA-3
Market Group:	Oncology
Lead Company:	Johnson & Johnson (JNJ)
Partner Companies:	Halozyme Therapeutics (HALO)
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	49% (5% Above Avg.)
Average Approval:	44%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Amivantamab (IV) + lazertinib	Amivantamab (SC) + lazertinib	Amivantamab (IV) + lazertinib vs. Amivantamab (SC) + lazertinib
Number of Patients	N/A	N/A	N/A
Number of Evaluable Patients	212	206	418
Overall Response Rate	33 %	30 %	N/A (P=0.001)
Median Duration of Response (DOR)	8.3 Months	11.2 Months	N/A
Progression-Free Survival (PFS) ***(Endpoint=Secondary)***	4.3 Months	6.1 Months	N/A
Hazard Ratio Progression-Free Survival (PFS) ***(Endpoint=Secondary)***	N/A	N/A	0.84 (P=0.20)
Hazard Ratio Overall Survival ***(Endpoint=Secondary)***	N/A	N/A	0.62 (P=0.02)

Johnson & Johnson announced first data from the Phase III PALOMA-3 study evaluating subcutaneous (SC) amivantamab combined with lazertinib in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion (ex19del) or L858R mutations. These data were presented in an abstract entitled "Subcutaneous amivantamab vs intravenous amivantamab, both in combination with lazertinib, in refractory *EGFR*-mutated, advanced non-small cell lung cancer (NSCLC): Primary results, including overall survival (OS), from the global, phase 3, randomized controlled PALOMA-3 trial" at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting on May 31, 2024.

Context

The company announced the submission of an application for the extension of the RYBREVANT marketing authorization (line extension) to the European Medicines Agency (EMA) seeking approval of SC amivantamab in combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR ex19del or L858R mutations and as monotherapy in adult patients with advanced NSCLC with activating EGFR exon 20 insertion mutations after failure of platinum-based therapy based on the PALOMA-3 data. Johnson & Johnson will submit regulatory applications seeking the approval of SC amivantamab in other markets, including the United States.

Design

PALOMA-3, which enrolled 418 patients, is a randomized, open-label Phase III study evaluating the pharmacokinetics (PK), efficacy and safety of subcutaneous amivantamab (administered via manual injection) combined with lazertinib compared to IV amivantamab and lazertinib in patients with EGFR-mutated advanced or metastatic NSCLC after progression on osimertinib and chemotherapy.

Per the abstract, SC ami at 1600 mg (2240 mg, ≥80 kg) was manually injected weekly for the first 4 weeks, then every 2 weeks; IV ami was given at the approved dose of 1050 mg (1400 mg, ≥80 kg). Laz was orally dosed at 240 mg daily.

Endpoints

The co-primary PK endpoints of the study were trough concentration (C_{trough} on Cycle [C] 2 Day [D] 1 or C4D1) and C2 area under the curve (AUCD1-D15). Key secondary endpoints were objective response rate and progression-free survival. Overall survival was a predefined exploratory endpoint. Prophylactic anticoagulation was recommended for the first four months of treatment.

Results

Results showed SC amivantamab was non-inferior to IV amivantamab, meeting both co-primary pharmacokinetic (PK) efficacy endpoints as measured by amivantamab levels in the blood (C_{trough} and area under the serum concentration time curve from day 1 to 15).

At a median follow-up of seven months, the overall response rate was 30 percent (95 percent confidence interval [CI], 24–37) in the subcutaneous arm and 33 percent (95 percent CI, 26–39) for IV (relative risk, 0.92; 95 percent CI, 0.70-1.23; *P*=0.001), meeting the noninferiority criteria. SC amivantamab also demonstrated longer duration of response (DoR), progression-free survival (PFS) and significant improvement in overall survival (OS) compared to IV administration during this time. Specifically, median DoR was numerically longer for SC amivantamab combined with lazertinib compared to IV (median, 11.2 vs 8.3 months among confirmed responders) as was PFS (median, 6.1 vs 4.3 months; hazard ratio [HR], 0.84; 95 percent CI, 0.64–1.10; *P*=0.20). A prespecified exploratory endpoint showed patients treated with SC amivantamab had significantly longer OS compared with IV (HR, 0.62; 95 percent CI, 0.42–0.92; nominal *P*=0.02). At 12 months, 65 percent of patients who received SC amivantamab combined with lazertinib were alive compared with 51 percent of those treated with the IV regimen. It is theorized that the efficacy seen with SC amivantamab may be linked to SC absorption via the lymphatic system, potentially enhancing immune-mediated activity.

Administration time was substantially shorter for SC amivantamab (median less than approximately five minutes) compared to IV administration (up to five hours), with significantly more patients reporting convenience with the SC administration (85 percent with SC amivantamab vs 35 percent with IV administration at end of treatment; *P*<0.001).

Per the abstract, Geometric mean ratios (GMRs) comparing SC ami+laz vs IV for C_{trough} were 1.15 (90% CI, 1.04–1.26) for C2D1 and 1.43 (90% CI, 1.27–1.61) for C4D1. GMR for C2 AUC_{D1-D15} was 1.03 (90% CI, 0.98–1.09).

Most Common Adverse Events

The overall safety profile of SC amivantamab is consistent with the known profile of IV administration. The most common all-grade adverse events (≥ 20 percent) for SC amivantamab compared to IV were paronychia (54 percent vs 51 percent), hypoalbuminemia (47 percent vs 37 percent) and rash (46 percent vs 43 percent), respectively. No Grade 4 or 5 IRRs were reported. The rate of IRRs for patients treated with SC amivantamab combined with lazertinib was shown to be approximately five-fold lower than that observed with the IV formulation (13 percent vs 66 percent, respectively). Prophylactic anticoagulation was used in most patients in the study and was found to be safe and effective in reducing the rate of venous thromboembolic events (VTE). Patients receiving prophylactic anticoagulation had lower rates of VTE (10 percent) than those without prophylaxis (21 percent). Furthermore, VTE incidence was lower in the SC arm compared to the IV arm (9 percent vs 14 percent, respectively) regardless of anticoagulation use. Severe bleeding risk was low and similar among patients receiving anticoagulants in the SC (2 percent) and IV (1 percent) arms.

Conclusion

Study results showed non-inferior efficacy and pharmacokinetics for SC amivantamab combined with lazertinib compared to intravenous (IV) administration, the currently approved formulation of RYBREVANT (amivantamab-vmjw). Administration time for SC amivantamab was reduced to approximately five minutes from five hours (across two days) and showed a five-fold reduction in infusion-related reactions (IRRs).

Comment

In May 2023, topline results from the PALOMA-3 trial showed that subcutaneous (SC) Rybrevant (given in combination with lazertinib) was well tolerated, improved the time and ease of administration, and meaningfully reduced infusion-related reactions (IRRs). The final data from the PALOMA-3 trial are now available. Impressive outcomes in terms of shorter infusion times, lower rates of IRRs and venous thromboembolism, with pharmacokinetics and efficacy comparable to the current intravenous (IV) administration indicate the potential of SC Rybrevant in improving the treatment experience for patients with EGFR exon 19 deletion or L858R mutations. It is further notable that PFS was extended and an OS benefit was observed with SC Rybrevant.

The first-line treatment landscape for *EGFR*-mutated NSCLC, which is currently dominated by AstraZeneca's Tagrisso, was disrupted by the pivotal MARIPOSA study results. These results indicated a new treatment option, namely Rybrevant + lazertinib, as the primary endpoint of PFS was shown to be superior to that for Tagrisso, and interim OS data trended in favor of the combination. However, there was significant debate regarding the regimen's toxicity profile, including severe infusion reactions associated with IV Rybrevant, compared to the orally available and relatively safe current standard of care Tagrisso. Therefore, from a quality of life perspective, Tagrisso monotherapy remained the preferred first-line standard of care. Additionally, the FLAURA2 trial results suggested that Tagrisso combined with chemotherapy could be a game changer in first-line *EGFR*-mutated NSCLC, as the median PFS significantly improved to 25.5 months compared to 16.7 months for Tagrisso monotherapy. However, in March 2024, further exploratory analysis of the MARIPOSA study confirmed that Rybrevant + lazertinib remained effective in *EGFR*-mutated NSCLC patients despite toxicity-related dose interruptions. Johnson & Johnson received priority review from the FDA for this combination in February 2024 for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or L858R substitution mutations. Consequently, the standard of care for first-line *EGFR*-mutated NSCLC remains uncertain. The updated results from the CHRYSALIS-2 trial and new data from the MARIPOSA subgroup analysis study have also been made public at ASCO 2024. Both studies have demonstrated the benefit of first-line treatment with Rybrevant + lazertinib.

The favorable results of the PALOMA trials, combined with the CHRYSALIS-2 and MARIPOSA subgroup trials, are already generating significant attention. The SC option for Rybrevant could potentially revolutionize the treatment paradigm for *EGFR*-mutated NSCLC, positioning the SC Rybrevant + lazertinib combination as the new standard of care.

Based on these results, we are raising SC Rybrevant's LOA by 5%.

Source:

PR Newswire 05/31/2024 (JNJ)
Globe Newswire 05/31/2024 (JNJ)
American Society of Clinical Oncology (ASCO) 05/31/2024 (Abstract LBA8505)
Citeline Analysis

Elahere for Ovarian Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - MIRASOL (FRa-High Platinum-Resistant)
Market Group:	Oncology
Lead Company:	AbbVie Inc. (ABBV)
Partner Companies:	Huadong Medicine (000963) Takeda Pharmaceutical (TAK)
Former Companies:	ImmunoGen (IMGN)
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

An abstract entitled "Phase 3 MIRASOL (GOG 3045/ENGOT-ov55) trial: Mirvetuximab soravtansine (MIRV) vs. investigator's choice chemotherapy (ICC) in older patients with platinum-resistant ovarian cancer (PROC) and high folate receptor-alpha (FRα) expression" was presented at the American Society of Clinical Oncology Annual Meeting on June 3, 2024.

Data from this study were last seen in December 2023.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

453 PROC pts with high FRα expression (VENTANA FOLR1 [FOLR1-2.1] RxDx Assay) with 1-3 prior therapies were randomized 1:1 to MIRV 6 mg/kg, adjusted ideal body weight, Day 1 of a 21-day cycle or ICC: paclitaxel, pegylated liposomal doxorubicin, or topotecan. With a data cutoff of March 6, 2023, 107 pts ≥ 65 were randomized to the MIRV arm; 92 pts ≥ 65 were randomized to the ICC arm.

Endpoints

The primary efficacy endpoint was PFS by investigator (INV) with key secondary endpoints ORR, OS, and patient-reported outcomes in hierarchical order; other endpoints included safety, tolerability, and duration of response.

Results

Baseline characteristics were well balanced across arms; the median age was 71 years for MIRV and 70 for ICC arm. In the MIRV arm, 57% had prior bevacizumab vs. 67% in the ICC arm, and 57% had prior PARPi experience vs. 58% in the ICC arm in pts ≥ 65. In the MIRV arm, 15% had one, 36% had two, and 49% had three prior lines of therapy, respectively, and in the ICC arm, 18% had one, 39% had two, and 42% had three prior lines of therapy, respectively. The nominal PFS HR was 0.62 (0.45, 0.86), favoring MIRV; nominal OS HR was 0.57 (0.37, 0.87), favoring MIRV, and the overall response rate was 39.3% for MIRV vs. 17.4% for ICC in pts ≥ 65.

Most Common Adverse Events

Compared with ICC, pts on MIRV were associated with lower rates of grade 3+ treatment-emergent AEs (45% vs 58%) and serious AEs (24% vs 38%). TEAEs leading to dose reductions in MIRV pts ≥ 65 compared to ICC were 34% vs 30%, dose delays were 49% vs 57%, and discontinuations were 10% vs. 23%, respectively. Ocular, gastrointestinal, and neurosensory adverse events were comparable to the intent to treat population.

Conclusion

MIRV demonstrated a PFS, ORR, and OS benefit in PROC compared to ICC. MIRV demonstrated a longer PFS, OS, and higher ORR vs ICC in the older population. Importantly, MIRV had fewer dose discontinuations than ICC, suggesting that TEAEs were more manageable. The efficacy data and the well-characterized safety profile support MIRV as the standard of care for pts with FRα positive PROC across all ages.

Comment

Elahere was first granted accelerated approved by the FDA in November 2022, as the first-in-class ADC for the treatment of FRα-high platinum resistant ovarian cancer (PROC) across all age groups. The drug's approval came following data from MIRASOL, the Phase III trial of Elahere versus investigator's choice of chemotherapy in this setting, in which Elahere demonstrated improvements in median PFS, ORR and OS over chemotherapy, becoming the first agent to show a meaningful OS benefit over single-agent chemotherapy in a Phase III PROC trial.

Data presented at ASCO further highlighted the clinical benefit of Elahere, specifically in FRα-high elderly PROC patients, especially significant for patients who may otherwise be unable to tolerate standard chemotherapy. Similarly to the larger trial population, Elahere showed improvements over single-agent chemotherapy across parameters measured in MIRASOL in patients 65 years and older, notably in median PFS (5.9 months versus 3.0 months), median OS (19.9 months versus 12.1 months) and median ORR (39.3% versus 17.4%), with similar safety signals to all patients enrolled in MIRASOL and fewer discontinuations in the elderly cohort compared to chemotherapy.

The data bolster Elahere's standing as drug-of-choice in high FRα expressers with PROC, especially as drugs like luveltamab tazevibulin and BAT8006 (China only) are currently in development for FRα-expressing PROC all-comers, and will seek approval for use in a larger patient population including Elahere's current market.

Source:

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 5580)
Citeline Analysis

Ceralasertib for Ovarian Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - CAPRI
Market Group:	Oncology
Lead Company:	AstraZeneca PLC (AZN)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	0% (Same As Avg.)
Average Approval:	N/A

An abstract entitled "Combination ATR and PARP Inhibitor (CAPRI): A phase 2 study of ceralasertib plus olaparib in patients with recurrent, platinum-sensitive epithelial ovarian cancer (cohort A)" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Context

Preclinical data have demonstrated synergy between poly (ADP-ribose) polymerase inhibitors (PARPi) and ataxia telangiectasia and Rad3-related kinase inhibitors (ATRi) regardless of homologous recombination deficiency (HRD) status.

Methods

The Researchers present results of an investigator-initiated study examining the combination of PAPRi and ATRi in patients (pts) with PSOC. Pts with PSOC and measurable disease by RECIST v1.1 were enrolled. Prior PARPi was permitted but not mandatory and there was no limit to number of prior regimens. Pts received ceralasertib (C) 160mg po once daily, days 1–7 and olaparib (O) 300mg po twice daily, on days 1–28 of a 28-day cycle until unacceptable toxicity or disease progression. Myriad MyChoice CDx and Caris Life Sciences MI Profile assays were used to determine presence of tumor genomic instability; HRD (positive if score >42) or loss of heterozygosity (LOH) (positive if 38% of tested genomic segments exhibited LOH).

Endpoints

The primary end points were efficacy based on objective response rate (ORR) and toxicity. Secondary endpoint was progression-free survival (PFS).

Results

Thirty-seven pts were enrolled and evaluable for toxicity; 33 pts were available for response evaluation. Median number of prior regimens was 1 (range 1-3) while 2 pts received prior PARPi. Germline homologous recombination (HR) gene mutations were present in 3 (8.1%) pts (1 BRCA2, 1 BRIP1, 1 RAD51C),10 (27%) pts had tumors exhibiting genomic instability (8 with HRD positive and 2 with LOH high), while 19 (51.4%) pts had tumors without genomic instability, and 5 (13.5%) pts had unknown status. Pts received a median of 8 cycles (range 1-50). ORR was 48.5% with 3 complete responses (CR) and 13 partial responses (PR) and median progression-free survival (mPFS) was 8.3 months (95% CI: 5.9, 10.7). ORR and mPFS in 16 pts with tumors without genomic instability was 43.8% (1 CR, 6 PR) and 7.6 months (95% CI: 5.4, 9.8). ORR in 10 pts with tumors with genomic instability was 40% (4 PR) with a mPFS of 8.3 months (95% CI: 5.1, 11.5). ORR in 3 pts with germline HR gene alterations was 100% (1 CR, 2 PR) with mPFS not reached. ORR in 4 pts with unknown status of genomic instability was 50% (1CR, 1PR).

Most Common Adverse Events

Fifteen (40.5%) pts experienced a grade (G) 3 toxicity event, most commonly anemia 21.6% (n=8) and diarrhea 5.4% (n=2). Two pts (5.4%) had

G4 thrombocytopenia. Dose reductions occurred in 14 pts (37.8%); one pt discontinued treatment due to toxicity (G2 fatigue and nausea).

Conclusions

C+O was well tolerated and active in pts with platinum sensitive HGSOC warranting further evaluation. Efficacy was seen regardless of the presence of tumor genomic instability.

Comment

Ceralasertib is a selective inhibitor of the ataxia telangiectasia and RAD3-related kinase (ATR) pathway, which controls checkpoints which ensure cell survival after DNA damage or replication stress. It has been proposed that a combination of the ATR inhibitor and Lynparza offers a promising strategy to overcome PARP inhibitor resistance, especially in *BRCA*-mutated cancers. As the current standard of care in platinum-sensitive ovarian cancer consists of platinum-based chemotherapy with or without bevacizumab or a PARP inhibitor, there is scope to explore other interventions capable of showing efficacy and mitigating safety concerns associated with the use of platinum chemotherapy.

In CAPRI, ceralasertib + Lynparza showed an ORR of 48.5% with a median PFS of 8.3 months in all patient groups irrespective of HRD status. Although promising, these results pale in comparison to platinum chemotherapy + paclitaxel, which showed an ORR of 66% in the ICON4/AGO-OVAR-2.2 trial, with a median PFS of 13 months. Combinations of platinum chemotherapy and maintenance bevacizumab have also been significantly more effective, with ORRs ≥ 57% in multiple trials irrespective of HRD status, and even more impressive median PFS values in combination with PARP inhibitors in this setting. Impressively though, in patients with germline HR mutations, the ceralasertib combination showed an ORR of 100%, while median PFS was not reached, comparing favorably to Lynparza alone in Study 42, where an ORR of 46% was observed.

Although AstraZeneca intends to continue studies into the efficacy of ceralasertib, a high bar for approval has been set, given the success and familiarity of platinum chemotherapy combinations in platinum-sensitive disease. Further data are anticipated by the end of 2024, but based on these interim results, the LOA for ceralasertib remains unchanged.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 5510)
Citeline Analysis

JNJ-69086420 for Prostate Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase I - CR108817
Market Group:	Oncology
Lead Company:	Johnson & Johnson (JNJ)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	-1%
Likelihood of Approval:	4% (1% Below Avg.)
Average Approval:	5%

Johnson & Johnson announced the data from Phase I study of JNJ-69086420 (JNJ-6420) to treat metastatic castration-resistant prostate cancer (mCRPC) at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. The abstract entitled "A Phase 1 study of JNJ-69086420 (JNJ-6420), an actinium-225 (^{225}Ac)-labeled antibody targeting human kallikrein 2 (hk2) to treat metastatic castration-resistant prostate cancer (mCRPC)" was presented at the meeting on June 3, 2024.

Design

Intravenous JNJ-6420 was escalated from 50 µCi to 400 µCi every 8-12 weeks in the outpatient setting with no residential radioprotective restrictions. Prior radioisotopic therapy was an exclusion criterion.

Endpoints

Primary objectives were safety and defining a recommended phase 2 dose (RP2D). Secondary objectives included preliminary assessment of clinical activity.

Results

As of January 5, 2024, 67 pts received ≥1 JNJ-6420 dose. At doses ≥150 µCi, the PSA50 rate was 45.6%. To date, across all dose cohorts, 31 pts (46%) remained on treatment for ≥24 weeks. Prolonged clinical, biochemical, and radiographic responses were noted in pts receiving doses of 150 µCi and higher. Durable responses included pts on treatment for 112 weeks (96 weeks since last dose), 88 weeks (13 weeks since last dose), and 46 weeks (after a single dose).

Most Common Adverse Events

35/57 (61.4%) experienced grade ≥3 TEAEs, and 21 (36.8%) had a serious TEAE. TEAEs of note included thrombocytopenia (63.2%) and interstitial lung disease (ILD, 9%). All instances of ILD occurred at cumulative doses ≥500 µCi and prior to implementation of pulmonary function surveillance. Grade ≥3 TEAEs (≥10%) included anemia (26.3%), thrombocytopenia (17.5%), lymphopenia (10.5%), and leukopenia (10.5%). 9/57 (15.8%) pts discontinued treatment due to TRAEs; 4 TRAEs resulted in death.

Conclusion

These data highlight hK2 as a target for targeted alpha-particle therapy.

Comments

Radioligand therapy is a rapidly developing drug class in the metastatic castration resistant prostate cancer (mCRPC) space. Currently, pipeline and approved therapies have used the transmembrane protein, PSMA, as a key target for therapeutic strategies due to its high level of expression on prostate cancer tumor cells. Johnson & Johnson's JNJ-69086420 is a first-in-class human kallikrein-related peptidase 2 (hK2) targeted radioligand, which delivers the high-energy alpha particle emitter actinium-255 to prostate cancer cells. The hK2 protein shares significant homology to prostate-specific antigen (PSA) and, as with PSMA, is minimally expressed in normal

non-prostate tissues.

Currently, there are only two radiotherapies approved for mCRPC, both with distinct drawbacks. The radium-233-based Xofigo, is the only approved alpha emitter on the market following the success of the Phase III ALSYMPCA trial. Notably, Xofigo is not conjugated to a targeting molecule specific to prostate cancer and is instead taken up into bone matrix following IV. Pluvicto is the only approved protein-targeting (PSMA) radioconjugate based on the results of the Phase III VISION trial. However, the beta-particles emitted by lutetium-177 in Pluvicto treatment are lower energy particles with higher levels of unwanted exposure to the surrounding cells compared to that of actinium-225, the potent alpha-particle emitter in JNJ-69086420. Therefore, there is a lucrative gap in the market for a first-in-class protein-targeting alpha emitter.

JNJ-69086420 is being investigated in a Phase I study in mCRPC patients who have progressed on at least one prior androgen receptor-targeted therapy. The primary endpoint of this study is safety, as measured by the incidence and severity of adverse effects. Given this, the results of the trial were not entirely positive. Serious treatment-related adverse effects (TRAEs) occurred in 32% of patients, with TRAEs leading to discontinuation in 14.7% of the patient population. Furthermore, 6.7% of patients had treatment-emergent interstitial lung disease (ILD) and two of these cases were fatal. If approved, JNJ-69086420 may be burdened with a black box warning for ILD and may need further subgroup analyses to discern which patients would have a stronger safety profile on the drug.

Currently, Fusion Pharmaceuticals' FPI-2265 is the only late-phase actinium-225 based radioconjugate being investigated in the Phase II TACTIST trial in heavily pre-treated mCRPC patients. To afford an indirect comparison, as FPI-2265 is being investigated in a similar patient population but is PSMA-targeted, JNJ-69086420's results do not look competitive to those of FPI-2265. The TACTIST trial had a lower discontinuation rate (8%) and most TRAEs were grade 1 and 2. The results of the secondary endpoint of clinical activity are more encouraging with JNJ-69086420, which achieved a PSA50 of 45%, more closely matched with FPI-2265's PSA50 OF 50%.

While this trial is only in the early phase, the current efficacy is not strong enough to mitigate the dose-limiting and consequential nature of JNJ-69086420's adverse events. Further testing of the use of the novel hK2-targeted radioligand is necessary and in the meantime, we are lowering the LOA by 1%.

Source:

Press Release 05/23/2024 (JNJ)
American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 5010)

ARV-766 for Prostate Cancer

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase I/II - w/Abiraterone
Market Group:	Oncology
Lead Company:	Novartis AG (NVS)
Partner Companies:	Arvinas (ARVN)
Former Companies:	N/A
Change to Likelihood of Approval:	2%
Likelihood of Approval:	13% (2% Above Avg.)
Average Approval:	11%

Arvinas announced updated results from the Phase I/II trial of ARV-766 in prostate cancer at the 2024 American Society of Clinical Oncology Annual Congress. The abstract entitled "ARV-766, a proteolysis targeting chimera (PROTAC) androgen receptor (AR) degrader, in metastatic castration-resistant prostate cancer (mCRPC): Initial results of a phase 1/2 study" was presented at the meeting on June 3, 2024.

Data from the study were last seen in October 2023.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website.

Design

Eligible patients had progressive mCRPC and ongoing androgen deprivation therapy. The Phase I dose escalation portion evaluated the safety and tolerability of escalating doses of ARV-766 (20–500 mg once daily [QD]) in patients who had progressed on ≥2 prior systemic therapies (including ≥1 NHA). The Phase II cohort expansion portion is evaluating the clinical activity and safety of 2 doses of ARV-766 (100 or 300 mg QD) in patients who had received 1–3 prior NHAs and ≤2 prior chemotherapy regimens. Safety was reported in all patients treated with ARV-766 across the Phase I/II study and clinical activity (proportion of patients with best prostate-specific antigen [PSA] declines of ≥50% [PSA_{50}] after ≥1 month of PSA follow-up) in the subgroup of patients with *AR* LBD mutations.

As of December 15, 2023, 103 patients received ARV-766 (34 in Phase I and 69 in Phase II). Patients had received a median of 4 prior therapies (range: 1–9), including 56% with ≥1 prior taxane and 46% with ≥2 prior NHAs. Patients with *AR* LBD mutations (n=30) had received a median of 4 prior therapies (range: 1–9), including 60% with ≥1 prior taxane and 57% with ≥2 prior NHAs.

Results

In 28 PSA-evaluable patients with *AR* LBD mutations, PSA_{50} was 50.0%. Preliminary pharmacokinetics indicated dose-dependent increases in ARV-766 exposure up to 320 mg QD, with exposure accumulation ranging from ≈5- to 8-fold at steady state.

Most Common Adverse Events

In Phase I, there were no dose-limiting toxicities, and a maximum tolerated dose was not reached. Across 103 Phase I/II patients, treatment-emergent adverse events led to dose reduction and treatment discontinuation, respectively, in 7 (7%) and 10 (10%). Any grade treatment-related adverse events (TRAEs) reported in ≥10% of patients were fatigue (36%; 3% grade 3), nausea (19%; 1% grade 3), diarrhea (15%; 1% grade 3), alopecia (14%), increased blood creatinine (13%; 0 grade 3), and decreased appetite (11%; 0 grade 3); there were no grade 4 TRAEs.

Conclusion

In the Phase I/II study of pretreated patients with mCRPC, ARV-766 was well tolerated and showed clinical activity in those with tumors harboring*AR* LBD mutations. ARV-766 warrants further development in advanced prostate cancer.

Comments

Proteolysis targeting chimeras (PROTACs) are a promising approach to cancer treatment, yet after over two decades of research, not a single PROTAC has gained FDA approval. Arvinas' ARV-766, is a second-generation PROTAC androgen receptor (AR) degrader, which has been designed to degrade both wild-type AR and all clinically relevant AR ligand-binding domain (LBD) mutants, including L720H, H875Y and T878A. This is a key addressable population, as these mutations develop in ~20-25% of men with metastatic castration-resistant prostate cancer (mCRPC) who have progressed on an androgen receptor pathway inhibitor (ARPI) and are associated with a poor prognosis.

Arvinas is looking to address this area of unmet need through running a Phase I/II study, investigating ARV-766 in mCRPC patients who have progressed on at least two systemic therapies, one of which is an ARPI. The data presented at ASCO 2024 only reports on the subgroup of patients with AR LBD mutations, but the early efficacy data look encouraging, with a PSA50 of 43% and unconfirmed ORR of 30%. The safety profile of ARV-766 looks to be clinically manageable, with very low levels of grade 3 treatment-related adverse effects (TRAEs). This is promising, as 58% of patients had received prior taxanes, which are associated with high toxicity and low tolerability in the later lines of treatment.

Bristol Myers Squibb is also developing the first-in-class AR degrader, CC-94676, for mCRPC patients who have progressed on at least one ARPI in a Phase I trial. In a cautious comparison we note that the activity seen in AR LBD mutant patients with CC-94676 (PSA50 40%) is comparable to ARV-766's PSA50. There is the potential for differentiation in terms of safety, as there were higher rates of grade 3 TREAs following CC-94676 treatment, including 9% of patients experiencing grade 3 QTc prolongation, which resulted in dose modifications and dose interruptions.

Based on ARV-766's compelling clinical profile to date, Arvinas have announced that they will prioritize bringing ARV-766 forward in pivotal development over their first-generation PROTAC AR degrader bavdegalutamide. ARV-766 also represents a greater market opportunity relative to that of bavdegalutamide, which only targets H875Y and T878A LBD mutations. ARV-766 is currently in the process of being out-licensed to Novartis, and with a pivotal Phase III trial pending regulatory discussions with the FDA in Q2 of 2024, exciting late-phase data for the novel drug class could be on the horizon. In the meantime, we are increasing the LOA by 2%.

Source:

Globe Newswire 05/23/2024 (ARVN)
American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 5011)

Verzenio for Prostate Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase II/III - CYCLONE 2
Market Group:	Oncology
Lead Company:	Eli Lilly and Company (LLY)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	11% (Same As Avg.)
Average Approval:	11%

An abstract entitled "CYCLONE 2: A phase 3 study of abemaciclib with abiraterone in patients with metastatic castration-resistant prostate cancer" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data from this study were last seen in May 2024.

Data in this event has been created solely from the abstract program.

Background

Oncogenic addiction to androgen receptor (AR) signaling drives mCRPC progression, highlighting the unmet need for novel treatment strategies to maximize AR-directed therapy. Preclinical evidence suggests a key role for CDK4/6 in sustained AR signaling, uncontrolled proliferation, and hormonal resistance in prostate cancer. Abemaciclib (ABEMA) is a potent CDK4/6 oral inhibitor that significantly augments the efficacy of endocrine therapy in hormonally driven (ER+) high-risk early-stage and metastatic breast cancer. ABEMA also showed single-agent activity in heavily pretreated mCRPC. Here, we report the primary results of CYCLONE 2, a Phase III study of ABEMA plus abiraterone (ABI) in pts with 1L mCRPC.

Methods

CYCLONE 2 was a seamless Phase II/III adaptive trial with a dose-finding safety lead-in. Randomization to the ABEMA or placebo (PBO) plus ABI and predniso(lo)ne was stratified by prior docetaxel receipt for mHSPC, measurable disease, and radiographic progression at study entry.

Endpoints

Primary endpoint was investigator-assessed radiographic progression-free survival (rPFS) per RECIST v1.1 and PCWG3. The study was powered at ~90%, assuming a HR of 0.55 for rPFS, at a cumulative 2-sided alpha level of 0.05.

Results

Between Nov 2018 and Jul 2022, 393 pts were randomized. Baseline characteristics were balanced across arms. Primary endpoint of rPFS was not met (HR 0.829; 95% CI, 0.619–1.111; p=0.2123), medians were 21.96 months for the ABEMA plus ABI group vs 20.28 months for the PBO plus ABI group. rPFS by blinded independent central review was consistent with investigator assessment (HR 0.842; 95% CI, 0.611–1.160). OS was a gated secondary endpoint and not inferentially tested (HR 0.927; 95% CI, 0.669–1.285; 38.9% maturity). Other secondary endpoints included time to PSA progression (HR 0.637; 95% CI, 0.474–0.856), time to symptomatic progression (HR 0.768; 95% CI, 0.522–1.131), and time to worst pain progression (HR 0.935; 95% CI 0.665–1.314).

Most Common Adverse Events

The most common grade ≥3 adverse events (AEs) reported in the ABEMA plus ABI group were anemia (13.6% vs 4.3% in the PBO plus ABI group), neutropenia (12.6% vs 0.5%) and ALT increased (8.7% vs 6.5%). Discontinuations of all study treatments due to AEs were 13.1% vs 4.3% in ABEMA plus ABI vs PBO plus ABI groups, while discontinuations of ABEMA or PBO alone due to AEs were 5.8% vs 1.6%, respectively.

Conclusions

In patients with mCRPC, adding abemaciclib to abiraterone did not significantly increase rPFS. While no OS detriment was observed, secondary endpoints were not meaningfully improved. Overall, the combination was well tolerated, and safety was consistent with the known profiles of the individual medicines.

Comments

Eli Lilly's Verzenio (abemaciclib) is a highly potent inhibitor of cyclin-dependent kinases 4 and 6 (CDK4/6) and is indicated in HR+/HER2- metastatic and high-risk early-stage breast cancer. It has also shown efficacy in the heavily pre-treated metastatic castration-resistant prostate cancer (mCRPC) space following results from the Phase II CYCLONE-1 trial.

Despite recent advances, management of heavily pretreated mCRPC remains a major clinical challenge with high rates of progression and mortality. The key drivers of disease progression are due to persistent reactivation of androgen receptor signalling pathways (AR) and resulting downstream activation of CDK4/6. Evidence for this mechanism underpins the design and initiation of the Phase III CYCLONE-2 trial, which assesses the efficacy of Verzenio in combination with abiraterone, an AR inhibitor, as a first-line treatment for patients with mCRPC. The utility of an AR in combination with a CDK4/6 inhibitor is unclear in prostate cancer, with few early-phase trials investigating the combination.

Unfortunately, as shown at ASCO 2024, the results for the combination were negative. Investigator assessment detailed that rPFS was not significantly improved by Verzenio in combination with abiraterone (22.0 months versus 20.3 months in the placebo and abiraterone group) and this was consistent with blinded independent central review. Objective response rate was greater in the placebo group (55% versus 45%) and PSA50 response rates were very similar in the Verzenio and placebo group (70.4% and 70.6%, respectively). Regarding subgroup analysis, patients at higher risk of progression and also those with radiographic disease, benefited most from the Verzenio and abiraterone combination, which could have allowed Verzenio to enter a population with high unmet need had it been more efficacious in the entire patient population.

The futility of the CYCLONE-2 results and the discontinuation of the Phase III CYCLONE-3 trial, which was investigating Verzenio in metastatic hormone-sensitive prostate cancer, concludes the development of Verzenio in the prostate cancer space. It remains to be seen if other CDK4/6 inhibitors such as Ibrance or Kisqali, manage to reach late-phase trials or if this drug class is obsolete in the prostate cancer space.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract 5001)
Citeline Analysis

Jevtana for Prostate Cancer

Event Date:	06/01/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - CHAARTED2
Market Group:	Oncology
Lead Company:	Sanofi (SNY)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Abiraterone/Prednisone	Cabazitaxel + Abiraterone/Prednisone	Cabazitaxel + Abiraterone/Prednisone vs. Abiraterone/Prednisone
Number of Patients	112	111	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Progression Free Survival *(Endpoint=Primary)*	9.9 Months	14.9 Months	N/A (P=0.049)
Median Time to PSA Progression *(Endpoint=Secondary)*	6.1 Months	10 Months	N/A (P=0.002)
Overall Survival *(Endpoint=Secondary)*	26.9 Months	25.0 Months	N/A (P=0.67)

The abstract entitled "Cabazitaxel with abiraterone versus abiraterone alone randomized trial for extensive disease following docetaxel: The CHAARTED2 trial of the ECOG-ACRIN Cancer Research Group (EA8153)" was presented at the American Society of Clinical Oncology Annual Meeting on June 1, 2024.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website. Citeline was unable to obtain updated data, if any, from the actual presentation at the ASCO conference.

Design

EA8153 (CHAARTED2) is a prospective randomized Phase II open label trial. Two hundred twenty-three (223) pts with metastatic CRPC previously treated with ADT + docetaxel for HSPC were randomized (1:1) to abiraterone/prednisone plus cabazitaxel 25 mg/m^2 for up to 6 cycles (n=111) or abiraterone/prednisone alone (n=112). Stratification factors included ECOG performance status (PS) of 0 vs. 1-2, time from initiation of ADT to development of CRPC of <12 vs. > 12 months, and presence vs. absence of visceral metastases.

Endpoints

The primary trial endpoint is progression-free survival (PFS), defined as time from randomization to radiographic progression, symptomatic

deterioration requiring discontinuation of treatment, or death. Key secondary endpoints include time to PSA progression (TTPP), overall survival (OS), and safety.

Results

After a median follow-up of 47.3 (0-61.2) months, median PFS was longer for the cabazitaxel + abiraterone/prednisone arm vs. abiraterone/prednisone alone arm (14.9 months [95% CI 9.9-18.6] vs. 9.9 months [95% CI, 7.0-12.6], p=0.049; hazard ratio [HR] 0.73, 80% CI 0.59-0.90). The advantage with the combination was more pronounced in patients < 65 years of age (15.6 vs. 9.8 months, p=0.08), ECOG PS of 0 (20.9 vs. 10.1 months, p=0.01), time to CRPC of < 12 months (12.9 vs. 5.1 months, p=0.006), and absence of visceral metastases (18.1 vs. 10.1 months, p=0.01). Median TTPP was also longer in the combination vs. the monotherapy arm (10 months [95% CI 8.5-13.5] vs. 6.1 months [95% CI 4.4-8], p=0.002). No difference in OS was observed between the 2 arms in the interim analysis (25.0 vs. 26.9 months, p=0.67).

Most Common Adverse Events

More grade >3 side effects were noted in the combination arm, as expected from use of cabazitaxel.

Conclusion

The addition of cabazitaxel to abiraterone/prednisone prolonged PFS in patients with metastatic CRPC who previously received ADT + docetaxel for HSPC compared to abiraterone/prednisone alone. No significant OS difference was noted between the two arms, but the study was not powered for this endpoint.

Comments

Androgen deprivation therapy (ADT) remains the cornerstone of treatment for metastatic prostate cancer and while the response to ADT is effective and almost universal, the durability of response in metastatic hormone-sensitive prostate cancer (mHSPC) is variable due to castration-resistance pathways eventually occurring. Once castration resistance emerges and there is progression to metastatic castration-resistant prostate cancer (mCRPC), fewer therapeutic options exist.

In the Phase II CHAARTED trial, the addition of docetaxel to ADT significantly increased the OS in mHSPC patients, from 34.4 months in the ADT monotherapy group to to 57.6 months. Following this trial, ADT in combination with docetaxel became the new standard of care for newly diagnosed mHSPC patients, however, the optimal treatment pathway for these patients following progression to mCRPC remained unclear. CHAARTED laid the groundwork for the Phase II CHAARTED2 trial, which aims to assess if the combination of abiraterone, a second-generation AR inhibitor, and Jevtana (cabazitaxel), a second-generation chemotherapy, could improve patient outcomes and prolong response to abiraterone in mCRPC patients who were on ADT had previously received docetaxel for mHSPC.

Sanofi's microtubule inhibitor, Jevtana (cabazitaxel) is already a well-established drug in its respective niche in mCRPC. It was approved based off the success of the Phase III TROPIC trial, which investigated Jevtana in patients who had progressed on docetaxel and demonstrated a clinically meaningful in the improvement of median OS of 15.1 months versus 12.7 months in the control arm.

It was thus expected that the results of the CHAARTED2, which were presented at ASCO 2024, would show encouraging results in the same setting to that of the TROPIC trial. The final analysis shows that the combination of Jevtana and abiraterone significantly improved mPFS by 5 months compared abiraterone alone (14.9 months versus 9.9 months). High-risk patients who had a shorter time from onset of ADT to progression to mCRPC had a notably strong PFS improvement of 7.8 months. While no significant difference was shown for OS, it was noted that the study was underpowered for that endpoint.

Treatment related adverse effects were clinically manageable with the Jevtana and abiraterone combination, with hypertension, fatigue and white cell count decrease being the most common Grade 3 adverse events. These were higher than those in the abiraterone alone group, but remained in line with expectations due to the addition of chemotherapy.

These results are significant, as abiraterone dominates the mCRPC treatment algorithm, and evidence for stronger efficacy in combination with Jevtana could provide an opportunity for Jevtana to increase its uptake in this space. However, for any significant changes in Jevtana uptake to occur, further late-phase trials would be necessary to assess the combination in patients who had no prior docetaxel treatment, as this is the setting in which abiraterone is predominantly used. Furthermore, in recent years there has been a shift away from the use of docetaxel and ADT alone for mHSPC due to the introduction of additional doublet and triplet therapies, including; ADT in combination with Erleada, Xtandi and Nubeqa (with docetaxel). This shift in treatment options limits the applicability of the CHAARTED2 results in general practice. Therefore, although effective in this setting, commercial prospects are restricted and it will be interesting to see if Jevtana has any ongoing development.

Source:

American Society of Clinical Oncology (ASCO) 06/01/2024 (Abstract LBA5000)
Citeline Analysis

Bavencio for Renal Cell Cancer (RCC)

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - JAVELIN Renal 101
Market Group:	Oncology
Lead Company:	Merck KGaA (MKKGY)
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

An abstract entitled "Avelumab + axitinib vs sunitinib in patients (pts) with advanced renal cell carcinoma (aRCC): Final overall survival (OS) analysis from the JAVELIN Renal 101 phase 3 trial" was presented at the American Society of Clinical Oncology Annual Meeting on June 3, 2024.

Data from the study were last seen in May 2021.

Data summarized in this event is solely based on data contained in the abstract from the ASCO abstract website.

Design
The JAVELIN Renal 101 Phase III trial compared first-line treatment with avelumab + axitinib vs sunitinib in aRCC. The trial previously met one of its primary objectives by showing significantly longer progression-free survival (PFS) with avelumab + axitinib vs sunitinib in pts with PD-L1+ tumors; longer PFS, higher objective response rate (ORR), and an acceptable safety profile were also observed in the overall population. OS data were immature. Here we report the final analysis.

Endpoints
Pts with untreated aRCC (any IMDC risk score) were randomized 1:1 to avelumab + axitinib or sunitinib. OS and PFS (by blinded independent central review) in pts with PD-L1+ tumors (SP263 assay) were independent primary endpoints. OS and PFS in the overall population were key secondary endpoints; response and safety were also analyzed.

Results
Of 886 pts randomized, 560 (63.2%) had PD-L1+ tumors. At data cutoff (August 31, 2023), median follow-up in the avelumab + axitinib and sunitinib arms was 73.7 and 73.6 months, respectively (≥68 months in all pts). Final efficacy data are shown in the Table. In the avelumab + axitinib and sunitinib arms, grade ≥3 TRAEs occurred in 66.8% vs 61.5%, respectively. Second-line therapy was received by 58.1% vs 69.4%, including a PD-(L)1 inhibitor in 18.8% vs 53.6%, respectively.

Conclusions
The JAVELIN Renal 101 trial provides the longest follow-up for immune checkpoint inhibitor + tyrosine kinase inhibitor combination treatment from a Phase III trial reported to date. OS analyses favored avelumab + axitinib vs sunitinib but did not reach statistical significance. PFS was longer with avelumab + axitinib vs sunitinib, and responses were durable in a subset of pts. Final analysis results confirm the long-term efficacy and manageable safety profile of avelumab + axitinib treatment in pts with aRCC.

Comments

The first-line renal cell carcinoma (RCC) treatment market is highly competitive, with immune-oncology (IO)/IO and IO/tyrosine kinase inhibitor (TKI) combinations dominating the space. IO/TKI combinations have become the first-line standard of care, but many of these

combinations have similar efficacy profiles.

The pivotal JAVELIN Renal 101 Phase III trial formed the basis for the US and European approval of immune-checkpoint inhibitor Bavencio (avelumab), in combination with TKI Inlyta (axitinib) for first-line RCC in in May and October 2019, respectively. The trial demonstrated a statistically significant improvement in PFS versus Sutent (13.8 months versus 8.5 months) , and the final OS data have now bee made public at ASCO 2024.

This was the longest follow-up for an immune checkpoint inhibitor and tyrosine kinase inhibitor combination treatment from a Phase III trial to date, and in a surprising turn of events, the mOS favored the Bavencio and Inlyta arm but did not reach statistical significance in either the PD-L1+ population (43.2 months versus 36.2 months; p=0.076) or overall population (44.8 months versus 38.9 months; p=0.067). Interestingly, there was a greater separation of the Kaplan Meier curves in the poor risk group than in the intermediate risk group.

Treatment-related adverse effects (TRAEs) were predictable and comparable to other IO/TKI combinations. The tolerability profile of Bavencio and Inlyta continues to be positive, with only 5% of patients discontinuing both drugs due to TRAEs. With treatment-related concerns and improving patient adherence becoming increasingly important in physician decision-making, this strong tolerability profile continues to be key for the Bavencio/Inlyta combination.

The disappointing OS data won't cause the combination to lose its FDA approval, however, as the trial is still considered positive through meeting one of its primary objectives—an significant improvement in PFS. And while statistically insignificant, the OS data is strong compared to that of other IO/TKI combinations, including that of Opdivo/Cabometyx, which showed OS of 35.1 months (versus 30.7 months in the Sutent arm) in updated Phase III CheckMate 9ER trial, also presented at ASCO 2024. However, it does leave room for the Keytruda and Lenvima combination to increase its influence in the treatment space following the hugely successful results from the Phase III CLEAR study.

Source:

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 4508)

Tecentriq for Small Cell Lung Cancer (SCLC)

Event Date:	06/03/2024
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - BEAT-SC (China & Japan)
Market Group:	Oncology
Lead Company:	Roche Holding AG (RHHBY)
Partner Companies:	Bristol Myers Squibb (BMY) Chugai Pharmaceutical (4519) Ono Pharmaceutical (4528:JP)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Atezolizumab + Cisplatin or Carboplatin + Etoposide (ACE) + Placebo	Atezolizumab + Cisplatin or Carboplatin + Etoposide (ACE) + Bevacizumab	ACE + Bevacizumab vs. ACE + Placebo
Number of Patients	N/A	N/A	333
Number of Evaluable Patients	N/A	N/A	333
Median Investigator-Assessed Progression-Free Survival (INV-PFS) ***(Endpoint=Primary)***	4.4 Months	5.7 Months	N/A (P=0.0060)
Median Overall Survival (OS) ***(Endpoint=Secondary)***	16.6 Months	13.0 Months	N/A (P=0.2212)

An abstract entitled "BEAT-SC: A randomized phase III study of bevacizumab or placebo in combination with atezolizumab and platinum-based chemotherapy in patients with extensive-stage small cell lung cancer (ES-SCLC)" was presented at the 2024 Annual Meeting of the American Society of Clinical Oncology on June 3, 2024.

Data from this trial were last seen in October 2023.

Data summarized in this event are solely based on data contained in the abstract from the ASCO abstract website.

Context

Atezolizumab combined with carboplatin and etoposide is approved as first-line treatment for patients with ES-SCLC, based on results from the Phase I/III IMpower133 trial.

Design

BEAT-SC is evaluating the efficacy and safety of bev combined with atezolizumab and platinum-based chemotherapy in patients with

ES-SCLC from Japan and China. Eligible patients had measurable ES-SCLC, were aged ≥20 y (≥18 y for patients from China), had an ECOG performance status of 0 or 1 and had no prior systemic treatment for ES-SCLC. Patients were randomized 1:1 to receive 4 cycles (21 days/cycle) of induction therapy with bev combined with atezolizumab + cisplatin or carboplatin + etoposide (ACE) or placebo combined with ACE, followed by maintenance therapy with bev + atezolizumab or placebo + atezolizumab, respectively.

Endpoints

The primary endpoint was investigator-assessed PFS (INV-PFS). Key secondary endpoints included OS and safety.

Results

The ITT population comprised 333 patients with a median age of 65.0 y; 82.6% of the patients were male, 57.7% were from China, 91.8% received carboplatin and 87.6% were current or former smokers. At data cutoff (June 30, 2023; median follow-up, 10.2 mo), median INV-PFS was 5.7 mo for bev + ACE vs 4.4 mo for placebo + ACE (HR, 0.70; 95% CI: 0.54, 0.90; *P*=0.0060; 2-sided α boundary=0.05). Median OS was 13.0 mo for bev + ACE vs 16.6 mo for placebo + ACE (HR, 1.22; 95% CI: 0.89, 1.67; *P*=0.2212; 2-sided α boundary=0.0079).

Most Common Adverse Events

Among the safety analysis population (n=330), bev + ACE was well tolerated and treatment-related adverse events (TRAEs) were generally similar between treatment arms.

Conclusion

BEAT-SC met its primary endpoint, demonstrating that the addition of bev to ACE significantly increased PFS vs placebo + ACE. OS data were immature at the first interim OS analysis, and the numerical OS improvement of bev + ACE was not shown vs placebo + ACE; OS follow-up will continue. No new safety signals were observed.

Comment

Although the PFS results from the BEAT-SC trial are promising for its potential application in extensive-stage small cell lung cancer (ES-SCLC), they are not significant enough to change the current treatment paradigm. For patients with ES-SCLC, the NCCN currently recommends a combination of platinum and etoposide with either Tecentriq or Imfinzi for first-line therapy, based on the median PFS (mPFS) and OS results from the IMpower133 and CASPIAN trials, respectively. The mPFS values reported in IMpower133 and CASPIAN were 5.2 months and 5.1 months, respectively, while the median OS values were 12.3 months and 13 months, respectively. The mPFS reported in the BEAT-SC trial is 5.7 months, which is comparable to these results, indicating that the addition of Avastin to chemotherapy and Tecentriq did not result in significant benefit. Payers may also be reluctant to accept the additional cost of bevacizumab (even if cheaper biosimilars are now available) for only a small efficacy benefit.

Source:

American Society of Clinical Oncology (ASCO) 06/03/2024 (Abstract 8001)
Citeline Analysis

Sacituzumab Tirumotecan for Triple-Negative Breast Cancer (TNBC)

Event Date:	06/02/2024
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - Recurrent/Metastatic (China)
Market Group:	Oncology
Lead Company:	Sichuan Kelun Pharmaceutical Co Ltd. (002422)
Partner Companies:	N/A
Former Companies:	KLUS
Change to Likelihood of Approval:	0%
Likelihood of Approval:	44% (33% Above Avg.)
Average Approval:	11%

	Comparator	Treatment	Difference Between Treatment and Comparator
Treatment Description	Chemotherapy	sac-TMT	sac-TMT vs Chemotherapy
Number of Patients	133	130	N/A
Number of Evaluable Patients	N/A	N/A	N/A
Median Progression-Free Survival Assessed by BICR ***(Endpoint=Primary)***	2.3 Months	5.7 Months	N/A
Progression-Free Survival Rate at 6 Months ***(Endpoint=Primary)***	11.1 %	43.4 %	N/A
Median Progression-Free Survival in Patients with Trophoblast Cell-Surface Antigen 2 (TROP2) H-score > 200 ***(Endpoint=Primary)***	1.9 Months	5.8 Months	N/A
Progression-Free Survival - Hazard Ratio ***(Endpoint=N/A)***	N/A	N/A	0.31 (P<0.00001)
Median Overall Survival ***(Endpoint=Secondary)***	9.4 Months	N/A	N/A
Overall Survival - Hazard Ratio ***(Endpoint=N/A)***	N/A	N/A	0.53 (P=0.0005)
Objective Response Rate (ORR) Assessed by BICR ***(Endpoint=Secondary)***	12.8 %	43.8 %	N/A

Kelun-Biotech announced data from the Phase III OptiTROP-Breast01 study of sacituzumab tirumotecan for triple-negative breast cancer (TNBC). The abstract entitled "The Phase 3 OptiTROP-Breast01 study of its anti-TROP2 ADC sacituzumab tirumotecan (sac-TMT) (formerly SKB264/MK-2870) in patients with previously treated locally recurrent or metastatic triple-negative breast cancer (TNBC)" was presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting on June 2, 2024.

Context

A Phase III global study led by MSD of sac-TMT plus pembrolizumab versus treatment of physician's choice (TPC) in TNBC who received neoadjuvant therapy and did not achieve a pathological complete response (pCR) at surgery and a Phase III study led by the company of sac-TMT in China for 1L treatment of unresectable locally advanced, recurrent or metastatic PD-L1-negative TNBC are also ongoing.

Design

Per the abstract, in this randomized Phase III trial, SKB264 was compared with physician's choice of chemotherapy (eribulin, vinorelbine, capecitabine, or gemcitabine) in pts with locally recurrent or metastatic TNBC who had received two or more prior therapies including at least one for the metastatic setting.

Endpoints

Per the abstract, the primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR). The TROP2 expression was determined by immunohistochemistry (IHC) using the semi-quantitative H-score method.

Results

Patients were randomly assigned (1:1) to receive sac-TMT (n=130) or chemotherapy (n=133). The median age was 51 years; 87% had visceral metastases; 26% received prior PD-1/PD-L1 inhibitors; 48% received three or more prior lines of chemotherapy for advanced disease. The primary endpoint of PFS was met based on interim analysis (data cut-off: Jun 21, 2023) with a 69% reduction in risk of progression or death (HR 0.31; 95% CI, 0.22 to 0.45; p<0.00001).

The median PFS, as assessed by BICR, was 5.7 months (95% CI, 4.3 to 7.2) with sac-TMT and 2.3 months (95% CI, 1.6 to 2.7) with chemotherapy; PFS rate at 6 months was 43.4% vs 11.1%. In the subset of patients with trophoblast cell-surface antigen 2 (TROP2) H-score > 200, the median PFS was 5.8 months with sac-TMT and 1.9 months with chemotherapy (HR 0.28; 95% CI, 0.17 to 0.48). At the first planned interim analysis for overall survival (OS) (data cut-off: Nov 30, 2023) with median follow-up of 10.4 months, OS was statistically significant in favor of sac-TMT (HR 0.53; 95% CI, 0.36 to 0.78; p=0.0005); the median OS was not reached (95% CI, 11.2 to NE) with sac-TMT and 9.4 months (95% CI, 8.5 to 11.7) with chemotherapy. The objective response rate (ORR) assessed by BICR was 43.8% with sac-TMT and 12.8% with chemotherapy.

Most Common Adverse Events

Most common grade ≥ 3 treatment-related adverse events (TRAEs) (sac-TMT vs. chemotherapy) were neutrophil count decreased (32.3% vs. 47.0%), anemia (27.7% vs. 6.1%) and white blood cell count (WBC) decreased (25.4% vs. 36.4%).

Conclusion

Per the abstract, sacituzumab tirumotecan monotherapy demonstrated statistically significant and clinically significant PFS and OS benefit over chemotherapy, with a manageable safety profile in pts with heavily pretreated advanced TNBC and limited treatment options.

Comment

The third-generation antibody-drug conjugate (ADC) sacituzumab tirumotecan is a TROP2-targeted ADC conjugated to a topoisomerase I inhibitor developed by Sichuan Kelun Pharmaceutical. The readout from the OptiTROP-Breast01 study that will be presented at ASCO 2024 provides encouraging late-phase data on sacituzumab tirumotecan as a monotherapy for TNBC patients who have progressed on at least two lines of treatment. These results shed light on a possible exciting new therapeutic option for the notoriously aggressive TNBC subtype, which is also associated with the highest rates of adverse outcomes, recurrence, and metastasis of all breast cancer subtypes.

Trodelvy is currently the only approved TROP2-targeted therapy recommended for heavily pretreated TNBC patients. It is favored by physicians due to established efficacy and brings high competition to the development of sacituzumab tirumotecan. Sacituzumab tirumotecan demonstrated a strong efficacy profile in OptiTROP-Breast01, with a relative 3.4-month median PFS (mPFS) improvement (5.7 vs. 2.3 months) over investigator’s choice of chemotherapy. Further impressive efficacy was seen in the patient subgroup with higher TROP2 levels, with the relative mPFS improvement increased by 3.9 months (5.8 months vs. 1.9 months). The median OS values were not yet reached at this interim analysis, which bodes well for the ADC’s efficacy. These results are modestly superior to Trodelvy’s Phase III ASCENT trial results, which reported an mPFS of 4.8 months (vs. 1.7 months for the comparator arm) in third-line and beyond patients with no brain metastases. In terms of safety and tolerability, sacituzumab tirumotecan demonstrated a manageable safety profile, with

mostly hematologic adverse effects, comparable to those seen for Trodelvy in the ASCENT study.

In addition to Trodelvy, sacituzumab tirumotecan will also be feeling increasing competitive pressure from another ADC in the pipeline, namely datopotamab deruxtecan, which has demonstrated positive PFS results in the Phase III TROPION-Breast01 trial, with a relative 2.0-month median improvement over the chemotherapy arm (6.9 months vs. 4.9 months). The TROPION-Breast02 trial has also been initiated for patients who are not eligible for PD-L1 treatment, who made up 26% of the patient population in the OptiTROP-BReast01 trial.

The data from OptiTROP-Breast01 come from an all-Chinese patient population, so it is likely that the results will need to be replicated in a Western patient population to stand a chance at regulatory success and approval. However, given that its target patients were heavily pretreated (48% having had ≥3 prior lines) and the high unmet need characterizing this segment, the results look very promising for sacituzumab tirumotecan.

Source:

Press Release 05/24/2024 (Kelun-Biotech)
Press Release 05/24/2024 (KLUS Pharma)
American Society of Clinical Oncology (ASCO) 06/02/2024 (Abstract 104)
Citeline Analysis

BIOMEDTRACKER
CITELINE COMMERCIAL

List of Biomedtracker ASCO Abstract Events

Event Date	Drug	Lead Company	Ticker	Event Type	Trial Name	Link
Acute Lymphoblastic Leukemia (ALL)						
06/03/2024	Blincyto	Amgen, Inc.	AMGN	Trial Data - Top-Line Results	Phase IV - Feasibility Study	518502
06/03/2024	Iclusig	Takeda Pharmaceutical Co. Ltd.	TAK	Trial Data - Updated Results	Phase III - Phallcon (vs. Imatinib, Ph+ ALL)	518552
06/03/2024	PMB-CT01	PeproMene Bio, Inc.		Trial Data - Updated Results	Phase I - r/r B-ALL	518880
06/03/2024	Rylaze	Jazz Pharmaceuticals plc	JAZZ	Trial Data - Retrospective Analysis	Phase II/III - PK Study	518907
06/03/2024	Tecartus	Gilead Sciences, Inc.	GILD	Trial Data - Updated Results	Phase I/II - ZUMA-3 (r/r Adults)	518909
05/31/2024	Obe-cel	Autolus Therapeutics plc	AUTL	Trial Data - Updated Results	Phase Ib/II - FELIX	517925
05/31/2024	CN-201	Curon Biopharmaceutical Limited		Trial Data - Top-Line Results	Phase Ib/II - (China)	519036
Acute Myelogenous Leukemia (AML)						
06/03/2024	Rezlidhia	Rigel Pharmaceuticals, Inc.	RIGL	Trial Data - Subgroup Analysis	Phase I/II - 2102-HEM-101	519841
06/03/2024	Lisaftoclax	Ascentage Pharma Group Corporation	6855	Trial Data - Updated Results	Phase Ib - China	517792
06/03/2024	Onureg	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - QUAZAR (Maintenance)	518524
06/03/2024	Venclexta	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase Ib/II - w/FLAG-IDA (MD Anderson)	518593
06/01/2024	Prexigebersen	Bio-Path Holdings, Inc.	BPTH	Trial Data - Updated Results	Phase II - BP1001-201 (w/Decitabine)	518583
Adenoid Cystic Carcinoma (ACC)						
05/31/2024	RGT-61159	Rgenta Therapeutics		Trial Data - Preclinical Results	Preclinical Studies	519525
Biliary Tract Cancer						
06/01/2024	Zanidatamab	Jazz Pharmaceuticals plc	JAZZ	Trial Data - Updated Results	Phase IIb - HERIZON-BTC-01	518749
06/01/2024	Ivonescimab	Summit Therapeutics plc	SMMT	Trial Data - Top-Line Results	Phase Ib/II - w/(AK117) (China)	519556
06/01/2024	CPI-613	Cornerstone Pharmaceuticals, Inc.		Trial Data - Updated Results	Phase Ib/II - BilT-04	518575
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - MK-3475-966/KEYNOTE-966	518630
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - MK-3475-966/KEYNOTE-966	519533
Bladder Cancer						
06/04/2024	LP-50	Lipella Pharmaceuticals Inc.	LIPO	Trial Data - Preclinical Results	Preclinical Studies	520064
06/03/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase I - Urothelial/Solid Tumors	518603
06/03/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase III - KEYNOTE-A39 (EV-302)	518604
06/03/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - KEYNOTE-A39 (EV-302)	519962

06/03/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate 901 (w/Ipilimumab)	518520
06/02/2024	CG0070	CG Oncology, Inc.	CGON	Trial Data - Final Results	Phase II - CORE1 (w/Keytruda)	517928
06/02/2024	Cabometyx / Cometriq	Exelixis, Inc.	EXEL	Trial Data - Top-Line Results	Phase I - w/ enfortumab vedotin	518510
06/02/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Retrospective Analysis	Phase II - KEYNOTE-057 (High Risk, Non-muscle)	518632
06/02/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Top-Line Results	Phase Ia- ASPEN-07	519653
06/02/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase III - KEYNOTE-A39 (EV-302)	518599
06/02/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase III - KEYNOTE-A39 (EV-302)	518600
06/02/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase Ib/II - KEYNOTE-869 (EV-103)	518601
06/02/2024	Balversa	Johnson & Johnson	JNJ	Trial Data - Subgroup Analysis	Phase III - THOR (2L)	518672
06/02/2024	Bavencio	Merck KGaA	MKKGY	Trial Data - Retrospective Analysis	Phase III - JAVELIN Bladder 100	517730
06/02/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase II - DESTINY-PanTumor02	520222
06/02/2024	ALX-148	ALX Oncology, Inc.	ALXO	Trial Data - Top-Line Results	Phase Ia - ASPEN-07	518783
06/02/2024	Tookad	ImPact Biotech Ltd.		Trial Data - Updated Results	Phase III - ENLIGHTED	519662
06/02/2024	Disitamab Vedotin	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase II - Perioperative w/ Toripalimab (China)	518868
06/01/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Updated Results	Phase II - TROPHY U-01	518645
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - KEYNOTE-361	518629
Brain Cancer (Malignant Glioma; AA and glioblastoma (GBM))						
06/04/2024	HF-1K16	HighField Biopharmaceuticals		Trial Data - Top-Line Results	Phase Ib/II - China	520071
06/03/2024	Zejula	GSK plc	GSK	Trial Data - Updated Results	Phase 0/II - Dose Expansion	518560
06/03/2024	Stivarga	Bayer AG	BAYN	Trial Data - Top-Line Results	Phase II/III - GBM AGILE (GCAR)	518564
06/03/2024	HyLeukin	NeoImmuneTech, Inc.	950220	Trial Data - Preclinical Results	Preclinical Studies	519835
06/03/2024	APL-101	Apollomics, Inc.	APLM	Trial Data - Top-Line Results	Phase II/III - FUGEN	518774
06/02/2024	BI 907828	Boehringer Ingelheim GmbH		Trial Data - Top-Line Results	Phase Ia - Glioblastoma	518977
06/02/2024	MN-166	MediciNova, Inc.	MNOV	Trial Data - Updated Results	Phase I/II - w/Temozolomide	518525
06/02/2024	Ojemda	Day One Biopharmaceuticals, LLC	DAWN	Trial Data - Updated Results	Phase I - PNOC014	518618
06/01/2024	Ojemda	Day One Biopharmaceuticals, LLC	DAWN	Trial Data - Updated Results	Phase II - FIREFLY-1	518617
06/01/2024	MDNA55	Medicenna Therapeutics Corp.	MDNA	Trial Data - Updated Results	Phase IIb - MDNA55-05 (rGBM)	518498
06/01/2024	Optune	NovoCure Limited	NVCR	Trial Data - Updated Results	TIGER (Germany)	518721
06/01/2024	BDTX-1535	Black Diamond Therapeutics, Inc.	BDTX	Trial Data - Top-Line Results	Phase I - 101	518951

06/01/2024	BDTX-1535	Black Diamond Therapeutics, Inc.	BDTX	Trial Data - Updated Results	Phase I - HGG	518952
06/01/2024	MK-0482	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase I - +/-Pembrolizumab	519549
06/01/2024	ST101 (Sapience)	Sapience Therapeutics, Inc.		Trial Data - Updated Results	Phase I/II - ST101-101	518913
06/01/2024	INB-200	IN8bio, Inc.	INAB	Trial Data - Updated Results	Phase I - Newly Diagnosed GBM (University of Alabama at Birmingham)	518943
06/01/2024	HyLeukin	NeoImmuneTech, Inc.	950220	Trial Data - Preclinical Results	Preclinical Studies	519773
06/01/2024	SONALA-001	SonALAsense, Inc		Trial Data - Updated Results	Phase I/II - SDT-201 (DIPG)	519015
Brain Cancer (Secondary; Metastases)						
06/03/2024	Optune	NovoCure Limited	NVCR	Trial Data - Updated Results	IDE - METIS (US)	518722
Breast Cancer						
06/03/2024	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Top-Line Results	Phase II - I-SPY2.2	519905
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase II - I-SPY2.2	519897
06/02/2024	Giredestrant	Roche Holding AG	RHHBY	Trial Data - Top-Line Results	Phase I/II - MORPHEUS- BREAST CANCER	518822
06/02/2024	Balversa	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase II - RAGNAR	519643
06/02/2024	Irinotecan Liposome (CSPC)	CSPC Pharmaceutical Group Limited	1093	Trial Data - Top-Line Results	Phase I - HE072-CSP-002 (China)	519071
05/31/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase II - I-SPY2.2	519523
Breast Cancer - Imaging						
06/02/2024	ABY-025	Affibody AB		Trial Data - Updated Results	Phase II/III - Affibody-3	518732
Cancer						
06/03/2024	FS222	invoX Pharma		Trial Data - Updated Results	Phase I - PK/PD	518876
06/01/2024	DK210	Deka Biosciences, Inc.		Trial Data - Top-Line Results	Phase I - First-in-Human	519043
06/01/2024	LM-101	LaNova Medicines		Trial Data - Top-Line Results	Phase I/II - Dose-Escalation & Expansion	519041
06/01/2024	Mekinist	Novartis AG	NVS	Trial Data - Updated Results	Phase II - EAY131-H	518579
Cervical Cancer						
06/03/2024	ISA101	ISA Pharmaceuticals B.V.		Trial Data - Top-Line Results	Phase II - w/Cemiplimab	518587
06/03/2024	SG001	CSPC Pharmaceutical Group Limited	1093	Trial Data - Top-Line Results	Phase II - PD-L1 Positive (China)	519046
06/03/2024	9MW2821	Mabwell Biotechnology	688062	Trial Data - Updated Results		519934
06/03/2024	PM-8002	BioNTech SE	BNTX	Trial Data - Top-Line Results	Phase Ib/IIa - PK/PD Study	519833
06/03/2024	Disitamab Vedotin	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase II - RC48-C018 (China)	518869
06/03/2024	Tivdak	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - innovaTV 301	518650
06/01/2024	ATG-008	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase I/II - TORCH-2	518218
06/01/2024	Loqtorzi	Coherus BioSciences, Inc.	CHRS	Trial Data - Updated Results	Phase I/II - TORCH-2 (China)	519768

Chemotherapy Induced Nausea and Vomiting (CINV)					
06/03/2024	Akynzeo	Helsinn Healthcare SA		Trial Data - Top-Line Results	Phase IV - GPL/CT/2022/008/IV	518589
Chronic Lymphocytic Leukemia (CLL)/Small Cell Lymphocytic Lymphoma (SLL) - NHL					
06/04/2024	Brukinsa	BeiGene, Ltd.	BGNE	Trial Data - Retrospective Analysis	Phase III - ALPINE (vs. Ibrutinib)	517961
06/03/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase II - MC1485	518633
06/03/2024	Imbruvica	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase II - CAPTIVATE (w/Venetoclax)	518562
Chronic Myelogenous Leukemia (CML)					
06/03/2024	Scemblix	Novartis AG	NVS	Trial Data - Top-Line Results	Phase Ib/II - Dose Assessment Study (Pediatric)	518709
05/31/2024	Scemblix	Novartis AG	NVS	Trial Data - Updated Results	Phase III - ASC4FIRST	519478
05/31/2024	Iclusig	Takeda Pharmaceutical Co. Ltd.	TAK	Trial Data - Updated Results	Phase II - OPTIC (CP-CML)	518551
Colorectal Cancer (CRC)					
06/03/2024	Tukysa	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase II - MOUNTAINEER (w/Trastuzumab)	518550
06/03/2024	ERAS-007	Erasca, Inc.	ERAS	Trial Data - Updated Results	Phase Ib/II - HERKULES-3 (w/encorafenib + cetuximab)	518853
06/03/2024	Lumakras	Amgen, Inc.	AMGN	Trial Data - Updated Results	Phase III - CodeBreak 300	519940
06/03/2024	DEP-SN38	Starpharma Holdings Limited	SPL	Trial Data - Final Results	Phase I/II - UK Hospitals	518049
06/03/2024	DEP-SN38	Starpharma Holdings Limited	SPL	Trial Data - Updated Results	Phase I/II - UK Hospitals	518804
06/03/2024	HyLeukin	NeoImmuneTech, Inc.	950220	Trial Data - Updated Results	Phase I/II - KEYNOTE A60	519837
06/02/2024	Zimberelimab	Arcus Biosciences, Inc.	RCUS	Trial Data - Top-Line Results	Phase Ib/II - ARC-9 (w/zimberelimab/FOLFOX +/- bevacizumab)	517962
06/02/2024	IBI-310	Innovent Biologics, Inc.	1801	Trial Data - Updated Results	Phase Ib/III - Neoshot (China)	518875
06/02/2024	Etrumadenant	Arcus Biosciences, Inc.	RCUS	Trial Data - Top-Line Results	Phase Ib/II - ARC-9 (w/zimberelimab/FOLFOX +/- bevacizumab)	517923
06/02/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate 8HW	517744
06/02/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase II - NEOPRISM-CRC (UK)	519647
06/02/2024	M9140	Merck KGaA	MKKGY	Trial Data - Updated Results	Phase Ia/Ib - First in Human	519017
06/02/2024	IM-96	Beijing Immunochina Pharmaceuticals Co., Ltd.		Trial Data - Top-Line Results	Phase I - YMCART9601 (China)	519101
06/01/2024	CR6086	Rottapharm Biotech		Trial Data - Top-Line Results	Phase I/II - w/(AGEN2034)	519095
06/01/2024	ABBV-400	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase I - First-In-Human	520204
06/01/2024	IBI-363	Innovent Biologics, Inc.	1801	Trial Data - Top-Line Results	Phase Ia/Ib - CIBI363A102 (China)	519546
06/01/2024	Fruzaqla	Takeda Pharmaceutical Co. Ltd.	TAK	Trial Data - Updated Results	Phase III - FRESCO (China)|Phase III - FRESCO-2 (Global)	518652
06/01/2024	Lonsurf	Otsuka Holdings Co., Ltd.	4578	Trial Data - Updated Results	Phase III - SUNLIGHT	518610
06/01/2024	Erbitux	Eli Lilly and Company	LLY	Trial Data - Top-Line Results	Phase IV - BERING-CRC	518496

06/01/2024	Balstilimab	Agenus Inc.	AGEN	Trial Data - Subgroup Analysis	Phase Ia/Ib - PK/PD Study (+/- Botensilimab)	517897
06/01/2024	Balstilimab	Agenus Inc.	AGEN	Trial Data - Top-Line Results	Phase I/II - w/(CR6086)	518727
06/01/2024	COM701	Compugen Ltd.	CGEN	Trial Data - Updated Results	Phase I - CPG-02-101	518734
06/01/2024	Tevimbra	BeiGene, Ltd.	BGNE	Trial Data - Top-Line Results	Phase II - China	518739
06/01/2024	Fadraciclib	Cyclacel Pharmaceuticals, Inc.	CYCC	Trial Data - Preclinical Results	Preclinical Studies	520044
06/01/2024	Tecentriq	Roche Holding AG	RHHBY	Trial Data - Top-Line Results	Phase II - OBERTO 301 - w/PolyPEPI1018	519611
06/01/2024	Braftovi	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase IV - BERING-CRC	518653
06/01/2024	Botensilimab	Agenus Inc.	AGEN	Trial Data - Subgroup Analysis	Phase Ia/Ib - PK/PD Study (+/- Balstilimab)	517838
06/01/2024	HLX04	Essex Bio-Technology Limited	1061	Trial Data - Updated Results	Phase II/III - ASTRUM-015 (China)	520070
06/01/2024	HLX-10	Shanghai Henlius Biotech Co. Ltd.	2696	Trial Data - Updated Results	Phase II/III - ASTRUM-015 (China)	518850
06/01/2024	PolyPEPI1018	Treos Bio Limited		Trial Data - Top-Line Results	Phase II - OBERTO 301 - w/Atezolizumab	518846
06/01/2024	ALX-148	ALX Oncology, Inc.	ALXO	Trial Data - Top-Line Results	Phase II - w/ Cetuximab + Pembrolizumab	518782
06/01/2024	TTX-080	Tizona Therapeutics, Inc.		Trial Data - Updated Results	Phase Ia/Ib - Monotherapy/Combination	519122
06/01/2024	COM902	Compugen Ltd.	CGEN	Trial Data - Updated Results	Phase I - CPG-02-101	518777
Colorectal Cancer (CRC) - Imaging						
06/01/2024	ColoAlert	Mainz Biomed N.V.	MYNZ	Trial Data - Retrospective Analysis	ColoFuture (EU)|eAArly DETECT (US)	519840
COVID-19 Prevention						
06/01/2024	Pemgarda	Invivyd, Inc.	IVVD	Trial Data - Updated Results	Phase III - CANOPY	519050
Cutaneous T-Cell Lymphoma (CTCL) - NHL						
06/03/2024	Lacutamab	Innate Pharma S.A.	IPHA	Trial Data - Updated Results	Phase II - TELLOMAK	518696
Desmoid Tumors						
06/01/2024	Ogsiveo	SpringWorks Therapeutics Inc.	SWTX	Trial Data - Updated Results	Phase III - DeFi (Desmoid/Fibromatosis)	518555
06/01/2024	Ogsiveo	SpringWorks Therapeutics Inc.	SWTX	Trial Data - Updated Results	Phase III - DeFi (Desmoid/Fibromatosis)	518556
05/31/2024	Ogsiveo	SpringWorks Therapeutics Inc.	SWTX	Trial Data - Updated Results	Phase III - DeFi (Desmoid/Fibromatosis)	518554
Diffuse Large B-Cell Lymphoma (DLBCL) - NHL						
06/03/2024	Polivy	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase III - POLARIX (vs. R-CHOP)	518591
06/03/2024	Breyanzi	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - TRANSFORM	518714
06/03/2024	CNTY-101	Century Therapeutics, Inc.	IPSC	Trial Data - Updated Results	Phase I - ELiPSE-1	518991
06/03/2024	Lunsumio	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase Ib/II - w/Polatuzumab Vedotin	518747
06/03/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Top-Line Results	Phase II - EPCORE NHL-6	518839

06/03/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Updated Results	Phase I/II - EPCORE NHL-2	518842
06/03/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Updated Results	Phase I/II - EPCORE NHL-2	518843
06/03/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Updated Results	Phase I/II - EPCORE NHL-2	518844
06/03/2024	AT101	AbClon Inc.	174900	Trial Data - Updated Results	Phase I/II - B-NHL Study	519056
06/02/2024	CB-010	Caribou Biosciences, Inc.	CRBU	Trial Data - Retrospective Analysis	Phase I - ANTLER	519699
06/01/2024	Adcetris	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - ECHELON-3	519603
Esophageal Cancer						
06/04/2024	AN0025	Adlai Nortye Biopharma Co., Ltd.	ANL	Trial Data - Top-Line Results	Phase Ib - China	520069
06/04/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-649	520281
06/03/2024	9MW2821	Mabwell Biotechnology	688062	Trial Data - Updated Results	Phase I/II - Dose - Escalation (China)	519054
06/01/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-649	518513
06/01/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate 648	519635
06/01/2024	Yervoy	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate 648	519633
06/01/2024	Camrelizumab	Jiangsu Hengrui Pharmaceuticals	600276:SS	Trial Data - Updated Results	Phase III - ESCORT-1st	518745
06/01/2024	Tevimbra	BeiGene, Ltd.	BGNE	Trial Data - Updated Results	Phase III - RATIONALE 306	518740
06/01/2024	Lytgobi	Otsuka Holdings Co., Ltd.	4578	Trial Data - Updated Results	Phase Ib - MK3475 - 990	519544
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase Ib - MK3475 - 990	519554
Follicular Lymphoma (FL)						
06/03/2024	Breyanzi	Bristol Myers Squibb Company	BMY	Trial Data - Subgroup Analysis	Phase II - TRANSCEND FL	518713
06/03/2024	Abexinostat	Xynomic Pharmaceuticals Holdings, Inc.	XYNO	Trial Data - Top-Line Results	Phase II - China	518522
06/03/2024	Gazyva	Roche Holding AG	RHHBY	Trial Data - Top-Line Results	Phase II - FLUORO	518553
06/03/2024	EO2463	Enterome Bioscience		Trial Data - Updated Results	Phase I/II - SIDNEY	517947
06/03/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Top-Line Results	Phase II - M23-362	520034
06/03/2024	TQ-B3525	Chia Tai Tianqing Pharmaceutical Group Co., Ltd		Trial Data - Top-Line Results	Phase II - China	518862
06/02/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Updated Results	Phase I/II - EPCORE NHL-2	517703
06/02/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Updated Results	Phase I/II - EPCORE NHL-1	517704
Gastric Cancer						
06/03/2024	CT041	CARsgen Therapeutics	2171	Trial Data - Updated Results	Phase I - Dose Escalation and Dose Expansion (China)	518927
06/03/2024	AK109	Akeso Inc.		Trial Data - Top-Line Results	Phase Ib/II - w/ AK104 +/- chemotherapy (China)	518919
06/02/2024	IBI-389	Innovent Biologics, Inc.	1801	Trial Data - Top-Line Results	Phase I - w/Sintilimab (China)	519932

06/01/2024	TST-001	Transcenta Holding Ltd.	6628	Trial Data - Updated Results	Phase I/IIa - TranStar102/TST001-1002 (China)	517798
06/01/2024	Domvanalimab	Arcus Biosciences, Inc.	RCUS	Trial Data - Updated Results	Phase II - EDGE-Gastric w/Zimberelimab	519584
06/01/2024	Zimberelimab	Arcus Biosciences, Inc.	RCUS	Trial Data - Updated Results	Phase II - EDGE-Gastric w/Domvanalimab	519583
06/01/2024	Minnelide	Minneamrita Therapeutics LLC		Trial Data - Top-Line Results	Phase I - +/- Paclitaxel	518793
06/01/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-649 (w/Ipilimumab)	519700
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - KEYNOTE-859	518626
06/01/2024	DHP107	Daehwa Pharmaceutical Co Ltd	067080:KS	Trial Data - Top-Line Results	Phase III - China	518725
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - KEYNOTE-585	518625
06/01/2024	VYLOY	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase III - Spotlight (w/mFOLFOX6)	518656
06/01/2024	TPX-4589	Bristol Myers Squibb Company	BMY	Trial Data - Top-Line Results	Phase I/II - Dose-escalation and Expansion Study (China)	519543
06/01/2024	IMC001	Immuno Cure BioTech Limited		Trial Data - Top-Line Results	Phase I - China	519600
06/01/2024	IMC002	Immuno Cure BioTech Limited		Trial Data - Top-Line Results	Phase I - China	519599
06/01/2024	FG-M108	FutureGen Biopharm		Trial Data - Top-Line Results	Phase III - w/CAPOX (China)	519088
Gastrointestinal Stromal Tumor (GIST)						
06/03/2024	IDRX-42	IDRx, Inc		Trial Data - Updated Results	Phase I/Ib - First-in-Human	520023
06/03/2024	Olverembatinib	Ascentage Pharma Group Corporation	6855	Trial Data - Updated Results	Phase Ib/II - Adults (China)	517790
06/01/2024	Bezuclastinib	Cogent Biosciences, Inc.	COGT	Trial Data - Updated Results	Phase III - PEAK	518731
Graft vs. Host Disease (GVHD) - Treatment						
06/03/2024	SER-155	Seres Therapeutics, Inc.	MCRB	Trial Data - Updated Results	Phase Ib - Safety and Tolerability	518716
Head and Neck Cancer						
06/04/2024	Libtayo	Regeneron Pharmaceuticals, Inc.	REGN	Trial Data - Updated Results	Phase II - OpcemISA	518354
06/04/2024	ISA101	ISA Pharmaceuticals B.V.		Trial Data - Updated Results	Phase II - OpcemISA	518260
06/04/2024	HB-200	HOOKIPA Pharma Inc.	HOOK	Trial Data - Updated Results	Phase I/II - HPV-Positive Cancers (HB-201/HB-202)	517706
06/04/2024	CUE-101	Cue Biopharma, Inc.	CUE	Trial Data - Updated Results	Phase I - First-in-Human (KEYNOTE-A78)	520015
06/04/2024	Xevinapant	Merck KGaA	MKKGY	Trial Data - Retrospective Analysis	Phase I/II - LA-SCCHN	517729
06/03/2024	PRGN-2012	Precigen, Inc.	PGEN	Trial Data - Updated Results	Phase I/II - U.S.	519877
06/03/2024	HX008	Lepu Biopharma Co., Ltd.	2157	Trial Data - Top-Line Results	Phase I/II - w/MRG003	520297
06/03/2024	MRG003	Lepu Biopharma Co., Ltd.	2157	Trial Data - Top-Line Results	Phase I/II - w/ HX008 (China)	520295
06/03/2024	Petosemtamab	Merus N.V.	MRUS	Trial Data - Updated Results	Phase I/II - Dose Finding/Expansion	517754
06/03/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - KEYNOTE-412	518634

06/03/2024	Tivdak	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase II - innovaTV 207	520084
06/02/2024	FID-007	Fulgent Pharma Holdings, Inc.		Trial Data - Top-Line Results	Phase I - 0C-18-2	519625
06/02/2024	NBTXR3	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase I/II - Study 1100 (w/Nivolumab or Pembrolizumab)	519663
06/02/2024	ASP-1929	Rakuten Medical, Inc.		Trial Data - Updated Results	Phase I/II - ASP-1929-181 w/Anti-PD1	517938
06/02/2024	Fianlimab	Regeneron Pharmaceuticals, Inc.	REGN	Trial Data - Top-Line Results	Phase I - +/- REGN2810	519678
06/02/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase II - DESTINY-PanTumor02	520211
06/01/2024	REGN6569	Regeneron Pharmaceuticals, Inc.	REGN	Trial Data - Top-Line Results	Phase I - w/Cemiplimab	518953
06/01/2024	TTX-080	Tizona Therapeutics, Inc.		Trial Data - Updated Results	Phase Ia/Ib - Monotherapy/Combination	519121
06/01/2024	Pepinemab	Vaccinex, Inc.	VCNX	Trial Data - Top-Line Results	Phase Ib/II - KEYNOTE B84 (w/Pembrolizumab)	518666
Hearing Loss - Chemotherapy-Induced						
06/02/2024	DB-020	Regeneron Pharmaceuticals, Inc.	REGN	Trial Data - Final Results	Phase Ib - 002 (Cisplatin-Receiving Patients)	518910
Hematologic Cancer						
06/03/2024	Orca-T	ORCA Bio Inc.		Trial Data - Updated Results	Phase Ib - Single-Arm Study	518930
06/03/2024	MK-4280	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase I/II - w/Pembrolizumab	518858
06/03/2024	MK-4280	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase I/II - w/Pembrolizumab	518859
06/01/2024	CS5001	CStone Pharmaceuticals (Suzhou) Co., Ltd	2616	Trial Data - Updated Results	Phase I - Dose Escalation/ Expansion (FIH) (Global)	517905
06/01/2024	Fadraciclib	Cyclacel Pharmaceuticals, Inc.	CYCC	Trial Data - Updated Results	Phase I/II - CYC065-101 (Lymphoma)	519612
06/01/2024	PA3-17	PersonGen BioTherapeutics (Suzhou) Co., Ltd.		Trial Data - Top-Line Results	Phase I - China	519096
06/01/2024	SUPLEXA	Alloplex Biotherapeutics, Inc.		Trial Data - Top-Line Results	Phase I - FIH (Australia)	519100
Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)						
06/04/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase II - w/Regorafenib	518623
06/04/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Top-Line Results	Phase III - CheckMate 9DW (w/Ipilimumab)	520060
06/04/2024	Stivarga	Bayer AG	BAYN	Trial Data - Top-Line Results	Phase II - w/Pembrolizumab	518565
06/03/2024	C-CAR031	AbelZeta Pharma Inc.		Trial Data - Updated Results	Phase I - First-In-Human (China)	519055
06/01/2024	SCT-510A	Sinocelltech Group Limited		Trial Data - Top-Line Results	Phase II/III - w/SCT-I10A (China)	519553
06/01/2024	SCT-I10A	Sinocelltech Group Limited		Trial Data - Top-Line Results	Phase II/III - w/(SCT510) (China)	519030
06/01/2024	VG-161	Virogin Biotech Ltd.		Trial Data - Updated Results	Phase I -Dose Ascending (China)	518960
06/01/2024	Lenvima	Eisai Co., Ltd.	4523:JP	Trial Data - Updated Results	Phase III - REFLECT (vs. Sorafenib)	518533
06/01/2024	Nelitolimod	TriSalus Life Sciences	TLSI	Trial Data - Updated Results	Phase Ib/II - PERIO-02	518570
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - KEYNOTE-240	518624
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase II - KEYNOTE-224	518628

06/01/2024	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - EMERALD-1	518660
06/01/2024	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase II - w/Tremelimumab or Bevacizumab	518661
06/01/2024	Camrelizumab	Jiangsu Hengrui Pharmaceuticals	600276:SS	Trial Data - Updated Results	Phase III - w/Rivoceranib	518744
05/30/2024	Camrelizumab	Jiangsu Hengrui Pharmaceuticals	600276:SS	Trial Data - Final Results	Phase III - w/Rivoceranib	519283
05/30/2024	Rivoceranib	Elevar Therapeutics, Inc.		Trial Data - Final Results	Phase III - w/Camrelizumab	519712
HER2+ Breast Cancer						
06/03/2024	Tykerb	Novartis AG	NVS	Trial Data - Updated Results	Phase III - NSABP B-41 (HER2+)	518505
06/03/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase II - DESTINY-Breast01 (HER2+)|Phase III - DESTINY-Breast02 (HER2+)|Phase III - DESTINY-Breast03 (HER2+)	518761
06/03/2024	Bria-IMT	BriaCell Therapeutics Corp.	BCT	Trial Data - Updated Results	Phase I/IIa - w/Retifanlimab	518766
06/03/2024	ARX788	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase II/III - ACE-Breast-02 (China)	517901
06/02/2024	Bria-IMT	BriaCell Therapeutics Corp.	BCT	Trial Data - Retrospective Analysis	Phase I/IIa - w/Retifanlimab	518765
06/02/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Retrospective Analysis	Phase II - DESTINY-Breast01 (HER2+)|Phase III - DESTINY-Breast02 (HER2+)|Phase III - DESTINY-Breast03 (HER2+)	518758
06/02/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase III - DESTINY-Breast03 (HER2+)	518760
06/02/2024	Nerlynx	Puma Biotechnology, Inc.	PBYI	Trial Data - Updated Results	Phase II - SUMMIT Basket (HER2mut, EGFRmut)	519605
06/02/2024	Tukysa	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase II - HER2 Altered Tumors	519984
06/01/2024	Halaven	Eisai Co., Ltd.	4523:JP	Trial Data - Top-Line Results	Phase III - EMERALD	517814
06/01/2024	Ibrance	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase II - PATRICIA II (Spain)	517917
06/01/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase I/II - DESTINY-Breast07	518756
06/01/2024	PF-07220060	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase I/IIa - C4391001	518950
Hodgkin's Lymphoma						
06/03/2024	Adcetris	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - ECHELON-1	518501
06/01/2024	Adcetris	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase III - BrECADD (Germany)	519591
HR+/HER2- Breast Cancer						
06/03/2024	H3B-6545	Eisai Co., Ltd.	4523:JP	Trial Data - Updated Results	Phase I/II - Monotherapy (HER2 Negative Subjects)	518789
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase III - TROPION-Breast01	518834
06/03/2024	Ibrance	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase IV - PALMARES-2	519878
06/03/2024	Verzenio	Eli Lilly and Company	LLY	Trial Data - Subgroup Analysis	Phase III - monarchE	519943
06/03/2024	Kisqali	Novartis AG	NVS	Trial Data - Updated Results	Phase III - MONALEESA-3 (HR+/HER2-)	518606
06/03/2024	Lynparza	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - OlympiA (gBRCA, Adjuvant)	518528

06/02/2024	Ibrance	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - PALLAS (HR+/HER2-)	518576
06/02/2024	Entinostat	Syndax Pharmaceuticals, Inc.	SNDX	Trial Data - Top-Line Results	Phase III - w/Exemestane (ER+/PR+/HER2-, China)	518563
06/02/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Updated Results	Phase III - TROPICS-02 (HR+/HER2- MBC)	518647
06/02/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Top-Line Results	Phase II - PRIMED	520267
06/02/2024	Orserdu	The Menarini Group		Trial Data - Updated Results	Phase Ib/II - ELECTRA - w/Abemaciclib	518675
06/02/2024	Orserdu	The Menarini Group		Trial Data	Phase Ib/II - ELEVATE	518676
06/02/2024	XZP-3287	Sihuan Pharmaceutical Holdings Group Ltd	460	Trial Data - Top-Line Results	Phase III - w/Fulvestrant (China)	518815
06/02/2024	H3B-6545	Eisai Co., Ltd.	4523:JP	Trial Data - Updated Results	Phase Ib - w/Palbociclib (HER2 Negative Subjects)	518788
06/02/2024	Bria-IMT	BriaCell Therapeutics Corp.	BCT	Trial Data - Retrospective Analysis	Phase I/IIa - w/Retifanlimab	519696
06/02/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase III - DESTINY-Breast06	519623
06/02/2024	BLU-222	Blueprint Medicines Corporation	BPMC	Trial Data - Updated Results	Phase I/II - VELA	517808
06/02/2024	CYH33	Shanghai HaiHe Pharmaceutical Co., Ltd.		Trial Data - Top-Line Results	Phase I - CYH33-G103 (China)	518939
06/02/2024	Imlunestrant	Eli Lilly and Company	LLY	Trial Data - Updated Results	Phase Ia/Ib - EMBER	518914
06/02/2024	Lerociclib	Pepper Bio, Inc.		Trial Data - Top-Line Results	Phase III - GB491-008 (China)	518735
06/02/2024	Alisertib	Puma Biotechnology, Inc.	PBYI	Trial Data - Updated Results	Phase II - TBCRC041 (+/- Fulvestrant)	518530
06/02/2024	PF-07248144	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase I - KAT6	519052
06/02/2024	TQB-2930	Sino Biopharmaceutical Limited	1177	Trial Data - Top-Line Results	Phase I/II - TQB2930-Ib/II-01 (China)	519044
06/01/2024	AC-699	Accutar Biotechnology, Inc.		Trial Data - Top-Line Results	Phase I - AC699-001	519047
06/01/2024	BB-1701	Bliss Biopharmaceutical (Hangzhou) Co., Ltd		Trial Data - Top-Line Results	Phase I - BB-1701-101 (US & China)	520003
06/01/2024	Inavolisib	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase II/III - INAVO120 (w/Palbociclib/Fulvestrant, PIK3CA-Mutant/HR+/HER2-)	518785
06/01/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase III - TROPION-Breast01	518832
06/01/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Top-Line Results	Phase II - +/- Pembrolizumab	519683
06/01/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Updated Results	Phase III - TROPICS-02 (HR+/HER2- MBC)	518646
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase II - w/Trodelvy	519559
06/01/2024	E7090	Eisai Co., Ltd.	4523:JP	Trial Data - Top-Line Results	Phase I - E7090-J081-102 (Japan)	518720
06/01/2024	Ibrance	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase II - w/Exemestane	519562
06/01/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Top-Line Results	Phase II - KEYNOTE-F21	519571
06/01/2024	Verzenio	Eli Lilly and Company	LLY	Trial Data - Top-Line Results	Phase III - postMONARCH	519560
05/31/2024	Kisqali	Novartis AG	NVS	Trial Data - Updated Results	Phase III - NATALEE (HR+/HER2- eBC)	518605
Leiomyosarcoma						

06/01/2024	Yondelis	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase I/II - SAINT	518507
Liposarcoma						
06/03/2024	Lete-cel	Adaptimmune Therapeutics plc	ADAP	Trial Data - Updated Results	Phase II - IGNYTE-ESO	519910
06/01/2024	BI 907828	Boehringer Ingelheim GmbH		Trial Data - Top-Line Results	Phase I - Dose Escalation Study	518975
Mantle Cell Lymphoma - NHL						
06/03/2024	Breyanzi	Bristol Myers Squibb Company	BMY	Trial Data - Subgroup Analysis	Phase I - TRANSCEND-NHL-001	519862
06/01/2024	Imbruvica	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase III - SYMPATICO (w/Venetoclax)	517919
06/01/2024	Venclexta	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase III - SYMPATICO (w/Ibrutinib)	519945
Marginal Zone Lymphoma - NHL						
06/03/2024	EO2463	Enterome Bioscience		Trial Data - Updated Results	Phase I/II - SIDNEY	517946
Melanoma						
06/03/2024	cytoTIL15	Obsidian Therapeutics, Inc.		Trial Data - Updated Results	Phase I - First in Human	518972
06/03/2024	RP-1	Replimune Group Inc.	REPL	Trial Data - Updated Results	Phase I/II - IGNYTE (+/- Nivolumab)	518792
06/03/2024	mRNA-4157	Moderna, Inc.	MRNA	Trial Data - Updated Results	Phase IIb - KEYNOTE-942 (w/Pembrolizumab)	519924
06/03/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase II - KEYNOTE-942 (w/mRNA-4157)	519859
06/03/2024	Tilsotolimod	Aceragen, Inc.	ACGN	Trial Data - Updated Results	Phase III - ILLUMINATE-301 (w/Ipilimumab)	519838
06/02/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Top-Line Results	Phase III - NADINA (Neoadjuvant)	519656
06/02/2024	Yervoy	Bristol Myers Squibb Company	BMY	Trial Data - Top-Line Results	Phase III - NADINA (Neoadjuvant)	519876
06/01/2024	Yervoy	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase II - M.D. Anderson Cancer Center	518497
06/01/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase II/III - RELATIVITY-047 (w/Relatlimab, 1st-Line)	518515
06/01/2024	Cotellic	Roche Holding AG	RHHBY	Trial Data - Final Results	Phase II - w/Atezolizumab +/- Vemurafenib (BRAFV600 Mutation; EU)	518526
06/01/2024	Lenvima	Eisai Co., Ltd.	4523:JP	Trial Data - Updated Results	Phase II - LEAP-004 (w/Pembrolizumab)	518534
06/01/2024	SCIB1	Scancell	SCLP	Trial Data - Updated Results	Phase II - SCOPE	518608
06/01/2024	Amtagvi	Iovance Biotherapeutics, Inc.	IOVA	Trial Data - Updated Results	Phase II - C-144-01	518612
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase II - Neo PeLe	518621
06/01/2024	Relatlimab	Bristol Myers Squibb Company	BMY	Trial Data - Top-Line Results	Phase II - w/Nivolumab (First-Line, University of Pittsburgh)	518688
06/01/2024	Relatlimab	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase II/III - RELATIVITY-047 (w/Nivolumab, 1st-Line)	519883
06/01/2024	EVX-01	Evaxion Biotech A/S	EVAX	Trial Data - Updated Results	Phase IIb - w/Keytruda	518962
06/01/2024	FCN-159	Fochon Pharmaceuticals Ltd.		Trial Data - Updated Results	Phase Ia/Ib - FCN-159-001	519009
06/01/2024	UV-1	Ultimovacs ASA	ULTIMO	Trial Data - Updated Results	Phase II - INITIUM	519588

06/01/2024	KD6001	Shanghai Kanda Biotechnology Co., Ltd.		Trial Data - Top-Line Results	Phase Ib/II - w/Toripalimab (China)	519057
06/01/2024	IBI-363	Innovent Biologics, Inc.	1801	Trial Data - Top-Line Results	Phase Ia/Ib - CIBI363A102 (China)	519545
06/01/2024	Tunlametinib	Shanghai Kechow Pharma Inc		Trial Data - Updated Results	Phase II - Advanced Melanoma (China)	519079
06/01/2024	BCD-145	BIOCAD		Trial Data - Top-Line Results	Phase I - Russia	519093
05/31/2024	Nidlegy	Philogen S.p.A.	PHIL	Trial Data - Updated Results	Phase III - PIVOTAL	519539
05/31/2024	MK-7684	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase I/II - MK-3475-02A (Substudy 02A)	518780
05/31/2024	MK-1308	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase I/II - MK-3475-02A (Substudy 02A)	519506
05/31/2024	SX-682	Syntrix Pharmaceuticals		Trial Data - Top-Line Results	Phase I/II- w/Pembrolizumab (Massachusetts General Hospital/NCI)	518814
05/31/2024	IMC-F106C	Immunocore, Ltd.	IMCR	Trial Data - Updated Results	Phase I/II - IMC-F106C-101	519522
05/31/2024	Amtagvi	Iovance Biotherapeutics, Inc.	IOVA	Trial Data - Updated Results	Phase II - IOV-COM-202	519521
05/31/2024	Tafinlar	Novartis AG	NVS	Trial Data - Updated Results	Phase III - COMBI-AD - w/Trametinib	518578
Menopause (including Hormone Replacement Therapy [HRT])						
06/01/2024	Veozah	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase IIIb - DAYLIGHT	518685
Merkel Cell Carcinoma						
06/01/2024	IFx-Hu2.0	TuHURA Biosciences, Inc.		Trial Data - Updated Results	Phase Ib - NMSC	519064
Mesothelioma						
06/03/2024	Rubraca	pharma&		Trial Data - Updated Results	Phase II - MiST	518538
06/03/2024	RSO-021	RS Oncology, LLC		Trial Data - Top-Line Results	Phase I/II - MITOPE (UK)	519066
06/03/2024	Zeltherva	SELLAS Life Sciences Group, Inc.	SLS	Trial Data - Updated Results	Phase I - w/Nivolumab (MSKCC)	518729
Multiple Myeloma (MM)						
06/04/2024	Darzalex Faspro	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase III - PERSEUS	518724
06/04/2024	Venclexta	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase III - CANOVA (w/Dexamethasone +/- Pomalidomide)	518594
06/04/2024	Tecvayli	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase I - MajesTEC-1	518797
06/04/2024	Tecvayli	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase I/II - MajesTEC-1	517916
06/04/2024	OriCAR-017	OriCell Therapeutics Co. Ltd.		Trial Data - Updated Results	Phase I - POLARIS (Zhejiang University)	519013
06/03/2024	Tecvayli	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase II - MM165	518794
06/03/2024	Tecvayli	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase I/II - MajesTEC-1	518795
06/03/2024	Tecvayli	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase III - MajesTEC-7	517909
06/03/2024	Carvykti	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase II - CARTITUDE-2	517743
06/03/2024	Carvykti	Johnson & Johnson	JNJ	Trial Data - Subgroup Analysis	Phase III - CARTITUDE-4	519872

06/03/2024	Talvey	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase III - MajesTEC-7	520403
06/03/2024	Mezigdomide	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase I/II - w/ Dexamethasone (RRMM)	518811
06/03/2024	Elrexfio	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase I/II - MagnetisMM-9	518818
06/03/2024	ABBV-383	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase I - TNB383B.0001 (U.S.)	518864
06/03/2024	ABBV-383	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase I - TNB383B.0001 (U.S.)	518865
06/03/2024	Sarclisa	Sanofi	SNY	Trial Data - Updated Results	Phase III - IMROZ (w/VRd)	518580
06/03/2024	Darzalex Faspro	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase III - PERSEUS	517904
06/03/2024	Blenrep	GSK plc	GSK	Trial Data - Top-Line Results	Phase I/II - 2000028918	518697
06/03/2024	Blenrep	GSK plc	GSK	Trial Data - Updated Results	Phase I/II - BelaRd Study	518698
06/03/2024	Blenrep	GSK plc	GSK	Trial Data - Updated Results	Phase III - DREAMM 7 (w/ Vd)	518699
06/03/2024	Abecma	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - KarMMa-3	518681
06/03/2024	Abecma	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - KarMMa-3	518682
06/02/2024	Blenrep	GSK plc	GSK	Trial Data - Updated Results	Phase III - DREAMM 8 (w/ Pd)	519655
Myelodysplastic Syndrome (MDS)						
06/03/2024	CA-4948	Dr. Reddy's Laboratories Ltd.	RDY	Trial Data - Updated Results	Phase I/IIa - TakeAim Leukemia	518718
06/03/2024	CA-4948	Dr. Reddy's Laboratories Ltd.	RDY	Trial Data - Updated Results	Phase I/IIa - TakeAim Leukemia	518719
06/03/2024	Venclexta	AbbVie Inc.	ABBV	Trial Data - Top-Line Results	Phase II - w/Decitabine	518592
06/03/2024	Rytelo	Geron Corporation	GERN	Trial Data - Updated Results	Phase II/III - IMerge (Transfusion-Dependent Subjects)	518508
06/03/2024	Reblozyl	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - COMMANDS	518613
06/03/2024	AMG 176	Amgen, Inc.	AMGN	Trial Data - Top-Line Results	Phase I - w/+/-Azacitidine	518750
06/01/2024	IMM01	ImmuneOnco Biopharmaceuticals (Shanghai) Inc.	1541	Trial Data - Top-Line Results	Phase I/II - IMM01-02	518982
06/01/2024	Onureg	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase II/III - CA055-026	518523
Myelofibrosis (MF)						
06/03/2024	CK0804	Cellenkos, Inc.		Trial Data - Updated Results	Phase Ib - LIMBER-TREG108 (w/Ruxolitinib)	518955
06/03/2024	INCB57643	Incyte Corporation	INCY	Trial Data - Updated Results	Phase I/II - LIMBER (-/+Ruxolitinib)	518753
06/03/2024	Ojjaara	GSK plc	GSK	Trial Data - Updated Results	Phase III - MOMENTUM (Vs. Danazol)	518571
06/03/2024	Ojjaara	GSK plc	GSK	Trial Data - Updated Results	Phase III - MOMENTUM (Vs. Danazol)	518572
06/03/2024	Vonjo	Swedish Orphan Biovitrum AB	SOBI	Trial Data - Updated Results	Phase III - PAC326	518558
06/03/2024	Vonjo	Swedish Orphan Biovitrum AB	SOBI	Trial Data - Updated Results	Phase III - PAC326	518559
06/01/2024	TQB3617	Chia Tai Tianqing Pharmaceutical Group Co., Ltd		Trial Data - Top-Line Results	Phase I - Advanced Malignant Tumors (China)	519901

05/31/2024	Pelabresib	MorphoSys AG	MOR	Trial Data - Updated Results	Phase III - MANIFEST-2 (w/Ruxolitinib)	518683
Nasopharyngeal Cancer						
06/03/2024	MRG003	Lepu Biopharma Co., Ltd.	2157	Trial Data - Top-Line Results	Phase I/II - w/ HX008 (China)	520294
06/03/2024	HX008	Lepu Biopharma Co., Ltd.	2157	Trial Data - Top-Line Results	Phase I/II - w/MRG003	520296
06/02/2024	Tabelecleucel	Pierre Fabre		Trial Data - Top-Line Results	Phase I/II - w/KEYTRUDA	518723
06/02/2024	LBL-007	BeiGene, Ltd.	BGNE	Trial Data - Top-Line Results	Phase I/II - w/Tislelizumab (China)	519608
06/02/2024	Loqtorzi	Coherus BioSciences, Inc.	CHRS	Trial Data - Updated Results	Phase III - JUPITER-02 (China)	518896
06/02/2024	Penpulimab	Akeso Inc.		Trial Data - Top-Line Results	Phase II - NPC ± Anlotinib Hydrochloride (China)	518827
06/02/2024	QL1706	Qilu Pharmaceutical Co., Ltd.		Trial Data - Top-Line Results	Phase II/III - Nasopharyngeal Carcinoma (China)	518891
Neuroblastoma						
06/01/2024	Iwilfin	Panbela Therapeutics, Inc.	PBLA	Trial Data - Top-Line Results	Phase II - Study 3b	518810
06/01/2024	Danyelza	Y-mAbs Therapeutics Inc.	YMAB	Trial Data - Retrospective Analysis	Phase II - 201 (Osteomedullary Disease)	518778
06/01/2024	Danyelza	Y-mAbs Therapeutics Inc.	YMAB	Trial Data - Updated Results	Phase II - 201 (Osteomedullary Disease)	518779
06/01/2024	Unituxin	United Therapeutics Corporation	UTHR	Trial Data - Updated Results	Phase III - Efficacy (ANBL0032; Neuroblastoma)	518614
Neuroendocrine Tumors (NET)						
06/03/2024	AlphaMedix	RadioMedix, Inc.		Trial Data - Top-Line Results	Phase II - Naive Patients	518838
06/02/2024	LBL-024	Nanjing Leads Biolabs, Inc.		Trial Data - Top-Line Results	Phase I/II - China	519657
06/01/2024	RYZ101	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase Ib/III - ACTION-1	519021
06/01/2024	Lutathera	Novartis AG	NVS	Trial Data - Updated Results	Phase III - NETTER-2	518651
Neurofibromatosis (NF)						
06/03/2024	Mirdametinib	SpringWorks Therapeutics Inc.	SWTX	Trial Data - Updated Results	Phase IIb - ReNeu	517937
06/01/2024	FCN-159	Fochon Pharmaceuticals Ltd.		Trial Data - Updated Results	Phase I/II - FCN-159-002	519008
Non-Hodgkin's Lymphoma (NHL)						
06/03/2024	SHR-A1921	Jiangsu Hengrui Pharmaceuticals	600276:SS	Trial Data - Top-Line Results	Phase I - B Cell Lymphoma (China)	518992
06/03/2024	PMB-CT01	PeproMene Bio, Inc.		Trial Data - Updated Results	Phase I - PMB-102	518881
06/03/2024	AVM0703	AVM Biotechnology		Trial Data - Top-Line Results	Phase I/II - WWRD Study	518922
06/03/2024	CB-010	Caribou Biosciences, Inc.	CRBU	Trial Data - Updated Results	Phase I - ANTLER	518940
06/03/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Updated Results	Phase I/II - EPCORE-NHL	518840
06/03/2024	Epkinly	Genmab A/S	GMAB	Trial Data - Updated Results	Phase I/II - EPCORE-NHL	518841
06/03/2024	Columvi	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase I/II - NP30179 (w/Gazyva)	518787

06/03/2024	Breyanzi	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase I - TRANSCEND	518712
06/03/2024	IMM-0306	ImmuneOnco Biopharmaceuticals (Shanghai) Inc.	1541	Trial Data - Top-Line Results	Phase I/II - IMM0306-I	519075
06/03/2024	EX103	Guangzhou Excelmab Inc.		Trial Data - Top-Line Results	Phase I - EX103-001	519069
06/03/2024	CN-201	Curon Biopharmaceutical Limited		Trial Data - Top-Line Results	Phase I - R/R B-Cell NHL (China)	519037
06/03/2024	BRL-201	Bioray Laboratories		Trial Data - Top-Line Results	Phase I/II - 2019-CAR-00CH1	519048
06/03/2024	LY007	Shanghai Longyao Biotechnology Co., Ltd		Trial Data - Top-Line Results	Phase I - LY007C1101	519788
06/02/2024	Columvi	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase I/II - NP30179 (w/Gazyva)	518786
06/01/2024	Zelenirstat	Pacylex Pharmaceuticals		Trial Data - Final Results	Phase I/IIa - First in Human (Canada)	519617
06/01/2024	CA-4948	Dr. Reddy's Laboratories Ltd.	RDY	Trial Data - Updated Results	Phase I/II - TakeAim Lymphoma	518717
06/01/2024	TRS-005	Zhejiang Teruisi Biopharmaceutical, Inc.		Trial Data - Top-Line Results	Phase I - Dose-escalating Study (China)	519097
06/01/2024	QL-301	QLSF Biotherapeutics		Trial Data - Top-Line Results	Phase I - QLF31907-101 (China)	519994
Non-Small Cell Lung Cancer (NSCLC)						
06/04/2024	Fyarro	AADi Bioscience, Inc.	AADI	Trial Data - Preclinical Results	Preclinical Studies	517819
06/04/2024	Lazertinib	Genosco, Inc.		Trial Data - Updated Results	Phase III - MARIPOSA	517847
06/03/2024	THIO	MAIA Biotechnology, Inc.	MAIA	Trial Data - Updated Results	Phase II - THIO-101 (w/Libtayo)	518854
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase II - TROPION-Lung05|Phase III - TROPION-LUNG01	518833
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Subgroup Analysis	Phase Ib - TROPION-Lung02 (w/Keytruda)	518835
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase II - TROPION-Lung05	518836
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase I/II - TROPION-PanTumor02 (China)	519937
06/03/2024	APL-101	Apollomics, Inc.	APLM	Trial Data - Updated Results	Phase II - KUNPENG (China)	518775
06/03/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase II - DESTINY-Lung01|Phase II - DESTINY-LUNG02	518762
06/03/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Final Results	Phase II - DESTINY-LUNG02	518764
06/03/2024	Oleclumab	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase II - COAST - w/Imfinzi	519847
06/03/2024	MCLA-129	Merus N.V.	MRUS	Trial Data - Updated Results	Phase I/II - MCLA-129-CL01	519870
06/03/2024	D-1553	InventisBio, Inc.		Trial Data - Top-Line Results	Phase I/II - D1553-106/IN10018-602 (China)	520389
06/03/2024	SHR-1701	Jiangsu Hengrui Pharmaceuticals	600276:SS	Trial Data - Top-Line Results	Phase II - +/- Chemo (China)	518973
06/03/2024	Anyara	NeoTX Therapeutics Ltd.		Trial Data - Top-Line Results	Phase IIa - w/Docetaxel	518230
06/03/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-9LA (Stage IV, w/Ipilimumab)	518521
06/03/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-77T (Neoadjuvant)	519786
06/03/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Top-Line Results	Phase II - EV-202	520019

06/03/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase II - KEYNOTE-782 (Biomarkers of Response)	518635
06/03/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase II - KEYNOTE-799 (w/Chemotherapy + Radiotherapy; Stage III NSCLC)	518637
06/03/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - KEYNOTE-671	518638
06/03/2024	Alecensa	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase III - ALINA (vs. Adjuvant Platinum-Based Chemotherapy, ALK Positive)	518582
06/03/2024	Monalizumab	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase II - COAST - w/Imfinzi	519846
06/03/2024	Tepmetko	Merck KGaA	MKKGY	Trial Data - Updated Results	Phase II - VISION (Adenocarcinoma)	518577
06/03/2024	Tabrecta	Novartis AG	NVS	Trial Data - Top-Line Results	Phase I/II - METalmark (w/amivantamab)	518573
06/03/2024	Retevmo	Eli Lilly and Company	LLY	Trial Data - Updated Results	Phase III - LIBRETTO-431	518742
06/03/2024	VIC-1911	VITRAC Therapeutics, LLC		Trial Data - Top-Line Results	Phase I - Dose escalation /Extension (China)	518711
06/03/2024	Rybrevant	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase III - PAPILLON	518707
06/03/2024	Rybrevant	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase II - PALOMA-2	519861
06/03/2024	CAN-2409	Candel Therapeutics, Inc.	CADL	Trial Data - Updated Results	Phase II - LuTK02	517700
06/03/2024	AB-16B5	Alethia BioTherapeutics Inc.		Trial Data - Top-Line Results	Phase II - w/Docetaxel	518693
06/03/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Updated Results	Phase II - w/Keytruda (EVOKE-02)	518648
06/03/2024	Xpovio	Karyopharm Therapeutics	KPTI	Trial Data - Top-Line Results	Phase I/II - STU 032017-003	518654
06/03/2024	Tagrisso	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - ADAURA	518684
06/03/2024	IN-10018	InxMed Co., Ltd.		Trial Data - Top-Line Results	Phase I/II - D1553-106/IN10018-602 (China)	519967
06/03/2024	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - AEGEAN	518664
06/03/2024	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase II - COAST - w/MEDI9447 or Monalizumab	518665
06/03/2024	PM-8002	BioNTech SE	BNTX	Trial Data - Top-Line Results	Phase Ib/IIa - PK/PD Study	519828
06/03/2024	MYTX-011	Mythic Therapeutics		Trial Data - Top-Line Results	Phase I - KisMET-01	519053
06/03/2024	Alisertib	Puma Biotechnology, Inc.	PBYI	Trial Data - Top-Line Results	Phase I/Ib - w/Osimertinib	518529
06/03/2024	BAY 2927088	Bayer AG	BAYN	Trial Data - Updated Results	Phase I - First in Human	519845
06/03/2024	Augtyro	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase I/II - TRIDENT-1	519899
06/02/2024	PF-07248144	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase I - KAT6	519629
06/02/2024	Zongertinib	Boehringer Ingelheim GmbH		Trial Data - Updated Results	Phase Ia/Ib - Beamion Lung 1	519045
06/02/2024	Balversa	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase II - RAGNAR	517927
06/02/2024	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - AEGEAN	519710
06/02/2024	Tagrisso	AstraZeneca PLC	AZN	Trial Data - Top-Line Results	Phase III - LAURA	519664
06/02/2024	Telisotuzumab Vedotin	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase II - LUMINOSITY	518389

06/02/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-816	519665
06/02/2024	Sunvozertinib	Dizal (Jiangsu) Pharmaceutical Co., Ltd.	688192	Trial Data - Updated Results	Phase I/II - WU-KONG1 (EGFR/HER2)	518959
06/01/2024	Olomorasib	Eli Lilly and Company	LLY	Trial Data - Updated Results	Phase I/II - w/KRAS G12C-Mutant Tumors	519578
06/01/2024	Glecirasib	Jacobio Pharmaceuticals Co. Ltd.	1167	Trial Data - Top-Line Results	Phase I/II - JAB-21822-1003 (China)|Phase I/II - w/ JAB3312 (China)	519593
06/01/2024	IBI-351	GenFleet Therapeutics		Trial Data - Top-Line Results	Phase Ib/II - w/Cetuximab (Europe)	519585
06/01/2024	GEN1046	BioNTech SE	BNTX	Trial Data - Top-Line Results	Phase II - GCT1046-04	518897
06/01/2024	JAB-3312	Jacobio Pharmaceuticals Co. Ltd.	1167	Trial Data - Top-Line Results	Phase I/II - JAB-21822 w/ (China)	520098
06/01/2024	AFM24	Affimed N.V.	AFMD	Trial Data - Updated Results	Phase I/IIa -w/Atezolizumab	518767
06/01/2024	APG-2449	Ascentage Pharma Group Corporation	6855	Trial Data - Updated Results	Phase I -Dose escalation(China)	517797
06/01/2024	Lazertinib	Genosco, Inc.		Trial Data - Updated Results	Phase I/Ib - CHRYSALIS-2	517877
06/01/2024	CAN-04	Cantargia AB	CANTA	Trial Data - Updated Results	Phase I/IIa - CANFOUR (BeNeLux/Scandinavia)	518737
06/01/2024	Rybrevant	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase I/Ib - CHRYSALIS-2 (w/Lazertinib)	519997
06/01/2024	Tecentriq	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase II - POPLAR vs. Docetaxel (After Platinum Failure)|Phase III - OAK (vs. Docetaxel)	518657
06/01/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Updated Results	Phase I/II - Epithelial Cancer	518643
06/01/2024	AB-106	Nuvation Bio, Inc.	NUVB	Trial Data - Updated Results	Phase II - TRUST-I (China)	518710
06/01/2024	Krazati	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - KRYSTAL-12	519573
06/01/2024	SY-5007	Shouyao Holdings Beijing Co Ltd		Trial Data - Top-Line Results	Phase I/II - RET-altered Advanced Solid Tumor (China)	519912
05/31/2024	Ivonescimab	Summit Therapeutics plc	SMMT	Trial Data - Top-Line Results	Phase III - HARMONi	519120
05/31/2024	Amivantamab SC	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase III - PALOMA-3	519541
05/31/2024	Sacituzumab Tirumotecan	Sichuan Kelun Pharmaceutical Co Ltd.	002422	Trial Data - Updated Results	Phase II - Advanced/Metastatic (China)	518965
05/31/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Updated Results	Phase III - EVOKE-01	519495
05/31/2024	Rybrevant	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase III - MARIPOSA	517846
05/31/2024	Lorbrena	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - CROWN (vs. Crizotinib)	519512
05/31/2024	Lazertinib	Genosco, Inc.		Trial Data - Top-Line Results	Phase III - PALOMA-3	520055
05/31/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase II - ICARUS-LUNG01	518828
Osteoporosis / Osteopenia						
06/01/2024	FKS518	Fresenius SE & Co. KGaA	FSNUY	Trial Data - Top-Line Results	Phase III - LUMIADE-3	519007
Osteosarcoma						
06/03/2024	HS-20093	GSK plc	GSK	Trial Data - Top-Line Results	Phase II - ARTEMIS-002 (China)	519068
06/01/2024	ZN-c3	Zentalis Pharmaceuticals	ZNTL	Trial Data - Final Results	Phase I/II - ZN-c3-003 (w/Gemcitabine)	517750
Ovarian Cancer						

06/03/2024	TILT-123	TILT Biotherapeutics Ltd.		Trial Data - Updated Results	Phase I - PROTA	518903
06/03/2024	Oregovomab	Shenzhen Hepalink Pharmaceutical Group Co., Ltd.	002399	Trial Data - Top-Line Results	Phase III - FLORA-5	518503
06/03/2024	DEP-SN38	Starpharma Holdings Limited	SPL	Trial Data - Final Results	Phase I/II - UK Hospitals	518151
06/03/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - ATHENA (w/Rubraca)	519959
06/03/2024	Lynparza	AstraZeneca PLC	AZN	Trial Data - Top-Line Results	Phase III - L-MOCA (Monotherapy)	518527
06/03/2024	Elahere	AbbVie Inc.	ABBV	Trial Data - Retrospective Analysis	Phase I - FOLR1-Positive|Phase III - FORWARD I|Phase III - MIRASOL (FRa-High Platinum-Resistant)|Phase III - SORAYA	518619
06/03/2024	Elahere	AbbVie Inc.	ABBV	Trial Data - Updated Results	Phase III - MIRASOL (FRa-High Platinum-Resistant)	518620
06/03/2024	PM-8002	BioNTech SE	BNTX	Trial Data - Top-Line Results	Phase Ib/IIa - PK/PD Study	519834
06/03/2024	Rubraca	pharma&		Trial Data - Final Results	Phase III - ATHENA (w/Opdivo)	518537
06/01/2024	APX-003	Pyxis Oncology	PYXS	Trial Data - Updated Results	Phase III - SCORES Study	519674
06/01/2024	Ceralasertib	AstraZeneca PLC	AZN	Trial Data - Top-Line Results	Phase II - CAPRI	518692
Pancreatic Cancer						
06/04/2024	AMP945	Amplia Therapeutics Limited	ATX	Trial Data - Updated Results	Phase Ib/IIa - ACCENT	517828
06/03/2024	HyLeukin	NeoImmuneTech, Inc.	950220	Trial Data - Updated Results	Phase Ib/IIa - KEYNOTE A60	519829
06/02/2024	IBI-389	Innovent Biologics, Inc.	1801	Trial Data - Top-Line Results	Phase I - w/Sintilimab (China)	519920
06/01/2024	SHR3162	Jiangsu Hengrui Pharmaceuticals	600276:SS	Trial Data - Top-Line Results	Phase I - w/mFolirinox (China)	518923
06/01/2024	MK-0482	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase I - +/-Pembrolizumab	519551
06/01/2024	Loqtorzi	Coherus BioSciences, Inc.	CHRS	Trial Data - Top-Line Results	Phase II - w/YH003 (Melanoma & PDAC)	519558
06/01/2024	BXCL701	BioXcel Therapeutics, Inc.	BTAI	Trial Data - Top-Line Results	Phase II - EXPEL PANC (w/Keytruda)	519620
06/01/2024	ADC-1013	Alligator Bioscience AB	ATORX	Trial Data - Updated Results	Phase Ib/II - OPTIMIZE-1 (EU)	518691
06/01/2024	CAN-04	Cantargia AB	CANTA	Trial Data - Updated Results	Phase I/IIa - CANFOUR (BeNeLux/Scandinavia)|Preclinical Studies	517816
06/01/2024	CPI-613	Cornerstone Pharmaceuticals, Inc.		Trial Data - Top-Line Results	Phase I/II - w/FOLFIRINOX	519532
06/01/2024	Avutometinib	Verastem, Inc.	VSTM	Trial Data - Updated Results	Phase I/II - RAMP205	518569
06/01/2024	Onivyde	Ipsen SA	IPSEY	Trial Data - Updated Results	Phase III - NAPOLI 3	518590
06/01/2024	Irinotecan Liposome (CSPC)	CSPC Pharmaceutical Group Limited	1093	Trial Data - Top-Line Results	Phase II - HE072-CSP-004 (China)	519070
06/01/2024	FG-M108	FutureGen Biopharm		Trial Data - Top-Line Results	Phase I - Dose Escalation/Expansion (China)	519913
Peripheral T-Cell Lymphoma (PTCL) - NHL						
06/03/2024	Adcetris	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase II -	518499
06/03/2024	Xpovio	Karyopharm Therapeutics	KPTI	Trial Data - Updated Results	Phase Ib - TOUCH	517791
06/03/2024	Xpovio	Karyopharm Therapeutics	KPTI	Trial Data - Updated Results	Phase Ib - TOUCH	518655

Primary Central Nervous System Lymphoma (PCNSL) - NHL						
06/03/2024	Yescarta	Gilead Sciences, Inc.	GILD	Trial Data - Top-Line Results	Phase I - w/Fludarabine + Cyclophosphamide	518702
06/02/2024	Rozlytrek	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase I/II - STARTRK-NG|Phase II - STARTRK-2|Phase II - TAPISTRY	520178
Prostate Cancer						
06/03/2024	Imdelltra	Amgen, Inc.	AMGN	Trial Data - Top-Line Results	Phase Ib - DeLLpro-300	518386
06/03/2024	ARV-766	Novartis AG	NVS	Trial Data - Updated Results	Phase I/II - w/Abiraterone	517705
06/03/2024	JNJ-69086420	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase I - CR108817	517881
06/02/2024	FG-3246	FibroGen, Inc.	FGEN	Trial Data - Top-Line Results	Phase Ib/II - w/ Enzalutamide (Xtandi)	517698
06/02/2024	PF-07248144	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase I - KAT6	519630
06/02/2024	64Cu-SAR-bisPSMA	Clarity Pharmaceuticals		Trial Data - Updated Results	Phase I/II - COBRA	519080
06/02/2024	PF-06821497	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase I/II - SCLC/FL/CRPC/DLBCL	518866
06/02/2024	Pluvicto	Novartis AG	NVS	Trial Data - Top-Line Results	Phase I - Progressive Metastatic CRPC	518800
06/02/2024	Pluvicto	Novartis AG	NVS	Trial Data - Updated Results	Phase II - TheraP	518802
06/02/2024	SHR3680	Jiangsu Hengrui Pharmaceuticals	600276:SS	Trial Data - Top-Line Results	Phase II - w/Docetaxel	518751
06/02/2024	SHR3680	Jiangsu Hengrui Pharmaceuticals	600276:SS	Trial Data - Updated Results	Phase III - HSPC	518752
06/02/2024	ODM-209	Orion Biotechnology Canada Ltd.		Trial Data - Top-Line Results	Phase I/II - STESIDES	519582
06/02/2024	HP-518	Hinova Pharmaceuticals Inc.		Trial Data - Top-Line Results	Phase I - Safety and Pharmacokinetics (AUS)	519003
06/02/2024	Talzenna	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - TALAPRO-2	517965
06/02/2024	Talzenna	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - TALAPRO-2	518584
06/02/2024	Talzenna	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - TALAPRO-2	518585
06/02/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Subgroup Analysis	Phase III - KEYLYNK-010	518631
06/02/2024	Nubeqa	Bayer AG	BAYN	Trial Data - Retrospective Analysis	Phase III - ARAMIS (nmCRPC)	518615
06/02/2024	Nubeqa	Bayer AG	BAYN	Trial Data - Retrospective Analysis	Phase III - ARASENS	518616
06/02/2024	Xtandi	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase III - TALAPRO-2	517966
06/02/2024	Xtandi	Astellas Pharma, Inc.	4503:JP	Trial Data - Retrospective Analysis	Phase III - EMBARK	518541
06/02/2024	Xtandi	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase III - ENZAMET	518542
06/01/2024	Xtandi	Astellas Pharma, Inc.	4503:JP	Trial Data - Top-Line Results	Phase III - w/Abiraterone/Prednisone (Alliance for Clinical Trials in Oncology)	518539
06/01/2024	Xtandi	Astellas Pharma, Inc.	4503:JP	Trial Data - Retrospective Analysis	Phase III - EMBARK	518540
06/01/2024	Jevtana	Sanofi	SNY	Trial Data - Top-Line Results	Phase II - CHAARTED2	519581

06/01/2024	Zytiga	Johnson & Johnson	JNJ	Trial Data - Top-Line Results	Phase III - w/Enzalutamide/Prednisone (Alliance for Clinical Trials in Oncology)	518511
06/01/2024	Verzenio	Eli Lilly and Company	LLY	Trial Data - Updated Results	Phase II/III - CYCLONE 2	518609
06/01/2024	Erleada	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase III - PRESTO	518607
06/01/2024	Pluvicto	Novartis AG	NVS	Trial Data - Updated Results	Phase III - PSMAfore	518803
06/01/2024	Pluvicto	Novartis AG	NVS	Trial Data - Updated Results	Phase III - PSMAfore	518801
Renal Cell Cancer (RCC)						
06/03/2024	Inlyta	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - KEYNOTE-426 (w/Pembrolizumab; First-Line)	520112
06/03/2024	Lenvima	Eisai Co., Ltd.	4523:JP	Trial Data - Updated Results	Phase III - CLEAR (First Line)	517772
06/03/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - KEYNOTE-426 (w/Axitinib; First-Line)	518636
06/03/2024	Tecentriq	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase III - IMmotion010 (Adjuvant Therapy)	518659
06/03/2024	Bavencio	Merck KGaA	MKKGY	Trial Data - Updated Results	Phase III - JAVELIN Renal 101	518680
06/02/2024	Lenvima	Eisai Co., Ltd.	4523:JP	Trial Data - Updated Results	Phase III - CLEAR (First Line)	518535
06/02/2024	Lenvima	Eisai Co., Ltd.	4523:JP	Trial Data - Top-Line Results	Phase I - w/belzutifan (China)	519906
06/02/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-67T (SC vs. IV)	518517
06/02/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-67T (SC vs. IV)	518519
06/02/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate 214 (w/Ipilimumab)	519666
06/02/2024	Welireg	Merck & Co., Inc.	MRK	Trial Data - Top-Line Results	Phase I - w/Lenvatinib (China)	518770
06/02/2024	Welireg	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase II - LITESPARK-013	518772
06/02/2024	Opdivo (Subcutaneous)	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase III - CheckMate-67T (SC vs. IV)	519723
06/02/2024	Zanzalintinib	Exelixis, Inc.	EXEL	Trial Data - Updated Results	Phase Ib/II - STELLAR-001	520326
06/02/2024	JTX-8064	Concentra Biosciences, LLC		Trial Data - Top-Line Results	Phase I/II - INNATE (w/JTX-4014)	520120
06/02/2024	JTX-4014	Concentra Biosciences, LLC		Trial Data - Top-Line Results	Phase I/II - INNATE (w/JTX-8064)	520143
06/01/2024	DFF332	Novartis AG	NVS	Trial Data - Updated Results	Phase I - CDFF332A12101	519059
Rhabdomyosarcoma						
06/02/2024	Torisel	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase III - IR Rhabdomyosarcoma (NCI)	518506
Skin Cancer - Squamous Cell Carcinoma (SCC)						
06/01/2024	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase II - KEYNOTE-629	518627
06/01/2024	IFx-Hu2.0	TuHURA Biosciences, Inc.		Trial Data - Updated Results		520215
Small Cell Lung Cancer (SCLC)						
06/04/2024	Surufatinib	HUTCHMED (China) Limited	HCM	Trial Data - Top-Line Results	Phase II - w/Anti-PD-1/L1 (China)	520087
06/03/2024	Tecentriq	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase III - BEAT-SC (China & Japan)	517964

06/03/2024	Socazolimab	Sorrento Therapeutics, Inc.	SRNEQ	Trial Data - Top-Line Results	Phase III - First Line SCLC (China)	518708
06/03/2024	Zepzelca	Jazz Pharmaceuticals plc	JAZZ	Trial Data - Updated Results	Phase Ib/II - w/Irinotecan	520052
06/03/2024	Tifcemalimab	Shanghai Junshi Biosciences Co., Ltd.	1877	Trial Data - Top-Line Results	Phase I/II - w/Toripalimab/Standard Chemotherapy (China)	518957
06/03/2024	HLX-10	Shanghai Henlius Biotech Co. Ltd.	2696	Trial Data - Updated Results	Phase III - ASTRUM-005 (ES-SCLC)	518852
06/03/2024	HPN328	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase I/II - +/-Atezolizumab	518882
06/03/2024	SC-0245	Shijiazhuang Sagacity New Drug Development Co., Ltd.		Trial Data - Top-Line Results	Phase I/II - SC0245-102 (w/Irinotecan)	519049
06/02/2024	Imdelltra	Amgen, Inc.	AMGN	Trial Data - Updated Results	Phase II - DeLLphi-301	519684
06/02/2024	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - ADRIATIC	519661
Soft Tissue Sarcoma - General						
06/01/2024	LVGN6051	Lyvgen		Trial Data - Top-Line Results	Phase I/II - w/Anlotinib	519534
06/01/2024	SQ3370	Shasqi, Inc.		Trial Data - Top-Line Results	Phase I/II - SQ3370-001	519745
06/01/2024	CEB-01	Cebiotex		Trial Data - Top-Line Results	Phase I - First-in-Human	519092
Solid Tumors						
06/04/2024	HB-0036	Huabo Biopharm		Trial Data - Top-Line Results	Phase I/II - China/US	520059
06/04/2024	ZGGS-15	Suzhou Zelgen Biopharmaceuticals Co., Ltd.		Trial Data - Top-Line Results	Phase I (China)	520068
06/04/2024	HB-700	HOOKIPA Pharma Inc.	HOOK	Trial Data - Preclinical Results	Preclinical Studies	520083
06/04/2024	ZG0895	Suzhou Zelgen Biopharmaceuticals Co., Ltd.		Trial Data - Top-Line Results	Phase I - Dose-Escalation & Expansion	520067
06/04/2024	SNK02	NKGen Biotech, Inc.	NKGNW	Trial Data - Top-Line Results	Phase I - Dose-Escalation	517764
06/04/2024	ATG-017	AstraZeneca PLC	AZN	Trial Data - Top-Line Results	Phase I - ERASER (Australia & U.S.)	517801
06/04/2024	HMPL-295	HUTCHMED (China) Limited	HCM	Trial Data - Updated Results	Phase I - China	520085
06/03/2024	MRG003	Lepu Biopharma Co., Ltd.	2157	Trial Data - Top-Line Results	Phase I/II - w/ HX008 (China)	518961
06/03/2024	23ME-00610	23andMe, Inc.		Trial Data - Updated Results	Phase I/IIa - Advanced Solid Malignancies	519001
06/03/2024	LM-108	LaNova Medicines		Trial Data - Top-Line Results	Phase I/II - +/- Pembrolizumab|Phase I/II - First-in-Human (FIH)|Phase I/II - LM108-01-103	518996
06/03/2024	D-1553	InventisBio, Inc.		Trial Data - Top-Line Results	Phase Ib/II - D1553-106/IN10018-602 (China)	519760
06/03/2024	IMM01	ImmuneOnco Biopharmaceuticals (Shanghai) Inc.	1541	Trial Data - Top-Line Results	Phase Ib/II - IMM01-04 (China)	518983
06/03/2024	HX008	Lepu Biopharma Co., Ltd.	2157	Trial Data - Top-Line Results	Phase I/II - w/ MRG003 (China)	520298
06/03/2024	MCLA-129	Merus N.V.	MRUS	Trial Data - Top-Line Results	Phase I/II - BTP-21711 (China)	518883
06/03/2024	MCLA-129	Merus N.V.	MRUS	Trial Data - Updated Results	Phase I/II - MCLA-129-CL01	518884
06/03/2024	SRK-181	Scholar Rock, LLC	SRRK	Trial Data - Updated Results	Phase I - DRAGON (+/-anti-PD-(L)1)	518890
06/03/2024	RP-2	Replimune Group Inc.	REPL	Trial Data - Updated Results	Phase I - RP2-001-18 -w/Nivolumab (UK)	518886

06/03/2024	BMC128	Biomica Ltd.		Trial Data - Top-Line Results	Phase I - POC - w/Opdivo (Israel)	518941
06/03/2024	Tuvusertib	Merck KGaA	MKKGY	Trial Data - Updated Results	Phase Ib - DDRiver Solid Tumors 301	517724
06/03/2024	Tuvusertib	Merck KGaA	MKKGY	Trial Data - Updated Results	Phase Ib - DDRiver Solid Tumors 301	517727
06/03/2024	AdAPT 001	EpicentRx, Inc.		Trial Data - Updated Results	Phase IIa/IIb - BETA PRIME	517837
06/03/2024	REGN7075	Regeneron Pharmaceuticals, Inc.	REGN	Trial Data - Updated Results	Phase I/II - w/Cemiplimab	517760
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase II - TROPION-PanTumor03	518829
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase I/II - TROPION-PanTumor02 (China)	518830
06/03/2024	DEP-SN38	Starpharma Holdings Limited	SPL	Trial Data - Final Results	Phase I/II - UK Hospitals	518160
06/03/2024	IN-10018	InxMed Co., Ltd.		Trial Data - Top-Line Results	Phase Ib/II - D1553-106/IN10018-602 (China)	519234
06/03/2024	Jemperli	GSK plc	GSK	Trial Data - Updated Results	Phase II - w/Capecitabine or 5-FU	519844
06/03/2024	Vitrakvi	Bayer AG	BAYN	Trial Data - Updated Results	Phase Ia - 14001 (Solids)|Phase II - NAVIGATE (TRK Fusion)	518695
06/03/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Top-Line Results	Phase I - POC - w/BMC128 (Israel)	517822
06/03/2024	RC88	RemeGen Ltd.	9995	Trial Data - Top-Line Results	Phase I/IIa - RC88-C001 (China)	519026
06/03/2024	EP0031	Ellipses Pharma Ltd.		Trial Data - Top-Line Results	Phase I/II - EP0031-101 (Global)	519014
06/03/2024	CBP-1008	Coherent Biopharma (Suzhou) Co., Ltd.		Trial Data - Updated Results	Phase I - CBP-1008-01 (China)	519011
06/03/2024	HS-20093	GSK plc	GSK	Trial Data - Top-Line Results	Phase I - ARTEMIS-001 (China)	519067
06/03/2024	CYCART-201	Celularity, Inc.	CELU	Trial Data - Preclinical Results	Preclinical Studies	519789
06/03/2024	MHB-088C	Minghui Pharmaceutical Ltd.		Trial Data - Top-Line Results	Phase I/II - MHB088C-CP001EN	519871
06/03/2024	PM-8002	BioNTech SE	BNTX	Trial Data - Top-Line Results	Phase Ib/IIa - PK/PD Study	519035
06/03/2024	PM-8002	BioNTech SE	BNTX	Trial Data - Updated Results	Phase Ib/IIa - PK/PD Study	519830
06/03/2024	GC-203	Shanghai Juncell Therapeutics		Trial Data - Top-Line Results	Phase I - Gynecologic Tumors (China)	517906
06/02/2024	LBL-024	Nanjing Leads Biolabs, Inc.		Trial Data - Top-Line Results	Phase I/II - China	519658
06/02/2024	CBP-1018	Coherent Biopharma (Suzhou) Co., Ltd.		Trial Data - Top-Line Results	Phase I - CBP-1018-101	519012
06/02/2024	BAT-8006	Bio-Thera Solutions Ltd.	688177	Trial Data - Updated Results	Phase I - Safety and Tolerability (China)	519660
06/02/2024	Vitrakvi	Bayer AG	BAYN	Trial Data - Updated Results	Phase I/II - SCOUT (Pediatric)|Phase Ia - 14001 (Solids)|Phase II - NAVIGATE (TRK Fusion)	519648
06/02/2024	Retevmo	Eli Lilly and Company	LLY	Trial Data - Updated Results	Phase I/II - LIBRETTO-121	517756
06/02/2024	MCLA-145	Merus N.V.	MRUS	Trial Data - Updated Results	Phase I - CL01/101	518746
06/02/2024	Balversa	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase II - RAGNAR	517896
06/02/2024	Dendrimer-Cabazitaxel	Starpharma Holdings Limited	SPL	Trial Data - Updated Results	Phase I/II - CTX-SPL9111-001 (UK & Australia)	518754
06/02/2024	HLX-10	Shanghai Henlius Biotech Co. Ltd.	2696	Trial Data - Updated Results	Phase II - MSI-H/dMMR	518851

06/02/2024	JAB-3312	Jacobio Pharmaceuticals Co. Ltd.	1167	Trial Data - Updated Results	Phase I/IIa - w/ JAB21822 (China)	519728
06/02/2024	CTL-002	CatalYm GmbH		Trial Data - Updated Results	Phase I/IIa - GDFATHER	517752
06/02/2024	BLU-222	Blueprint Medicines Corporation	BPMC	Trial Data - Updated Results	Phase I/II - VELA	518963
06/02/2024	IBI-389	Innovent Biologics, Inc.	1801	Trial Data - Top-Line Results	Phase I - w/Sintilimab (China)	519005
06/02/2024	LBL-007	BeiGene, Ltd.	BGNE	Trial Data - Top-Line Results	Phase I/II - w/Tislelizumab (China)	518998
06/01/2024	KT-253	Kymera Therapeutics, Inc.	KYMR	Trial Data - Updated Results	Phase I - KT253-AL-101	518999
06/01/2024	23ME-00610	23andMe, Inc.		Trial Data - Updated Results	Phase I/IIa - Advanced Solid Malignancies	519000
06/01/2024	TSC-204	TScan Therapeutics	TCRX	Trial Data - Top-Line Results	Phase I - w/TSC-200	519002
06/01/2024	JCXH-211	Immorna (Hangzhou) Biotechnology Co., Ltd.		Trial Data - Top-Line Results	Phase I - Safety and Tolerability	519004
06/01/2024	TU-2218	TiumBio Co., Ltd.	321550	Trial Data - Top-Line Results	Phase Ib/IIa - w/Pembrolizumab (U.S & South Korea)	518989
06/01/2024	GRWD5769	Grey Wolf Therapeutics, Ltd.		Trial Data - Top-Line Results	Phase I/II - EMITT-1	518990
06/01/2024	AU-007	Aulos Bioscience, Inc.		Trial Data - Updated Results	Phase I/II - First-in-Human	518993
06/01/2024	ABM-1310	ABM Therapeutics, Inc		Trial Data - Updated Results	Phase I - w/Cobimetinib	518994
06/01/2024	PRJ1-3024	MingMed Guangzhou Inming Biopharmaceutical Technology Co., Ltd.		Trial Data - Top-Line Results	Phase I/II - China	518995
06/01/2024	GT101	Grit Biotechnology, Inc.		Trial Data - Top-Line Results	Phase I - GT101-101 (China)	518986
06/01/2024	CPI-0209	MorphoSys AG	MOR	Trial Data - Updated Results	Phase I/II - Dose Escalation	518885
06/01/2024	Decoy20	Indaptus Therapeutics, Inc.	INDP	Trial Data - Updated Results	Phase I - Dose Escalation and Expansion	519185
06/01/2024	CS5001	CStone Pharmaceuticals (Suzhou) Co., Ltd	2616	Trial Data - Updated Results	Phase I - Dose Escalation/ Expansion (FIH) (Global)	517840
06/01/2024	CS5001	CStone Pharmaceuticals (Suzhou) Co., Ltd	2616	Trial Data - Updated Results	Phase I - Dose Escalation/ Expansion (FIH) (Global)	518988
06/01/2024	TJ-L14B/ABL503	I-Mab Biopharma Co., Ltd	IMAB	Trial Data - Updated Results	Phase I - 1001	518969
06/01/2024	WTX-124	Werewolf Therapeutics, Inc.	HOWL	Trial Data - Updated Results	Phase I/Ib - +/- Pembrolizumab	518970
06/01/2024	Olomorasib	Eli Lilly and Company	LLY	Trial Data - Updated Results	Phase Ia/Ib/II - w/KRAS G12C-Mutant Tumors	518968
06/01/2024	Tifcemalimab	Shanghai Junshi Biosciences Co., Ltd.	1877	Trial Data - Updated Results	Phase I - First-in-Human	518958
06/01/2024	ERAS-601	Erasca, Inc.	ERAS	Trial Data - Updated Results	Phase I/Ib - FLAGSHP-1	518956
06/01/2024	GD2-SADA	Y-mAbs Therapeutics Inc.	YMAB	Trial Data - Preclinical Results	Preclinical Studies	519586
06/01/2024	XTX-202	Xilio Therapeutics, Inc.	XLO	Trial Data - Updated Results	Phase I/IIa - FIH	518979
06/01/2024	LVGN6051	Lyvgen		Trial Data - Updated Results	Phase I - MK-3475-A31/KEYNOTE-A31	518981
06/01/2024	SNS-101	Sensei Biotherapeutics, Inc.	SNSE	Trial Data - Updated Results	Phase I/II - w/Libtayo	518984
06/01/2024	ATG-022	Antengene Corporation	6996	Trial Data - Updated Results	Phase I - CLINCH (Australia/China)	518985
06/01/2024	MRG004A	Lepu Biopharma Co., Ltd.	2157	Trial Data - Top-Line Results	Phase I/II - Advanced or Metastatic Solid Tumours	519358

06/01/2024	BT8009	Bicycle Therapeutics, plc	BCYC	Trial Data - Updated Results	Phase I/II - Duravelo-1	517726
06/01/2024	ZG-005	Suzhou Zelgen Biopharmaceuticals Co., Ltd.		Trial Data - Updated Results	Phase I/II - ZG005-001 (China)	518912
06/01/2024	ELI-002	Elicio Therapeutics		Trial Data - Top-Line Results	Phase Ib/II - AMPLIFY-7P	517778
06/01/2024	IOV-3001	Iovance Biotherapeutics, Inc.	IOVA	Trial Data - Preclinical Results	Preclinical Studies	519622
06/01/2024	MP0317	Molecular Partners AG	MOLN	Trial Data - Final Results	Phase I - First-in-Human (Netherlands/France)	518916
06/01/2024	NDI-101150	Nimbus Therapeutics, Inc.		Trial Data - Updated Results	Phase I/II - w/ Pembrolizumab	517799
06/01/2024	Sudocetaxel Zendusortide	Theratechnologies Inc.	THTX	Trial Data - Updated Results	Phase I - TH1902-CTR-0001	517763
06/01/2024	BA3071	BioAtla, Inc.	BCAB	Trial Data - Updated Results	Phase I/II - +/- Nivolumab	517728
06/01/2024	TransCon IL-2	Ascendis Pharma A/S	ASND	Trial Data - Updated Results	Phase I/II - I'll Believe Trial	518931
06/01/2024	KB-0742	Kronos Bio, Inc.	KRON	Trial Data - Updated Results	Phase I/II - MYC-Amplified	518933
06/01/2024	BGB-15025	BeiGene, Ltd.	BGNE	Trial Data - Top-Line Results	Phase Ia/Ib - w/Tislelizumab	518934
06/01/2024	CLN-619	Cullinan Therapeutics, Inc.	CGEM	Trial Data - Updated Results	Phase I - +/- Pembrolizumab	517731
06/01/2024	HFB3010	HiFiBiO Therapeutics		Trial Data - Top-Line Results	Phase I - HFB-301001-01	518925
06/01/2024	HFB-200301	HiFiBiO Therapeutics		Trial Data - Top-Line Results	Phase Ia/Ib - Dose Escalation & Expansion (w/Tislelizumab)	518926
06/01/2024	Tuvusertib	Merck KGaA	MKKGY	Trial Data - Top-Line Results	Phase Ib - DDRiver Solid Tumors 320 (w/M4076)	518936
06/01/2024	Tuvusertib	Merck KGaA	MKKGY	Trial Data - Updated Results	Phase Ib - DDRiver Solid Tumors 320 (w/M4076)	518937
06/01/2024	NGM707	NGM Biopharmaceuticals, Inc.	NGM	Trial Data - Updated Results	Phase I/II - w/ Pembrolizumab	518944
06/01/2024	STC-15	STORM Therapeutics Ltd		Trial Data - Top-Line Results	Phase I - PK/PD	518945
06/01/2024	Zelenirstat	Pacylex Pharmaceuticals		Trial Data - Final Results	Phase I/IIa - First in Human (Canada)	518947
06/01/2024	Botensilimab	Agenus Inc.	AGEN	Trial Data - Updated Results	Phase Ia/Ib - PK/PD Study (+/- Balstilimab)	518860
06/01/2024	IMC-002	ImmuneOncia Therapeutics, Inc.		Trial Data - Updated Results	Phase I - Dose-Escalation/Expansion (Korea)	518848
06/01/2024	MASCT-I	SYZ Cell Therapy Co.		Trial Data - Updated Results	Phase I - w/Ifosfamide	518845
06/01/2024	Lumakras	Amgen, Inc.	AMGN	Trial Data - Updated Results	Phase Ib/II - CodeBreak 101 (KRAS G12C Mutations; Monotherapy)	518870
06/01/2024	CTX-471	Compass Therapeutics Inc.	CMPX	Trial Data - Updated Results	Phase Ib - CTX-471-001	517711
06/01/2024	BI-1808	BioInvent International AB	BINV	Trial Data - Updated Results	Phase I/IIa Keynote-D20 (US/EU)	517780
06/01/2024	CLD-201	Calidi Biotherapeutics, Inc.	CLDI	Trial Data - Preclinical Results	Preclinical Studies	519597
06/01/2024	BT5528	Bicycle Therapeutics, plc	BCYC	Trial Data - Updated Results	Phase I/II - +/-Nivolumab	517725
06/01/2024	FF-10832	FUJIFILM Holdings Corp.	TYO:4901	Trial Data - Top-Line Results	Phase IIa - w/Keytruda	518816
06/01/2024	TAK-102	Noile-Immune Biotech, Inc.	4893	Trial Data - Updated Results	Phase I - GPC3-Expressing Tumors (Japan)	518819
06/01/2024	Nitric Oxide (AIT)	Beyond Air, Inc.	XAIR	Trial Data - Updated Results	Phase Ia/Ib - First-In-Human	519985

06/01/2024	CUE-102	Cue Biopharma, Inc.	CUE	Trial Data - Updated Results	Phase I - CUE-102-01	518812
06/01/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase II- DESTINY-PanTumor02	518755
06/01/2024	Debio 0123	Debiopharm S.A.		Trial Data - Top-Line Results	Phase I - Debio 0123-102	518769
06/01/2024	Welireg	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase I/II - LITESPARK-001	518771
06/01/2024	HyLeukin	NeoImmuneTech, Inc.	950220	Trial Data - Updated Results	Phase Ib/IIa - KEYNOTE A60	518798
06/01/2024	NP-G2-044	Novita Pharmaceuticals, Inc.		Trial Data - Top-Line Results	Phase I/II - w/Anti-PD-1 Therapy	518809
06/01/2024	Balversa	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase II - Asian Patients|Phase II - RAGNAR	518667
06/01/2024	Balversa	Johnson & Johnson	JNJ	Trial Data - Updated Results	Phase II - RAGNAR	518668
06/01/2024	Fadraciclib	Cyclacel Pharmaceuticals, Inc.	CYCC	Trial Data - Updated Results	Phase I/II - CYC065-101	518674
06/01/2024	Tevimbra	BeiGene, Ltd.	BGNE	Trial Data - Top-Line Results	Phase II - BGB-A317-212 (China)	518738
06/01/2024	Q901	Qurient Co., Ltd.	115180	Trial Data - Updated Results	Phase I/II - Dosage Exploration (U.S & Korea)	518733
06/01/2024	Rozlytrek	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase II - TAPISTRY	518700
06/01/2024	Opdivo	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase I/II - w/ BA3071	519682
06/01/2024	Zepzelca	Jazz Pharmaceuticals plc	JAZZ	Trial Data - Updated Results	Phase Ib/II - w/Irinotecan	518567
06/01/2024	Alecensa	Roche Holding AG	RHHBY	Trial Data - Top-Line Results	Phase I/II - Solid or CNS Tumors	518581
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06/01/2024	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase II - EV-202	518597
06/01/2024	JSKN003	Alphamab Oncology	9966	Trial Data - Top-Line Results	Phase I/II - PK/PD Study (China)	519024
06/01/2024	JSKN003	Alphamab Oncology	9966	Trial Data - Updated Results	Phase I - JSKN003-101 (AUS)	519025
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06/01/2024	VC-004	Jiangsu Vcare PharmaTech Co. Ltd.,		Trial Data - Top-Line Results	Phase I/II - VC004-101 (China)	519029
06/01/2024	ZGGS-18	Suzhou Zelgen Biopharmaceuticals Co., Ltd.		Trial Data - Top-Line Results	Phase I/II - ZGGS18-001 (China)	519031
06/01/2024	GT201	Grit Biotechnology, Inc.		Trial Data - Top-Line Results	Phase I/II - GRIT-CD-MED-CHN-001 (China)	519032
06/01/2024	IBI-343	Innovent Biologics, Inc.	1801	Trial Data - Top-Line Results	Phase Ia/Ib - CIBI343A101 (Australia)	519038
06/01/2024	ABBV-706	AbbVie Inc.	ABBV	Trial Data - Top-Line Results	Phase I - First-in-Human Study	518373
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06/01/2024	GI-102	GI Innovation		Trial Data - Top-Line Results	Phase I/IIa - GII-102-P101 (South Korea)	519061
06/01/2024	Docetaxel	CSPC Pharmaceutical Group Limited	1093	Trial Data - Top-Line Results	Phase I - Adults w/Advanced Solid Tumors	519058
06/01/2024	PM-1032	Biotheus Inc.		Trial Data - Top-Line Results	Phase I/IIa - China	519033

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06/01/2024	CRB-701	Corbus Pharmaceuticals Holdings, Inc.	CRBP	Trial Data - Updated Results	Phase I - Dose-Escalation (China)	519587
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06/01/2024	LTC-004	Leto Laboratories		Trial Data - Top-Line Results	Phase I - LTC004-101	519084
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06/01/2024	SPH5030	Shanghai Pharmaceuticals Holding Co., Ltd	601607	Trial Data - Top-Line Results	Early Phase I Study (China)	519086
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06/01/2024	GT316	Grit Biotechnology, Inc.		Trial Data - Top-Line Results	Phase I - GRIT-CD-CHN-316-002 (China)	519078
06/01/2024	WTX212	Westlake Therapeutics		Trial Data - Top-Line Results	Phase I - Reboot-101	519077
06/01/2024	Sigvotatug Vedotin	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase I - SGNB6A-001	518928
06/01/2024	Nemvaleukin Alfa	Mural Oncology plc	MURA	Trial Data - Updated Results	Phase II - ARTISTRY-3	518690
06/01/2024	Adcetris	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase II - w/Keytruda	518500
06/01/2024	RBS-2418	Riboscience LLC		Trial Data - Updated Results	Phase Ia/Ib - Dose Escalation/Expansion	519073
06/01/2024	HRS-1167	Merck KGaA	MKKGY	Trial Data - Top-Line Results	Phase I - HRS-1167-I-101 (China)	519020
06/01/2024	QL-301	QLSF Biotherapeutics		Trial Data - Top-Line Results	Phase I - QLF31907-101 (China)	519074
06/01/2024	CHS-114	Coherus BioSciences, Inc.	CHRS	Trial Data - Updated Results	Phase I/II - Dose Escalation/Expansion	518949
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06/01/2024	KSQ-4279	Roche Holding AG	RHHBY	Trial Data - Top-Line Results	Phase I - KSQ-4279-1101 (US)	517920
06/01/2024	SOMCL-15-290	CSPC Pharmaceutical Group Limited	1093	Trial Data - Top-Line Results	Phase I - Advanced Solid Tumors (China)	519091
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06/01/2024	SUPLEXA	Alloplex Biotherapeutics, Inc.		Trial Data - Top-Line Results	Phase I - FIH (Australia)	519099
06/01/2024	LB1410	L&L Biopharma Co., LTD.		Trial Data - Top-Line Results	Phase I - Keyplus-001 (China)	519098
05/31/2024	NB003	Ningbo Tai Kang Medical Technology Co., Ltd.		Trial Data - Top-Line Results	Phase I - Dose Ecalation/Expansion	519072
05/31/2024	Stivarga	Bayer AG	BAYN	Trial Data - Updated Results	Phase I/II - REGOMUNE	518566
05/31/2024	Amtagvi	Iovance Biotherapeutics, Inc.	IOVA	Trial Data - Updated Results	Phase II - IOV-COM-202	518611
05/31/2024	Relatlimab	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase I/II - RELATIVITY-048 (w/Nivolumab and BMS-986205 or Ipilimumab)	518689
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05/30/2024	NC410	NextCure, Inc.	NXTC	Trial Data - Top-Line Results	Phase Ib/II - w/KEYTRUDA	519368

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06/03/2024	Lete-cel	Adaptimmune Therapeutics plc	ADAP	Trial Data - Updated Results	Phase II - IGNYTE-ESO	518677
Tenosynovial Giant Cell Tumor (TGCT) / Pigmented Villonodular Synovitis (PVNS)						
06/04/2024	Vimseltinib	Deciphera Pharmaceuticals, Inc.	DCPH	Trial Data - Updated Results	Phase III - MOTION	518705
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06/03/2024	Retevmo	Eli Lilly and Company	LLY	Trial Data - Updated Results	Phase III - LIBRETTO-531	519893
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Triple-Negative Breast Cancer (TNBC)						
06/03/2024	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase I - TROPION-PanTumor01	518831
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06/03/2024	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase III - DESTINY-Breast04 (HER2-low)	518763
06/03/2024	Bavencio	Merck KGaA	MKKGY	Trial Data - Top-Line Results	Phase III - A-Brave	519875
06/02/2024	Cosela	G1 Therapeutics Inc.	GTHX	Trial Data - Updated Results	Phase II - w/ Sacituzumab Govitecan	518305
06/02/2024	myChoice CDx	Myriad Genetics, Inc.	MYGN	Trial Data - Updated Results	Phase II - Cisplatin vs. Paclitaxel	518726
06/02/2024	Bria-IMT	BriaCell Therapeutics Corp.	BCT	Trial Data - Retrospective Analysis	Phase I/IIa - w/Retifanlimab	519697
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06/01/2024	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Updated Results	Phase III - ASCENT (TNBC)	518644
Uterine (Endometrial) Cancer						
06/03/2024	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - DUO-E	518662
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06/03/2024	Jemperli	GSK plc	GSK	Trial Data - Retrospective Analysis	Phase III - RUBY	518703
06/03/2024	Jemperli	GSK plc	GSK	Trial Data - Updated Results	Phase III - RUBY	518704
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06/03/2024	Sintilimab	Innovent Biologics, Inc.	1801	Trial Data - Updated Results	Phase I/II - FRUSICA-1 (China)	518010
06/03/2024	Imlunestrant	Eli Lilly and Company	LLY	Trial Data - Updated Results	Phase Ia/Ib - EMBER	519946

06/03/2024	Fruzaqla	Takeda Pharmaceutical Co. Ltd.	TAK	Trial Data - Updated Results	Phase I/II - FRUSICA-1 (China)	517826
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06/01/2024	Kimmtrak	Immunocore, Ltd.	IMCR	Trial Data - Updated Results	Phase I/II - IMCgp100-102|Phase III - IMCgp100-202	518640
06/01/2024	Kimmtrak	Immunocore, Ltd.	IMCR	Trial Data - Updated Results	Phase I/II - IMCgp100-102	518641
06/01/2024	Kimmtrak	Immunocore, Ltd.	IMCR	Trial Data - Updated Results	Phase III - IMCgp100-202	518642
06/01/2024	Hepzato Kit (Drug)	Delcath Systems, Inc.	DCTH	Trial Data - Updated Results	Phase III - FOCUS	518531

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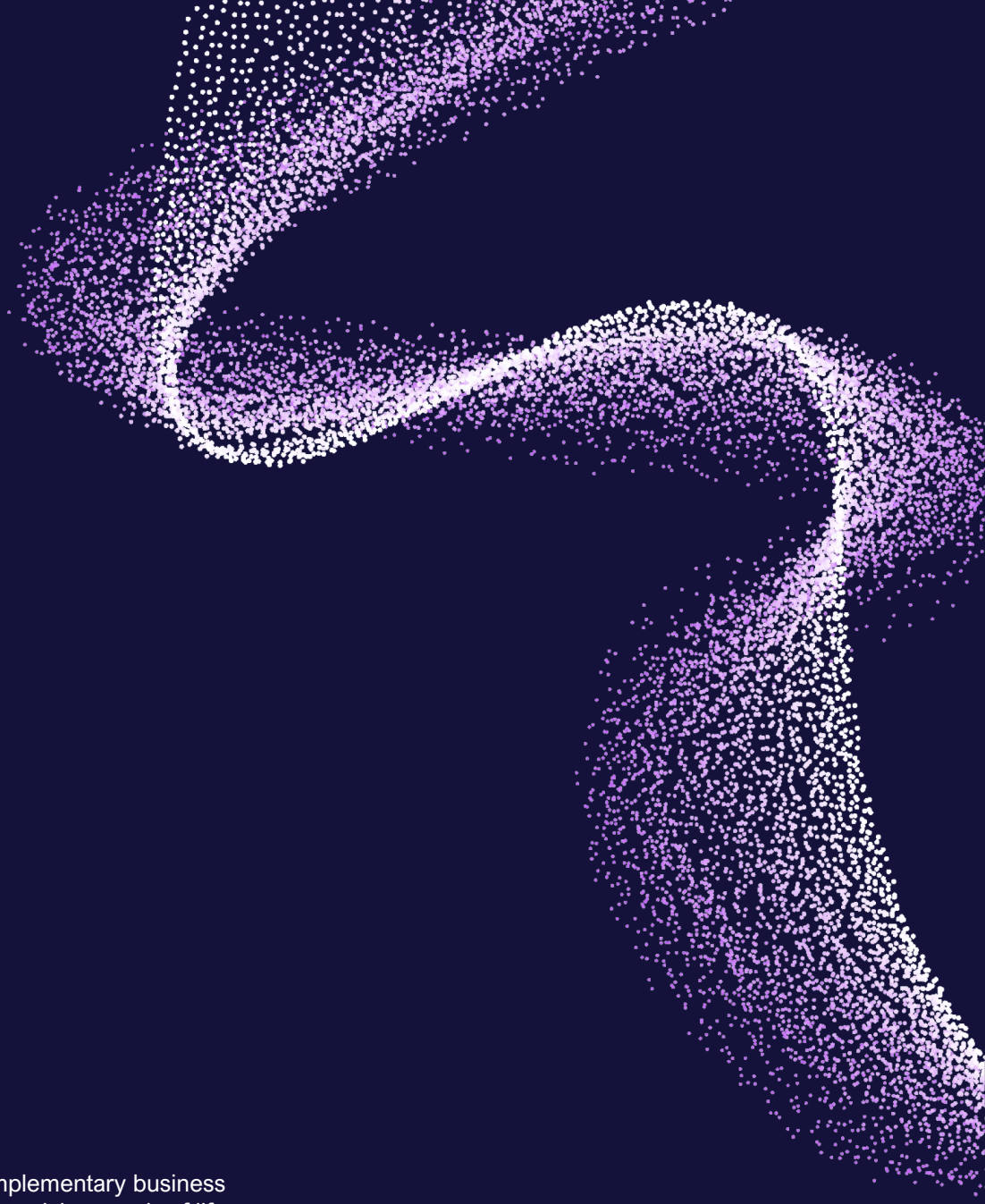

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