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Conference Report

2023 Pre-ASCO Report

May 2023

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Summary

Abstracts from the 2023 Annual Meeting of the American Society of Clinical Oncology (ASCO) were released May 25th at 5pm EDT. The 2023 ASCO meeting will be held in Chicago from June 2-6, 2023.

We have highlighted some key abstracts with analyses. Included at the end of the report is a list of the ASCO data events we have added from the Thursday release and Friday morning announcements. While this is just a brief overview, we will be available to discuss any data of interest in further detail. Please email Biomedtracker. Additionally, keep an eye out for our ASCO weekend updates and live-coverage when the meeting takes place.

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

- **June 4 – ASCO Weekend Update**
- **Shortly following the conference – Post-ASCO Report and Podcast**
- **June 19 – Post-ASCO Webinar**

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 BiomedSupport@sagientresearch.com.

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Breyanzi for Chronic Lymphocytic Leukemia (CLL)/Small Cell Lymphocytic Lymphoma (SLL) - NHL

Event Date:	05/25/2023
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase I/II - TRANSCEND-CLL-004
Market Group:	Oncology
Lead Company:	Bristol Myers Squibb Company (BMY)
Partner Companies:	N/A
Former Companies:	Celgene Juno Therapeutics
Change to Likelihood of Approval:	1%
Likelihood of Approval:	15% (4% Above Avg.)
Average Approval:	11%

	Treatment	Treatment
Treatment Description	Breyanzi (Primary Efficacy Analysis Set at DL2)	Breyanzi (Full Efficacy Set at DL2)
Number of Patients	49	87
Number of Evaluable Patients	N/A	N/A
Complete Response Rate ***(Endpoint=Primary)***	18.4 % (P=0.0006)	18.4 %
Objective Response Rate ***(Endpoint=N/A)***	42.9 % (P=0.3931)	47.1 %
uMRD in Blood ***(Endpoint=N/A)***	63.3 %	64.4 %
uMRD in Marrow ***(Endpoint=N/A)***	59.2 %	58.6 %

Progression-Free Survival ***(Endpoint=N/A)***	11.9 Months	18.0 Months

Bristol Myers Squibb announced the presentation of data from the primary analysis of the Phase I/II TRANSCEND CLL 004 study of Breyanzi (lisocabtagene maraleucel) in patients with relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting. The abstract entitled "Lisocabtagene maraleucel (liso-cel) in R/R chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL): Primary analysis of TRANSCEND CLL 004" will be presented at the meeting on June 6, 2023.

Data from this study were last seen in January 2023.

Context

Results from TRANSCEND CLL 004 will be discussed with health authorities.

Design

TRANSCEND CLL 004 is a Phase I/II open-label, multicenter study evaluating Breyanzi in patients with relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma. The Phase I dose escalation portion of the study assessed the safety and recommended dose for the subsequent Phase II expansion cohort. The Phase II portion of the study is evaluating Breyanzi at the recommended dose from the Phase I monotherapy arm.

The TRANSCEND CLL 004 trial included a broad population of patients with relapsed or refractory CLL or SLL with high unmet need who had received at least two prior lines of therapy, including a BTKi (n=117). The prespecified primary efficacy analysis set (PEAS; n=49) consisted of a subset of patients who had experienced disease progression following treatment with a BTKi and failure of BCL2i-based regimens, representing a patient population with advanced and aggressive disease, and who were treated with the target dose of 100 x 10^6 CAR-positive viable T-cells of Breyanzi.

Endpoints

The primary endpoint of the Phase II portion of the study was complete response rate, including complete remission with incomplete bone marrow recovery, based on independent review committee according to the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) 2018 guidelines.

Results

High rates of undetectable minimal residual disease (uMRD) were observed across patients treated with Breyanzi, with a uMRD rate 63.3% in the blood (95% CI: 48.3-76.6) and 59.2% in the bone marrow (95% CI: 44.2-73.0), which was associated with an increase in progression-free survival. The overall response rate (ORR) was 42.9% (95% CI: 28.8-57.8; p=0.3931), with a median duration of response of 35.3 months (11.01-NR). Data were consistent between the PEAS and the broad patient population evaluated in the study, including heavily pretreated patients with a median of five prior lines of therapy (2 – 12) and high-risk disease, with a CR rate of 18.4% (95% CI: 10.9-28.1), demonstrating the clinical benefit of Breyanzi for a broad patient population with relapsed or refractory CLL or SLL.

At a median follow-up of 21.1 months, results show that Breyanzi delivered statistically significant complete response (CR) rates, the study's primary endpoint, in 18.4% of patients in the primary efficacy analysis set (95% CI: 8.8-32; p=0.0006).

Most Common Adverse Events

Among all treated patients in the study (n=117), including subgroups of heavily pretreated patients, Breyanzi exhibited a manageable safety profile, and no new safety signals were observed. Any grade cytokine release syndrome (CRS) occurred in 84.6% of patients, with Grade 3 CRS occurring in 8.5% of patients. No Grade 4/5 CRS events were reported. Any grade neurologic events (NE) were reported in 45.3% of patients, with Grade 3 NE reported in 17.9% of patients and one case (0.9%) of Grade 4 NE reported. No Grade 5 NE were reported. Among patients who achieved a CR, no disease progression or deaths were observed, with median duration of response not reached.

Conclusion

Per the abstract, Breyanzi demonstrated durable CR/CRi, high uMRD rates, and a manageable safety profile in pts with heavily pretreated, high-risk R/R CLL/SLL and high unmet need.

Comment

CAR T-cell therapy has shown impressive success within B-cell malignancies with approvals for aggressive diseases such as diffuse large B cell lymphoma (DLBCL) and acute lymphoblastic leukemia, however, surprisingly it's story in chronic lymphocytic leukemia (CLL) has, until now, been largely underwhelming. Data released in the ASCO 2023 abstract from the Phase I/II TRANSCEND-004 trial, investigating Breyanzi - Bristol Myers Squibb's CD19-directed CAR T-cell therapy, in multi-refractory CLL patients mark the first positive results for a CAR-T cell therapy in the CLL space. In January this year, it was announced the study met the primary endpoint of complete response rate compared to historical control in the prespecified subset of patients with relapsed/refractory CLL that was refractory to a BTK inhibitor and pretreated with a BCL-2 inhibitor. The release of numerical data demonstrates 18.4% of patients, both in the primary efficacy cohort and broad patient population group, achieved complete responses, with median duration of response unreached at 21.1 months follow up. The median number of prior therapies for this population was five, and an achievement of an 18.4% complete response rate in such highly-refractory patients is remarkable. Despite current therapies providing patients with life expectancies which rival that of an age-matched general population, the potential to offer deep and durable remissions remains a major area of unmet need in CLL - especially within patients who have failed on both a BTKi and BCL2i. Armed with these data from TRANSCEND, Breyanzi looks primed to potentially address this need and reform the heavily pre-treated landscape for CLL patients.

However, TRANSCEND's design may cause bumps in Breyanzi's road to approval. The single-arm nature of the trial may pose as a limitation, with FDA chief Califf calling for a reform of the accelerated approval pathway amongst other top officials advocating for limited use of single arm trials. Although Califf did recognise that single-arm trials can sometimes be necessary, such as in rare diseases where there are no other effective treatments for comparison, which may act as a saving grace for TRANSCEND. Another concern for the trial is that the primary efficacy data is derived from a small sample population of only 49 patients. Breyanzi previously achieved accelerated approval in DLBCL based off response data from a single arm trial, however the population size much larger with 256 evaluable patients. The clinical benefit of Breyanzi in DLBCL was also arguably a lot more prominent, with a 53% complete response rate and overall response rate of 73% from this trial. In the TRANSCEND data from the ASCO abstract, the overall response rate in the primary efficacy group was reported at 42.9% and was not significant. Whilst the complete response data looks promising to offer transformative outcomes for heavily relapsed hard-to-treat CLL patients, the complete dataset may not be compelling enough to outweigh the trial pitfalls to secure Breyanzi accelerated approval. It may come unexpectedly if the FDA calls for more data in a larger patient population.

If Breyanzi is to be approved, it will enter the market largely uncontested, with currently limited treatment options for CLL patients who progress following BTKi and BCL2i treatment. Eli Lilly's Jaypirca is currently in Phase III investigation for this patient population and has shown impressive data thus far, and non-covalent BTKis are beginning to look set to become the standard of care treatment for BTKi and BCL2i pre-treated patients, following their approval. This would likely leave Breyanzi reserved for fourth line and beyond. However, where Jaypirca struggles to compete with Breyanzi is in its complete response data, which will be the key differentiator for Breyanzi and likely the driver behind physicians choice to prescribe the CAR T therapy as a third-line option.

Bristol Myers Squibb (BMS) announced at the 41st annual JP Morgan conference this year that they plan to file for approval of Breyanzi in CLL in the upcoming year. Considering Breyanzi's launch into both European and Japanese markets for DLBCL, it can be assumed BMS will strategize the same approach to launch Breyanzi into all major

markets for CLL as well. The therapy, however, may face more of a struggle to pull uptake in single payer healthcare markets due to the high cost of CAR T-cell therapy. Strong evidence that Breyanzi can offer durable remissions will be imperative to justify the high cost treatment in these countries. In January 2023, Yescarta, a CD19-directed CAR T-cell therapy, gained a positive recommendation from the National Institute for Health and Care Excellence (NICE) for its use in refractory DLBCL, marking the first positive recommendation for a personalised immunotherapy. This was supported by its impressive data in a poor prognosis and limited treatment disease space. Though Breyanzi's complete response data is compelling considering the current lack of deep remissions attained with the current CLL treatments, it remains questionable whether the complete dataset is strong enough to warrant cost effectiveness for single payer systems. Nevertheless, these results from TRANSCEND represent one of the first strong indicators for the plausibility of remission in multi-refractory patients and mark a breakthrough for CAR T-cell therapy within the CLL space. We are raising the LOA by 1%.

Source:

Business Wire 05/25/2023 (BMY)
American Society of Clinical Oncology (ASCO) (Abstract 7501)
Citeline Analysis 05/26/2023

Venclexta for Chronic Lymphocytic Leukemia (CLL)/Small Cell Lymphocytic Lymphoma (SLL) - NHL

Event Date:	05/25/2023
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase III - A041702 (w/Ibrutinib + Obinutuzumab; NCI)
Market Group:	Oncology
Lead Company:	AbbVie Inc. (ABBV)
Partner Companies:	Roche (RHHBY)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

	Comparator	Treatment
Treatment Description	Ibrutinib + Obinutuzumab	Ibrutinib + Venetoclax + Obinutuzumab
Number of Patients	N/A	N/A
Number of Evaluable Patients	N/A	N/A
Median Progression-Free Survival at 14 Months	87.5 %	85 %
Events Observed	29	35

The abstract entitled "Results of a phase 3 study of IVO vs IO for previously untreated older patients (pts) with chronic lymphocytic leukemia (CLL) and impact of COVID-19 (Alliance)" will be presented at ASCO on June 2-6, 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.

Context

The Alliance DSMB approved release of data on November 4, 2022 after meeting the protocol defined futility threshold at the second planned event-driven interim analysis. Data were locked on December 15, 2022.

Design

Alliance for Clinical Trials in Oncology A041702 is a multicenter trial designed to evaluate if IVO with response-guided

discontinuation of I improves progression free survival (PFS) versus IO with indefinite I in treatment-naïve, older CLL pts. IO is given in standard fashion, and in the IVO arm V is added at C3D1 and continued until C14D28. After 14 cycles, pts undergo response evaluation including CT scans and bone marrow biopsy with central MRD assessment by flow cytometry. Pts in IVO arm with uMRD CR discontinue I; all others continue I until progression or unacceptable toxicity. Eligible pts were age ≥70 years (amended to ≥65). Pts had CrCl ≥ 40 mL/min, bilirubin ≤ 1.5 x ULN, and no other life-limiting intercurrent illness. Pts were stratified based on Rai stage and +/- del17p13.1 by FISH, and randomized 1:1 to IO:IVO. With 431 evaluable pts, the trial had 90% power to detect significant improvement in PFS using a one-sided log-rank test with one-sided type 1 error rate of 2.5%.

Results

Between January 4, 2019 and July 15, 2022, 465 pts were registered (IO:232, IVO:233). Median age was 74; 67% of pts were men. Rai stage 3-4 was seen in 55% and del17p in 13%.

With median follow-up of 14 months, PFS of IO was 87.5% compared to 85% on IVO. Events were observed in 29 pts on IO (4 progressions, 23 deaths, 2 pts started other therapy) and 35 on IVO (7 progressions, 28 deaths). The predefined futility boundary was crossed, with a hazard ratio (HR) of 1.20 (95% CI: 0.73-1.97) in favor of IO. COVID-19 was the leading cause of death in both arms, (11 COVID-19 deaths on IO, 19 on IVO), with 13 and 11 additional deaths from other causes, respectively. Censoring pts with COVID-19 related deaths, PFS HR is 0.82 (95% CI: 0.44-1.53) in favor of IVO.

Most Common Adverse Events

Grade 3+ toxicity and discontinuation in year 1 of therapy were similar between arms.

Conclusion

This study demonstrates that PFS for IVO is not superior to IO for treatment-naive older CLL pts in the setting of the COVID-19 pandemic. Study treatment is ongoing, and long-term follow-up will determine if there are advantages to IVO, with special attention to MRD and therapy discontinuation.

Comment

These results from the Phase III Alliance trial come as a disappointment, with the triplet combination of Imbruvica, Venclexta and Gazyva failing to improve progression free survival compared to the doublet of Venclexta and Gazyva in first-line chronic lymphocytic leukemia (CLL). The disruption the COVID-19 pandemic has had on the data from this trial leaves uncertainty for the success of this combination regimen. The censoring of patients with COVID-19 related deaths leading to a shift in PFS HR in favor of IVO is a positive indication that the triplet regimen still has potential to improve patient outcomes and warrants further investigation. Yet, the adjusted PFS HR of 0.82 suggests only moderate benefit.

The safety information obtained, despite the tribulations of this trial, is positive, with grade 3+ toxicity and discontinuation rates reported to be similar between both arms. This could be considered a small win for the combination therapy as it may work towards dispelling physician concerns over the additional toxicity that comes with using a triplet regimen. However, unless long-term follow-up data can reveal IVO to significantly improve undetectable minimal residual disease and extend progression free survival, these safety data remain trivial.

In 2022, the Phase III GLOW trial, which evaluates Imbruvica and Venclexta combination in treatment naïve CLL patients, met its primary endpoint and subsequently secured European approval. This represented the first BTKi and BCL2i combination regimen to enter the market. However, its uptake has been lackluster, with many physicians expressing concerns of front-loading treatment. Moreover, AbbVie has not announced any plans to file a regulatory submission for the doublet regimen to the FDA. Considering the underwhelming traction the doublet therapy has received across markets, it begs to question how successful a triplet regimen would be. In order for IVO to

differentiate itself and prove to be a compelling therapy it will likely need to demonstrate deep and durable remissions for patients, which cannot be obtained by the use of Imbruvica monotherapy or Venclexta and Gazyva combination. Long-term data will be imperative to determine this, however, considering these results at ASCO, it does not look promising.

Other triplet BTKi + BCL2i + CD20 monoclonal antibody regimens are also being evaluated in CLL and have also demonstrated disappointing results thus far. The triplet regimen of Calquence, Gazyva and Venclexta is being investigated in the front-line and relapsed/refractory settings in various Phase II and Phase III trials. In late 2021, a Phase II study exploring this triplet regimen in frontline patients failed to meet its primary endpoint of undetectable minimal residual disease in the bone marrow. Collectively, the data does not currently bode well for triplet regimens and their future within the CLL space is uncertain. The Phase III ACE-CL-311 trial investigating Calquence, Gazyva and Venclexta in front-line CLL patients is due to read-out this year and may serve as a clearer indication for how triplet regimens will fit into the CLL treatment landscape.

Source:

American Society of Clinical Oncology (ASCO) 05/25/2023 (Abstract 7500)
Citeline Analysis 05/26/2023

Vectibix for Colorectal Cancer (CRC)

Event Date:	05/25/2023
Event Type:	Trial Data - Final Results (Clinical Analysis)
Trial Name:	Phase III - PARADIGM
Market Group:	Oncology
Lead Company:	Amgen, Inc. (AMGN)
Partner Companies:	Beta Pharma Takeda Pharmaceutical (TAK)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

The abstract entitled "Efficacy of panitumumab in patients with left-sided disease, MSS/MSI-L, and *RAS*/*BRAF* WT: A biomarker study of the phase III PARADIGM trial." will be presented at ASCO on June 2-6, 2023.

Data from this study were last seen in April 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

Baseline plasma circulating tumor DNA (ctDNA; >10 ng/mL and >10 nM DNA) from patients (pts) enrolled in the biomarker study was assessed using a custom panel (PlasmaSELECT-R 91, PGDx). The efficacy (OS, progression-free survival [PFS], response rate [RR], and curative resection rate [R0]) of PAN plus mFOLFOX6 compared with BEV plus mFOLFOX6 according to *RAS*, *BRAF (V600E)*, and MSI status and primary tumor location was evaluated.

Results

Among 802 pts in the full analysis set, 733 (91%) had evaluable pretreatment samples for ctDNA analysis. Of these pts, 53 (7.2%) and 78 (10.6%) pts had *RAS* and *BRAF* (*V600E*) mutations, respectively, and 20 (2.7%) pts had MSI high (MSI-H) status. In left-sided mCRC pts with MSS/MSI-L and *RAS*/*BRAF* WT, OS tended to be longer with PAN vs BEV (40.6 [95% CI, 36.3-44.4] vs 34.8 [95% CI, 31.3-41.2] months, respectively; HR, 0.79 [95% CI, 0.64–0.97]). Although PFS was comparable between PAN (13.6 months [95% CI, 12.6–15.3]) and BEV (12.6 months [95% CI, 11.3–14.1]; HR, 0.95 [95% CI, 0.77–1.17]), RR and R0 resection rates were higher with PAN (RR: 83.2% [95% CI, 78.0–87.6]; R0: 18.8% [95% CI: 14.2–24.1]) compared with BEV (RR: 66.4% [95% CI, 60.0–72.3]; R0: 10.0% [95% CI: 6.5–14.5]). OS was similar or inferior to PAN vs BEV regardless of the primary sidedness in pts with MSI-H or *RAS*/*BRAF* mutations.

Conclusion

These results support PAN + mFOLFOX6 as a first-line therapy for left-sided pts with MSS/MSI-L and *RAS*/*BRAF* WT

Comment

Set up to demonstrate Vectibix's superiority to bevacizumab when added to first-line chemotherapy in *KRAS/NRAS* wild-type colorectal cancer, the PARADIGM trial led to slightly more questions than answers. Results from the trial were presented one year ago at ASCO 2022 and showed that Vectibix + mFOLFOX6 led to a statistically significant OS improvement in both the left-sided primary tumor population, as well as in the intent-to-treat population versus bevacizumab + mFOLFOX6. OS is confounded by subsequent therapies, although the post-progression systemic treatments were well balanced between the trial's arms. However, median PFS values observed in PARADIGM were not different in the two arms of the trial, and sidedness was not used as a stratification factor. In addition, the trial recruited only Japanese patients, and although the study's authors indicated that the results should not differ in Western patients, the applicability of the results to the Western population may need to be verified.

In a bid to assess potential biomarkers and tease out any patient populations that may benefit more from the addition of Vectibix to mFOLFOX, multi-omics analyses of plasma circulating tumor DNA samples were conducted, with the results presented at the ASCO 2023 meeting. The data indicate that left-sided mCRC patients with MSS/MSI-L and *RAS/BRAF* WT tumors benefited more from the addition of Vectibix (mOS: 40.6 months vs. 34.8 months for bevacizumab), thus supporting the use of Vectibix over bevacizumab in this patient population. In MSI-H or *RAS/BRAF* mutated tumors (regardless of sidedness), the OS values in the Vectibix arm were similar or inferior to those for bevacizumab. It remains to be seen, however, whether physicians will make the switch from what has been the standard of care in the first-line *RAS/BRAF* WT or left side setting—bevacizumab + chemotherapy—to branded and thus premium-priced Vectibix, especially as bevacizumab biosimilars are now widely available and the therapy is deeply entrenched in the treatment algorithm.

Source:

American Society of Clinical Oncology (ASCO) 05/25/2023 (Abstract 3508)
Citeline Analysis 05/26/2023

Enhertu for Colorectal Cancer (CRC)

Event Date:	05/25/2023
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - DESTINY-CRC02
Market Group:	Oncology
Lead Company:	Daiichi Sankyo Co., Ltd. (4568)
Partner Companies:	AstraZeneca (AZN)
Former Companies:	N/A
Change to Likelihood of Approval:	5%
Likelihood of Approval:	18% (7% Above Avg.)
Average Approval:	11%

The abstract entitled "Trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-overexpressing/amplified (HER2+) metastatic colorectal cancer (mCRC): Primary results from the multicenter, randomized, phase 2 DESTINY-CRC02 study." will be presented at ASCO on June 2-6, 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

This was a multicenter Phase II study. Eligible patients (pts) had centrally confirmed HER2+ (immunohistochemistry [IHC] 3+ or IHC 2+/in situ hybridization [ISH]+) mCRC. Pts with *RAS* wild-type (wt) or mutant (m) mCRC were eligible. Pts had received prior standard therapy, unless contraindicated; prior anti-HER2 therapy was allowed. In stage 1, 80 pts were randomized 1:1 to 5.4 (n = 40) or 6.4 (n = 40) mg/kg T-DXd Q3W. In stage 2, an additional 42 pts received 5.4 mg/kg T-DXd.

Endpoints

Primary endpoint was confirmed objective response rate (cORR) by blinded independent central review (BICR). Secondary endpoints included duration of response (DoR), progression-free survival (PFS), overall survival (OS), and safety.

Results

At data cutoff (Nov 1, 2022), most pts in the 5.4 and 6.4 mg/kg T-DXd arms had HER2 IHC 3+ (78.0% and 85.0%), *RAS* wt tumors (82.9% and 85.0%), and a median of 3 and 4 prior lines of therapy, respectively. cORR was 37.8% (95% CI, 27.3-49.2%) in the 5.4 mg/kg arm and 27.5% (95% CI, 14.6-43.9%) in the 6.4 mg/kg arm (all partial responses in both arms). Grade ≥3 treatment-emergent adverse events (AEs) were observed in 41/83 pts (49.4%) and 23/39 pts (59.0%) in the 5.4 and 6.4 mg/kg T-DXd arms, respectively.

Most Common Adverse Events

Serious AEs were observed in 20/83 pts (24.1%) and 12/39 pts (30.8%) in the 5.4 and 6.4 mg/kg arms, respectively. Independently adjudicated drug-related interstitial lung disease occurred in 7/83 pts (8.4%) with 5.4 mg/kg T-DXd and 5/39

pts (12.8%) with 6.4 mg/kg T-DXd, and most events were grade 1/2 (1 grade 5 in the 6.4 mg/kg arm).

Conclusion

T-DXd showed promising antitumor activity in pts with HER2+ mCRC at both 5.4 and 6.4 mg/kg doses. Antitumor efficacy was observed irrespective of *RAS* mutation status at 5.4 mg/kg T-DXd, and in those with prior anti-HER2 therapy. Overall, safety was consistent with the known safety profile of T-DXd and favored the 5.4 mg/kg dose.

Comment:

HER2-targeted antibody-drug conjugate Enhertu is currently in Phase II trials for second-line and later mCRC. The drug is also included off-label in the NCCN's recommendations for *RAS/BRAF* WT *HER2*-amplified mCRC in all metastatic lines of therapy. The NCCN included this recommendation after Enhertu demonstrated impressive efficacy and reasonable safety in the Phase II DESTINY-CRC01 trial, despite the lack of an official FDA approval. This early recommendation positioned Enhertu well within this patient population, pending confirmatory results from the Phase II DESTINY-CRC02 trial. As such, the positive primary results from this latter trial that will be presented at ASCO 2023, could set the scene for the official entry of Enhertu in the CRC treatment algorithm. Lower than the ORR from the DESTINY-CRC01, the cORR observed in DESTINY-CRC02 (37.8% in the 5.4mg/kg arm) is still a positive result for Enhertu, especially as these patients had received a median of 3 prior therapies, but is not very dissimilar from all the HER2-targeting agents currently vying for a spot within the CRC space. For comparison, Tukysa's ORR from the Phase II MOUNTANEER trial was 38%, with 3.6% CRs (n = 3) and a median DoR of 12.4 months, while results from the HERACLES and MyPathway trials, showed that trastuzumab + Perjeta and trastuzumab + lapatinib led to ORRs of 32% and 30%, respectively.

The safety and tolerability data, however, highlight a potentially problematic incidence of drug-related interstitial lung disease (ILD), as well as one yet unspecified grade 5 event. Featuring in Enhertu's blackbox warning for the drug's approved indications, ILD is a serious side effect which could negatively impact the drug's uptake in CRC, especially in a heavily pretreated metastatic population.

Additionally, with *RAS/BRAF* WT *HER2*-amplified patients making up less than 5% of the CRC population, and with trastuzumab (either as Herceptin or biosimilars) and Perjeta also recommended by the NCCN guidelines for off-label use, and withTukysa recently approved for the same population, Enhertu's uptake will likely be severely limited in this indication. Nevertheless, based on these data, we are raising Enhertu's LOA by an additional 5%.

Source:

American Society of Clinical Oncology (ASCO) 05/25/2023 (Abstract 3501)
Citeline Analysis 05/26/2023

Tecentriq for Colorectal Cancer (CRC)

Event Date:	05/25/2023
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase II - AtezoTRIBE
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:	1%
Likelihood of Approval:	35% (9% Below Avg.)
Average Approval:	44%

	Comparator	Treatment	Comparator	Treatment
Treatment Description	ITT Population: FOLFOXIRI/Bev	ITT Population: FOLFOXIRI/Bev/Atezo	pMMR Population: FOLFOXIRI/Bev	pMMR Population: FOLFOXIRI/Bev/Atezo
Number of Patients	N/A	N/A	N/A	N/A
Number of Evaluable Patients	N/A	N/A	N/A	N/A
Median Progression-Free Survival *(Endpoint=Primary)*	11.5 Months	13.1 Months (P=0.15)	11.5 Months	13 Months (P=0.073)
mPFS2 *(Endpoint=Secondary)*	19.9 Months	22.6 Months (P=0.164)	19.9 Months	21 Months (P=0.269)
m2nd PFS *(Endpoint=Secondary)*	5.7 Months	6.3 Months (P=0.228)	5.7 Months	6.3 Months (P=0.27)

mOS *(Endpoint=Secondary)*	27.2 Months	33 Months (P=0.136)	26.9 Months	30.8 Months (P=0.172)

The abstract entitled "FOLFOXIRI plus bevacizumab and atezolizumab as upfront treatment of unresectable metastatic colorectal cancer (mCRC): Updated and overall survival results of the phase II randomized AtezoTRIBE study" will be presented at ASCO on June 2-6, 2023.

Data from this study were last seen in June 2022.

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 study had 85% power to detect a HR for PFS (time from randomization to 1st PD or death [PD1]) of .66 in favor of arm B with 1-sided α error of .10.

Endpoints

Secondary endpoints included PFS2 (time from randomization to PD on any treatment given after PD1 or death [PD2]), 2nd PFS (time from PD1 to PD2), and OS. MMR, TMB, IS IC were correlated to clinical outcome.

Results

218 pts (arm A/B:73/145) were enrolled. Main pts' characteristics were right-sided 44%/45%, *RAS* mut 71%/74%, *BRAF* mut 14%/8%, dMMR 7%/6%, high TMB 10%/12%, high IS IC 32%/32%. At a median follow-up of 37.0 mos, 175 (80%, arm A/B: 64/111) PD1, 150 (69%, arm A/B: 53/97) PD2, and 118 (54%, arm A/B: 43/75) OS events were collected. Out of 175 pts with a PD1 event, 135 (77%, arm A/B:50/85) received a subsequent treatment; among them, 121 pts (arm A/B: 43/78) had a PD2 event.

In the ITT population, significant interactions between treatment and MMR status (P_{int} .011), TMB (P_{int} .008), and IS IC (P_{int} .037) were reported in terms of PFS. Only IS IC was associated with a differential OS benefit (P_{int} .065), with pts bearing IS IC-high tumors deriving benefit from adding atezo (HR 0.43, 95%CI 0.19-1.00), differently than those with IS IC-low tumors (HR 1.09, 95%CI 0.65-1.83). In the pMMR group, significant interactions between treatment and TMB and IS IC were reported in terms of PFS (P_{int} .016 and .051, respectively) and OS (P_{int} .043 and .063, respectively). Pts bearing IS IC-high tumors derived higher OS benefit from adding atezo (HR 0.44, 95%CI 0.19-1.03), than those with IS IC-low tumors (HR 1.15, 95% CI 0.67-1.97).

Conclusion

Pts with IS IC-high and/or TMB high pMMR mCRC seem to derive a survival benefit from adding atezo to FOLFOXIRI/bev as upfront treatment. These findings deserve confirmation in a properly designed Phase III trial.

Comment

Combinations of angiogenesis inhibitors and immune checkpoint inhibitors have shown impressive activity in other solid tumors such as renal cell carcinoma, and the Phase II AtezoTRIBE trial set out to provide evidence of benefit from adding PD-L1 inhibitor Tecentriq to first-line treatment (chemotherapy and angiogenesis inhibitor bevacizumab) in patients with newly diagnosed metastatic colorectal cancer. Data from the trial has already shown that Tecentriq improved the PFS in such patients, with a relatively modest benefit in pMMR patients. Albeit with high P values, the OS update at a median follow-up of 37 months provides further evidence of this benefit, with a median OS of 33 months in the Tecentriq arm (versus 27.2 months in the FOLFOXIRI/bevacizumab arm; P = 0.136) in the intention-to-treat population. In the pMMR population, which represented most of the patients enrolled, the median

OS was 30.8 months in the Tecentriq arm (versus 26.9 months in the comparator arm; P = 0.172).

AtezoTRIBE also employed the use of Oncocyte's DetermaIO, an immune-related 27-gene expression signature able to predict benefit from immune checkpoint inhibition in triple-negative breast cancer, and the results from this analysis, published in 2022, indicated that the method could be useful in predicting the benefit of adding Tecentriq to chemotherapy (FOLFOXIRI) and bevacizumab through the identification of CRC patients exhibiting certain gene expression signatures. Additionally, post-hoc subgroup analyses from AtezoTRIBE that will be presented at ASCO 2023 indicate a correlation between tumor mutational burden and Immunoscore IC (Veracyte's IHC biomarker measuring CD8 and PD-L1 cell densities and their proximity), with pMMR patients with a high Immunoscore IC result more likely to derive benefit from the addition of an immune checkpoint inhibitor to chemotherapy and bevacizumab.

Although the pMMR population would be a more lucrative one because of its size, an investigator-led Phase III COMMIT trial is currently assessing Tecentriq in combination with chemotherapy and bevacizumab in newly-diagnosed dMMR/MSI-H CRC patients, which represent only 5% of metastatic CRC cases. As such, it remains to be seen whether Roche, armed with the knowledge gained from AtezoTRIBE, will try to reinforce Tecentriq's data in CRC by backing up a bigger and more powered Phase III development programme covering both pMMR and dMMR patients in this indication.

Source:

American Society of Clinical Oncology (ASCO) 05/25/2023 (Abstract 3500)
Citeline Analysis 05/26/2023

DKN-01 for Gastric Cancer

Event Date:	05/25/2023
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase IIa - DisTinGuish
Market Group:	Oncology
Lead Company:	Leap Therapeutics, Inc. (LPTX)
Partner Companies:	BeiGene (BGNE) Eli Lilly (LLY)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	12% (1% Above Avg.)
Average Approval:	11%

	All Treatment	Treatment	Treatment	Treatment	Treatment
Treatment Description	DKN-01 + Tislelizumab + Capecitabine + Oxaliplatin (All Patients)	DKN-01 + Tislelizumab + Capecitabine + Oxaliplatin (PD-L1-Low (vCPS < 5) Patients)	DKN-01 + Tislelizumab + Capecitabine + Oxaliplatin (PD-L1-High (vCPS > 5) Patients)	DKN-01 + Tislelizumab + Capecitabine + Oxaliplatin (DKK1-High Patients)	DKN-01 + Tislelizumab + Capecitabine + Oxaliplatin (DKK1-Low Patients)
Number of Patients	22	N/A	N/A	N/A	N/A
Number of Evaluable Patients	22	N/A	N/A	N/A	N/A
Median Overall Survival (OS) (Overall ITT Population) ***(Endpoint=Secondary)***	19.5 Months	18.7 Months	22.0 Months	16.9 Months	24.4 Months

Median Progression-Free Survival (PFS) (Overall ITT Population) ***(Endpoint=Secondary)***	11.3 Months	10.7 Months	11.6 Months	11.3 Months	12.0 Months
Objective Response Rate (ORR) (Overall ITT Population) ***(Endpoint=Primary)***	73 %	86 %	67 %	90 %	67 %

Leap Therapeutics announced the presentation of new long-term follow-up data from Part A of the Phase II DisTinGuish study evaluating DKN-01 in combination with BeiGene's tislelizumab and chemotherapy in first-line patients with advanced gastric or gastroesophageal junction adenocarcinoma (GEA) at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting. The abstract entitled "A phase 2 study (DisTinGuish) of DKN-01 in combination with tislelizumab + chemotherapy as first-line (1L) therapy in patients with advanced gastric or GEJ adenocarcinoma (GEA)" will be presented at the meeting on June 5, 2023.

Data from the study were last seen in November 2022.

Context

Part C is enrolling approximately 160 first-line HER2- GEA cancer patients in a randomized controlled trial of DKN-01 in combination with tislelizumab and chemotherapy compared to tislelizumab and chemotherapy. The Company anticipates completing enrollment in the randomized controlled clinical trial in late 2023 and seeing data from the ongoing colorectal cancer trial in the coming months.

Per the abstract, further evaluation of biomarkers is also ongoing.

Design

The DisTinGuish study is a Phase II study of DKN-01 in combination with tislelizumab, with or without chemotherapy as first-line or second-line therapy in patients with inoperable, locally advanced, G/GEJ adenocarcinoma. The study is being conducted in three parts in the United States, the Republic of Korea, the United Kingdom, and Germany. Part A enrolled 25 first-line HER2- GEA cancer patients to receive DKN-01 in combination with tislelizumab and capecitabine and oxaliplatin. Part B enrolled 52 second-line GEA cancer patients whose tumors expressed high levels of DKK1 to receive DKN-01 in combination with tislelizumab. Tislelizumab is provided for the study through a clinical collaboration with BeiGene.

Per the abstract, this multi-center, single arm Part A of the DisTinGuish study investigated DKN-01 + tislelizumab + CAPOX as 1L therapy in advanced HER2(-) GEA, regardless of DKK1 and PD-L1 expression levels. Tumor DKK1 and PD-L1 were assessed by central laboratories.

Endpoints

Per the abstract, the primary endpoint was ORR in a modified intent to treat population (>1 dose DKN-01); secondary endpoints included PFS and OS in the ITT population.

Results

Findings Part A DisTinGuish

- Median overall survival (OS) of 19.5 months and median progression-free survival (PFS) of 11.3 months exceeds benchmark results in the overall first-line patient population (n=25)
- OS and PFS results in all four important biomarker subgroups

- 18.7 months OS and 10.7 months PFS in PD-L1-low (vCPS < 5) patients (n=16)
- 22.0 months OS and 11.6 months PFS in PD-L1-high (vCPS > 5) patients (n=6)
- 16.9 months OS and 11.3 months PFS in DKK1-high patients (n=12)
- 24.4 months OS and 12.0 months PFS in DKK1-low patients (n=9)

- Additional patient with a partial response after 22 months on therapy improves objective response rate (ORR) to 73% in the overall modified intent-to-treat population (n=22), with one (5%) complete response (CR), 15 (68%) partial responses (PR), 5 (23%) best responses of stable disease (SD), and 1 (5%) non-evaluable (NE)
  - 86% ORR in PD-L1-low patients (n=14: 12 PR, 2 SD)
  - 67% ORR in PD-L1-high patients (n-6: 1 CR, 3 PR, 1 SD, 1 NE)
  - 90% ORR in DKK1-high patients (n=10: 9 PR, 1 NE)
  - 67% ORR in DKK1-low patients (n=9: 1 CR, 5 PR, 3 SD)

Per the abstract, twenty-five patients were enrolled from September 2020 to April 2021. As of January 23, 2023: Median age was 61 years (22, 80); 17 patients had GEJ adenocarcinoma; 8 had gastric cancer. Twenty-one patients had tumors with evaluable DKK1 expression. Twenty-two patients had tumors with evaluable PD-L1 expression; the majority (73%) were low expressors (vCPS <5%). Median (m) duration on treatment is 11.3 months (mo). Seven patients remain on study, with 4 on-treatment beyond 2 years.

Most Common Adverse Events

Consistent with previous results, combination was well tolerated with manageable toxicity, with most adverse events related to DKN-01 being low-grade (76%).

Per the abstract, treatment related adverse events (TRAEs) were mild with most G1/2. The most common AEs related to the study drug regimen were nausea (72%), diarrhea (64%) and fatigue (60%). Five patients experienced G3 DKN-01-TRAEs including decreased neutrophil count (1), diarrhea (1), vomiting (1), hypophosphatemia (2), and pulmonary embolism (1).

Conclusion

The long-term follow-up data for DKN-01 in combination with tislelizumab and chemotherapy indicates a well-tolerated treatment with the enhanced response rate, survival, and quality of life for advanced GEA patients. Median overall survival and progression-free survival for patients treated with DKN-01 plus tislelizumab and chemotherapy exceeded current PD-1 combination benchmarks, especially for those patients with low expression of PD-L1. Together with the previously reported data on the outcomes with DKN-01 for patients with high DKK1 expression, these results provide support for the ongoing randomized controlled clinical trial in first-line GEA patients.

Comment

These data demonstrate the DKN-01 + tislelizumab combination to have an impressive clinical benefit and substantially improve survival outcomes in a patient population with poor prognosis. Opdivo is currently the only targeted therapy for frontline HER2 negative gastric cancer and is the standard of care in combination with chemotherapy. In comparison to the results from the Phase III CheckMate-649 trial, from which Opdivo was approved, DKN-01 and tislelizumab combination looks to be a fierce competitor for Bristol Myers Squibb's PD-1 flagship and could potentially dethrone it from its title of standard of care. In CheckMate-649 the median overall survival was 13.8 months in the intention-to-treat population and the progression-free survival for patients with PD-L1 CPS ≥ 5 was reported as 7.7 months. In these long-term follow-up data from DisTinGuish, the median overall survival was reported as 19.5 months and the progression free survival for patients with PD-L1 CPS ≥ 5 was 11.6 months, both of which look to be markedly higher than those reported in CheckMate-649. Moreover, the survival benefit appears to be consistent regardless of DKK1 expression, although the objective response rate is

substantially higher in the DKK1-high subgroup (90% vs 67%), which could potentially warrant the combination regimen approval without the restriction of DKK1 expression.

Whilst these data poise DKN-01 and tislelizumab to confidently compete with Opdivo, the HER2-negative frontline market looks set to become increasingly crowded with potential approvals of novel agents zolbetuximab and bemarituzumab, alongside a possible label expansion for Keytruda in combination with Lenvima. In particular, zolbetuximab has shown impressive Phase III efficacy and safety data in CLDN18.2-positive HER2-negative gastric cancer patients, and also looks set to rivel Opdivo. Investigation into the overlap between DKN-01 overexpression and CLDN18.2 overexpression could prove useful to discern how directly the DKN-01 + tislelizumab and zolbetuximab regimens will compete and if DKN-01 will be able to carve itself a significant niche. Moreover, mature data from a double-arm Phase III trial will be crucial to further predict the likely success of DKN-01 and tislelizumab in a market that's set to become progressively competitive. Whilst we await later phase data, we are raising the likelihood of approval by 3%.

Source:

PR Newswire 05/25/2023 (LPTX)
American Society of Clinical Oncology (ASCO) (Abstract 4027, Poster 335)
Citeline Analysis 05/26/2023

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

Event Date:	05/25/2023
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - IMbrave050
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%

The abstract entitled "Efficacy, safety and patient reported outcomes (PROs) from the phase III IMbrave050 trial of adjuvant atezolizumab (atezo) + bevacizumab (bev) vs active surveillance in patients with hepatocellular carcinoma (HCC) at high risk of disease recurrence following resection or ablation" will be presented at the 2023 American Society of Clinical Oncology (ASCO) annual meeting on June 2-6, 2023.

Data from this study were last seen in April 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

IMbrave050 enrolled HCC pts at high risk of recurrence following resection or ablation. Pts were randomized to Arm A (atezo + bev) or Arm B (active surveillance). Pts in Arm A received atezo 1200 mg + bev 15 mg/kg IV q3w for a period of one year (17 cycles). Pts in Arm B underwent active surveillance for one year and were eligible to crossover to atezo + bev following independent review facility (IRF) confirmation of recurrence. Pts completed the IL42–EORTC QLQ-C30 (reduced) questionnaire at baseline and then at every odd treatment/surveillance visit through Cycle 17.

Endpoints

The primary endpoint was IRF-assessed RFS. Pre-specified exploratory analyses included change from baseline in global health status (GHS)/quality of life (QoL), physical functioning, role functioning, emotional functioning, and social functioning. Clinically meaningful deterioration was defined as a ≥ 10-point decrease.

Results

The ITT population included 334 pts in both Arms A and B. With a median follow-up time of 17.4 mo (clinical cutoff date:

21 Oct 2022), IRF-RFS HR was 0.72 (95% CI: 0.56, 0.93; P = 0.0120). In ITT pts, IL42 completion rates remained ≥ 93% in both arms from baseline through treatment/surveillance Cycle 17. Mean scores at baseline in both arms were high and similar, as measured by the GHS/QoL and physical, role, emotional and social functioning scales. Mean changes from baseline were not considerable through Cycle 17 and were similar between arms as evidenced by overlapping 95% CIs. Pts' GHS/QoL and functioning was maintained through Cycle 17, with no clinically meaningful deterioration observed at any time.

Most Common Adverse Events

In the safety population, Grade 3 or 4 adverse events occurred in 41% of 332 Arm A pts and 13% of 330 Arm B pts.

Conclusion

Statistically significant and clinically meaningful improvement in RFS was seen in pts receiving atezo + bev vs active surveillance. Atezo + bev safety was generally manageable, and consistent with the established safety profiles of each therapeutic agent and with the underlying disease. PRO outcome analyses revealed similar overall health-related QoL (HRQoL) and functioning between atezo + bev and active surveillance, and that treating high-risk pts with HCC with adjuvant atezo + bev following procedures with curative intent did not result in a clinically meaningful deterioration in HRQoL or function.

Comment

These first numerical results for Tecentriq in combination with bevacizumab as an adjuvant treatment for high-risk early-stage HCC are favorable. In topline results released in January this year, Roche announced its flagship HCC combination had met its primary endpoint of recurrence-free survival (RFS). These updated results for IMbrave050 demonstrate Tecentriq plus bevacizumab reduced the risk of recurrence by 28%. Currently, early-stage HCC patients are primarily treated with liver transplants or surgical resection, or with locoregional therapies if they are not candidates for surgery. However, outcomes for these patients are poor, and 70–80% of patients who have undergone surgery will see their cancer return within five years.

While the efficacy data is a positive step towards providing a treatment option alongside surgery for these high-risk early-stage patients, the safety data complicates matters. Grade 3 or 4 adverse events occurred in 41% of patients in the Tecentriq plus bevacizumab arm, which greatly surpasses the 13% grade 3 or 4 adverse event rate in the surveillance arm.

Although Roche is the first to announce positive results for an immunotherapy in early-stage HCC, Bristol Myers Squibb is also testing the combination of Opdivo and Yervoy in the adjuvant setting in the Phase III CheckMate 9DX trial; however, data are not expected until later this year. Despite its head start, it is anticipated the FDA will request longer-term data from IMbrave050 before granting approval due to the uncertainty around adverse events. Therefore, monopoly over the currently untouched first-line market will depend on which combination can demonstrated both superior efficacy and safety in this patient population.

Source:

American Society of Clinical Oncology (ASCO) (Abstract 4002)
Citeline Analysis

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

Event Date:	05/25/2023
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - HIMALAYA
Market Group:	Oncology
Lead Company:	AstraZeneca PLC (AZN)
Partner Companies:	Amgen (AMGN) Bristol Myers Squibb (BMY) Pfizer (PFE)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

The abstract entitled "Outcomes by occurrence of immune-mediated adverse events (imAEs) with tremelimumab (T) plus durvalumab (D) in the phase 3 HIMALAYA study in unresectable hepatocellular carcinoma (uHCC)" will be presented at the 2023 American Society of Clinical Oncology (ASCO) annual meeting on June 2, 2023.

Data from this study were last seen in June 2022.

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

This exploratory analysis assessed the association between imAEs and outcomes in HIMALAYA. Safety was assessed in participants (pts) who received ≥1 dose of STRIDE (T 300 mg [one dose] plus D 1500 mg once every 4 weeks [Q4W]) or D (1500 mg Q4W). imAEs were AEs of special interest associated with drug exposure and consistent with an immune-mediated mechanism of action with no found alternate etiology. Median OS (mOS) and OS rates were estimated using the Kaplan–Meier method. OS hazard ratios (HRs) and 95% CIs were calculated using Cox modeling, with imAEs as a time-varying covariate and stratified by etiology (HBV/HCV/others), ECOG (0/1), and macro-vascular invasion (yes/no) for pts with vs without imAEs of any grade. Pts with >1 imAE were counted once.

Results

In total, 388 pts (STRIDE) and 388 pts (D) were included in the analysis. An improvement in OS was seen with STRIDE in pts with imAEs vs pts without (HR, 0.73; 95% CI, 0.56–0.95). OS rates at 6, 12, and 24 months (mo) were higher for STRIDE in pts with imAEs vs pts without. The association between imAEs and OS was less clear for D and may be limited by small pt number. In a landmark analysis of pts with vs without imAEs within 6 mo of STRIDE (n=307) or D (n=287), OS

HRs (95% CIs) were 0.65 (0.47–0.90) and 1.39 (0.95–2.04), respectively.

Most Common Adverse Events

Any grade imAEs, Grade 3 or 4 imAEs, and imAEs leading to discontinuation occurred in 139 (35.8%), 49 (12.6%), and 22 (5.7%) pts, respectively for STRIDE and 64 (16.5%), 25 (6.4%), and 10 (2.6%) pts, respectively for D. imAEs requiring high-dose steroids (≥40 mg prednisone or equivalent daily) occurred in 78 (20.1%) pts for STRIDE and 37 (9.5%) pts for D.

Conclusion

In HIMALAYA, imAEs with STRIDE or D were manageable and generally low grade. In this exploratory analysis, the occurrence of imAEs was associated with improved OS for STRIDE, generally consistent with findings for other ICIs.

Comment

HCC has notably been a tricky indication for monotherapies to show activity, owing to the aggressive nature of the disease, so it is often treated with harsher combination therapies. In 2019, Tecentriq plus bevacizumab was the first therapy to show remarkable efficacy (42% reduction in the risk of death) over previous standard-of-care Nexavar in the front-line advanced HCC setting; however, high levels of toxicity are often seen with this combination. Imfinzi in combination with Imjudo, also coined the STRIDE regimen, was the second combination approved in 2022 following data (22% reduction in the risk of death) that just fell shy of the data seen with Tecentriq + bevacizumab. However, the 57% rate of grade 3 or 4 adverse events seen with the Tecentriq plus bevacizumab combination is inferior to the 26% of grade 3 or 4 adverse events in HIMALAYA.

This exploratory analysis investigating the relationship between immune-mediate adverse events (imAEs) and patient response to STRIDE suggests overall survival is greater in patients that experience imAEs. As treatment algorithms have moved on from cytotoxic chemotherapies to more efficacious immunotherapies, a new class of side effects, termed imAEs have been seen due to the immunologic toxicities related to immunotherapy treatment. In HIMALAYA, 35.8% of patients treated with STRIDE developed any grade imAEs, and grade 3 or 4 imAEs occurred in 12.6% of patients. The rate of imAEs are substantially greater in patients treated with STRIDE compared to patients treated with Imfinzi alone, where only 16.5% of patients developed any grade imAEs and 6.4% were grade 3 or 4. Interestingly, a higher OS rate was seen at six, 12, and 24 months in patients who developed imAEs than in patients who didn't. At 12 months, 69.1% of patients treated with STRIDE that developed imAEs were alive compared to 55.2% of patients who did not develop imAEs when treated with STRIDE. Furthermore, the median OS of 23.2 months in the STRIDE imAE arm was far superior to the 14.1-month median OS in the STRIDE no imAE arm. Therefore, it is hypothesized that both the anti-tumor response and the development of imAEs represent a robust immune reaction, which could lead to a longer survival time.

Source:

American Society of Clinical Oncology (ASCO) (Abstract 4004)
Citeline Analysis

Reblozyl for Myelodysplastic Syndrome (MDS)

Event Date:	05/25/2023
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - COMMANDS
Market Group:	Oncology
Lead Company:	Merck & Co., Inc. (MRK)
Partner Companies:	Bristol Myers Squibb (BMY)
Former Companies:	Acceleron Pharma Celgene
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	Epoetin alfa	Reblozyl	Reblozyl vs Epoetin alfa
Number of Patients	176	178	354
Number of Evaluable Patients	154	147	301
Red Blood Cell Transfusion Independence (RBC-TI) ≥12 Weeks with Mean Hemoglobin Increase ≥1.5 g/dL) ***(Endpoint=Primary)***	31.2 %	58.5 %	N/A (P
Hematologic Improvement-erythroid (HI-E) ≥8 Weeks ***(Endpoint=Secondary)***	51.3 %	74.1 %	N/A (P
RBC-TI, 24 Weeks ***(Endpoint=Secondary)***	29.2 %	47.6 %	N/A (P=0.0006)
RBC-TI ≥12 Weeks ***(Endpoint=Secondary)***	46.1 %	66.7 %	N/A (P=0.0002)

Bristol Myers Squibb announced first results from the Phase III COMMANDS study of Reblozyl (luspatercept-aamt). Results from the study will be featured in an abstract entitled "Efficacy and safety results from the COMMANDS trial: A phase 3 study evaluating luspatercept vs epoetin alfa in erythropoiesis-stimulating agent (ESA)-naive transfusion-dependent (TD) patients (pts) with lower-risk myelodysplastic syndromes (LR-MDS)" at the American Society of Clinical Oncology (ASCO) Annual Meeting on June 2, 2023 and in an oral presentation entitled "Luspatercept Versus Epoetin Alfa for Treatment (TX) of Anemia in ESA-naive Lower-risk Myelodysplastic Syndromes (LR-MDS) Patients (Pts) Requiring RBC Transfusions: Data From the Phase 3 COMMANDS Study" at the European Hematology Association (EHA) Congress on June 10, 2023.

Data from the study were last seen in October 2022.

"Efficacy and safety results from the COMMANDS trial: A phase 3 study evaluating luspatercept vs epoetin alfa in erythropoiesis-stimulating agent (ESA)-naive transfusion-dependent (TD) patients (pts) with lower-risk myelodysplastic syndromes (LR-MDS)" (Abstract 7003)

Context

A supplemental Biologics License Application for *Reblozyl* is currently under Priority Review with the U.S. Food and Drug Administration (FDA) for treatment of anemia in ESA-naïve adult patients with very low- to intermediate-risk MDS who may require RBC transfusions with an assigned Prescription Drug User Fee Act (PDUFA) goal date of August 28, 2023. The European Medicines Agency has also validated the Type II Variation for *Reblozyl* in this patient population. *Reblozyl* is being developed and commercialized through a global collaboration with Merck following Merck's acquisition of Acceleron Pharma in November 2021.

Design

Eligible patients were ≥18 years old with lower-risk MDS who require transfusions. Patients were randomized 1:1 to receive subcutaneous Reblozyl (starting dose 1.0 mg/kg, titration up to 1.75 mg/kg) once every 3 weeks or epoetin alfa (starting dose 450 IU/kg, titration up to 1050 IU/kg) weekly for ≥24 weeks.

Per the abstract, eligible pts were ≥ 18 years old with IPSS-R-defined LR-MDS with or without RS, < 5% bone marrow blasts, sEPO levels < 500 U/L, required RBC transfusions (defined as 2–6 RBC units/8 weeks [wk] for ≥ 8 wk immediately prior to randomization), and were ESA naive.

Endpoints

The primary endpoint evaluated in the COMMANDS study is RBC transfusion independence (RBC-TI) for 12 weeks with a mean hemoglobin increase of ≥1.5 g/dL. Key secondary endpoints include erythroid response (HI-E) of at least 8 weeks during weeks 1-24 of the study, RBC-TI ≥12 weeks and RBC-TI for 24 weeks.

Results

At the time of the interim analysis, 147 evaluable patients received *Reblozyl* and 154 evaluable patients received epoetin alfa, with median treatment durations of 41.6 and 27 weeks, respectively. Results showed 58.5% (n=86) of patients receiving *Reblozyl* vs. 31.2% (n=48) of patients receiving epoetin alfa achieved the primary endpoint of RBC-TI of at least 12 weeks with concurrent mean hemoglobin (Hb) increase of at least 1.5 g/dL within the first 24 weeks (p<0.0001). HI-E increase of at least 8 weeks was achieved by 74.1% (n=109) of *Reblozyl* patients vs. 51.3% (n=79) of epoetin alfa patients (p<0.0001). Patients treated with *Reblozyl* achieved more durable responses vs. epoetin alfa, with a median duration of response of RBC-TI ≥12 weeks (Week 1 to end of treatment) of 126.6 vs. 77 weeks. Within the first 24 weeks of treatment, RBC-TI of at least 24 weeks was achieved by 47.6% (n=70) of *Reblozyl* patients vs. 29.2% (n=45) of epoetin alfa patients (P=0.0006). Benefit with *Reblozyl* was also observed in clinically relevant subgroups.

Most Common Adverse Events

Results showed a consistent safety profile and no new safety signals.

Per the abstract, treatment-emergent adverse events (TEAEs; any grade) were reported by 164 (92.1%) luspatercept and

150 (85.2%) epoetin alfa pts; 8 (4.5%) and 4 (2.3%) pts discontinued due to TEAEs. Treatment-related AEs were reported by 54 (30.3%) luspatercept and 31 (17.6%) epoetin alfa pts. AML progression was reported in 4 (2.2%) luspatercept and 5 (2.8%) epoetin alfa pts. Overall rates of death were comparable between arms during treatment and post-treatment (32 [18.0%] luspatercept, 32 [18.2%] epoetin alfa pts).

Conclusion

Results showed nearly twice as many patients treated with Reblozyl achieved superior transfusion independence with concurrent hemoglobin increase vs. epoetin alfa, including in clinically relevant subgroups. Reblozyl demonstrated a durable response, with nearly 2.5 years median transfusion independence, 1 year longer than epoetin alfa.

"Luspatercept Versus Epoetin Alfa for Treatment (TX) of Anemia in ESA-naive Lower-risk Myelodysplastic Syndromes (LR-MDS) Patients (Pts) Requiring RBC Transfusions: Data From the Phase 3 COMMANDS Study" (Abstract S102)

Results

Data to be presented at EHA included both efficacy and safety consistent with results at ASCO, and showed *Reblozyl* demonstrated favorable outcomes compared to epoetin alfa across common MDS mutations (SF3B1, SF3B1a, ASXL1, TET2, DNMT3A, EZH2, IDH2, U2AF1) and had a probability of achieving clinical benefit, regardless of overall mutational burden.

Conclusion

Additional results, to be presented during the plenary session at the European Hematology Association Congress, show Reblozyl demonstrated clinical benefit across patients with spectrum of MDS mutations.

Comment

The release of this ASCO abstract containing data from the Phase III COMMANDS trial demonstrate Reblozyl to greatly improve outcomes for transfusion-dependent lower-risk MDS patients over standard of care epoetin alfa. In line with the release of topline data late last year, the abstract details the study to have met its primary endpoint of RBC transfusion independent ≥12 weeks with a concurrent mean hemoglobin increase ≥1.5 g/dL during weeks 1-24. Reblozyl treatment resulted in an absolute improvement of 27.3% compared to epoetin alfa - a highly significant benefit ($p<0.0001$). With nearly double the percentage of patients achieving the primary endpoint on Reblozyl treatment, these results stage an undeniably compelling case for Reblozyl to displace epoetin alfa as the standard of care treatment.

However, the safety data suggests Reblozyl is more toxic compared to epoetin alfa and potentially less tolerable, with higher rates of treatment-related adverse events and more patients discontinuing treatment on Reblozyl. One of the primary treatment goals for low-risk MDS patients is to improve quality of life, and therefore the toxicity profile of Reblozyl has a weighted role in the drug's benefit-risk profile. Nevertheless, the remarkable haematological improvements could arguably outweigh the additional toxicity. Further analysis stratifying the treatment-related adverse events by grade between the two arms will prove more indicative towards Reblozyl's benefit-risk profile in comparison to epoetin alfa. If the additional treatment-related adverse events consist of higher grade toxicities then this could potentially hinder Reblozyl in its bid to become the new standard of care.

Subgroup analysis investigating Reblozyl's affect in non-RS+ and RS+ patients may also be useful to determine if the drug has utility in an all-comer patient population and to further evaluate its commercial potential. Access to the front-line setting could prove a lucrative label expansion opportunity for Reblozyl as there are currently limited treatment options currently available for these patients outside of Erythropoiesis-stimulating agents, yet Reblozyl will need to demonstrate efficacy regardless of RS status to maximise revenue. For now, we wait to see if further safety

and subgroup analyses will be presented in the oral abstract on June 2nd.

Source:

Business Wire 05/25/2023 (BMY)
American Society of Clinical Oncology (ASCO) (Abstract 7003)
European Hematology Association (EHA) (Abstract S102)
Citeline Analysis

AB-101 (Artiva) for Non-Hodgkin's Lymphoma (NHL)

Event Date:	05/25/2023
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase I/II - +/- Rituximab
Market Group:	Oncology
Lead Company:	Artiva Biotherapeutics, Inc.
Partner Companies:	N/A
Former Companies:	N/A
Change to Likelihood of Approval:	1%
Likelihood of Approval:	12% (1% Above Avg.)
Average Approval:	11%

Artiva Biotherapeutics announced the presentation of initial data from the dose-escalation stage of its ongoing Phase I/II clinical trial of AB-101 in combination with rituximab for the treatment of relapsed/refractory B-cell non-Hodgkin lymphoma (B-NHL) at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting. The abstract entitled "AB-101, an allogeneic, non–genetically modified, natural killer (NK) cell therapy, evaluated as monotherapy or in combination with rituximab in R/R non-Hodgkin lymphoma" will be presented on June 5, 2023.

Design

The Phase I/II clinical trial in B-NHL is assessing AB-101 in an outpatient treatment regimen delivered in cycles, with each cycle consisting of three days of conditioning chemotherapy (250 mg/m^2 or 500 mg/m^2 of cyclophosphamide and 30 mg/m^2 of fludarabine) followed by four weekly doses of AB-101 at one billion or four billion cells per dose, each with IL-2 cytokine support. Monotherapy consists of one cycle only, while combination therapy allows for up to four cycles, each with two to three doses of rituximab (375 mg/m^2).

Patients had received a median of four prior lines of therapy, and 67% were refractory to the prior line of therapy. Approximately two-thirds have aggressive B-NHL. In the rituximab combination cohort, 89% had been treated with prior CAR-T therapy. At the time of the data cut, 15 patients in the monotherapy and nine patients in the combination cohorts were evaluable for assessment of safety.

Results

The Objective Response Rate (ORR) in seven efficacy evaluable patients treated with one billion cells per dose of AB-101 in combination with rituximab was 57.1% overall, including three Complete Responses (CRs) and one Partial Response (PR). Three of the responses were seen in patients who failed prior CAR-T therapy, and at the time of the data cut, three patients had ongoing responses and were progression free for 5+, 7+ and 9+ months.

Most Common Adverse Events

AB-101 was well tolerated at one and four billion cells per dose. Up to 16 doses of AB-101 at one billion cells per dose were administered in combination with rituximab in an outpatient setting. Myelosuppression, consistent with standard

lymphodepletion regimens, was the most common Grade ≥ 3 toxicity, but was manageable with standard of care. No prolonged cytopenias were observed. No observations of ICANS / neurotoxicity or GvHD were noted even after 16 doses per patient. Two patients (8%) had Grade 1 reports of CRS, based on low-grade fevers which resolved within five to 24 hours without the usage of steroids and/or tocilizumab. The most common SAEs reported in the monotherapy cohort were febrile neutropenia (Grade 3+, n=2) and malignant neoplasm progression (Grade 3+, n=2; Grade 1-2, n=1). In the combination cohort, only one unrelated Grade 3 SAE of pyrexia was noted. There were no treatment-related AEs leading to discontinuation of AB-101.

Conclusion

Per the abstract, 4 weekly doses of AB-101 given alone or with RTX appeared to be safe and well tolerated without the serious/severe toxicities associated with CAR-T therapies. Preliminary efficacy of the combination treatment is encouraging. The study is ongoing and continues to enroll the combination cohorts and the 4e9 cells/dose level.

Comment

These are encouraging, albeit early results for AB-101, an off-the-shelf enhancer of antibody-dependent cellular cytotoxicity. AB-101 consists of NK cells isolated from cord blood sourced from donors with a high affinity variant of the receptor CD16 and a KIR-B haplotype. These initial results show good activity in seven heavily pretreated patients with a 57% ORR and a 43% CR rate for AB-101 combined with rituximab. Although patients were treated in the outpatient setting, each 28-day cycle started with three-days of conditioning chemotherapy to deplete lymphocytes. Patients received four weekly doses of AB-101 each cycle (allogeneic NK cells have a short half-life) and the trial allowed for up to four cycles. While the conditioning regimen adds to the toxicity, there were no treatment-related adverse events leading to discontinuation of AB-101 and there were no observations of ICANS/neurotoxicity or graft versus host disease. There was one grade 5 event in the trial (cardiac arrythmia) which led to a clinical hold that was lifted after determination that it was not related to AB-101. After the clinical hold, the protocol was amended to exclude patients with a history of significant cardiac disease.

Comparable therapies include Fate Therapeutics FT516, which in 2021 reported a 73% ORR and a 55% CR rate in 11 patients (Fate Therapeutics has since suspended the program as aprt of a large downsizing of the company), and Gamida Cell's GDA-201 which in 2020 reported a 74% ORR and a 68% CR rate in 19 patients. A multicenter Phase I/II trial expected to enroll 99 patients initiated in 2022 and is evaluating GDA-201 in combination with rituximab. The expansion phase of the trial will enroll patients with follicular lymphoma and DLBCL.

As we await updated results for AB-101 combined with rituximab, we are raising the LOA by 1%. Also on the horizon, is initiation of a Phase II trial for Hodgkin's lymphoma of AB-101 combined with Affimed's AFM13, an NK cell engager targeting CD30 and CD16.

Source:

Business Wire 05/25/2023 (Artiva Biotherapeutics)
American Society of Clinical Oncology (ASCO) (Abstract 7529)
Citeline Analysis

Talzenna for Prostate Cancer

Event Date:	05/25/2023
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase III - TALAPRO-2
Market Group:	Oncology
Lead Company:	Pfizer Inc. (PFE)
Partner Companies:	BioMarin (BMRN)
Former Companies:	Medivation
Change to Likelihood of Approval:	0%
Likelihood of Approval:	94% (2% Above Avg.)
Average Approval:	92%

	Placebo	Treatment	Difference Between Treatment and Placebo
Treatment Description	Placebo + Ezalutamide	Talazoparib + Ezalutamide	Talazoparib + Ezalutamide vs Placebo + Ezalutamide
Number of Patients	N/A	N/A	N/A
Number of Evaluable Patients	199	200	399
Radiographic Progression-Free Survival by BICR ***(Endpoint=Primary)***	N/A	13.8	N/A
Radiographic Progression-Free Survival by BICR - Hazard Ratio	N/A	N/A	0.45 (P
Radiographic Progression-Free Survival by BICR - Hazard Ratio (BRCA1/2 subgroup)	N/A	N/A	0.20 (P
Radiographic Progression-Free Survival by BICR - Hazard Ratio (Without BRCA1/2 Alteration)	N/A	N/A	0.68 (P=0.06)

Overall Survival - Hazard Ratio	N/A	N/A	0.69 (P=0.07)
Global Health Status/Quality of Life (GHS/QoL)	19.3 %	27.1 %	N/A
Global Health Status/Quality of Life (GHS/QoL) - Hazard Ratio	N/A	N/A	0.69 (P=0.03)

The abstract entitled "TALAPRO-2: Phase 3 study of talazoparib (TALA) + enzalutamide (ENZA) versus placebo (PBO) + ENZA as first-line (1L) treatment for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) harboring homologous recombination repair (HRR) gene alterations" will be presented at the meeting on June 4, 2023.

Data from the study were last seen in February 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

Per the abstract, the researchers report results of the prespecified, independently powered analysis of pts with mCRPC with HRR gene alterations from Cohorts 1 and 2. From February 2019 to January 2022, 399 pts (169 from Cohort 1) were randomized 1:1 to receive TALA 0.5 mg or PBO (all received ENZA 160 mg) once daily. Randomization was stratified by prior abiraterone or docetaxel for castration-sensitive PC (yes vs no). Key eligibility criteria: mildly or asymptomatic mCRPC with disease progression at study entry, HRR-deficient status prospectively confirmed by tumor tissue and/or ctDNA testing (genes tested: ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, RAD51C), ECOG PS ≤1, ongoing androgen deprivation therapy, no prior life-prolonging therapy for CRPC.

Endpoints

Per the abstract, primary endpoint: radiographic progression-free survival (rPFS) by BICR per RECIST 1.1 and PCWG3.

Results

Per the abstract, 200 pts received TALA + ENZA and 199 PBO + ENZA. TALA + ENZA significantly improved rPFS by BICR (HR 0.45; 95% CI, 0.33–0.61; 2-sided*P*< 0.001; median PFS not reached vs 13.8 months). The HR for rPFS by BICR was 0.20 (95% CI, 0.11–0.36; *P*< 0.001) for the *BRCA1/2* subgroup (n=155) and 0.68 (95% CI, 0.46–1.02; *P* = 0.06) in those without a *BRCA1/2* alteration (n=240). The first interim analysis of OS was immature: 21.5% (TALA + ENZA) and 26.6% (PBO + ENZA) pts had died; HR 0.69 (95% CI, 0.46–1.03; *P* = 0.07). TALA + ENZA delayed time to PSA progression, cytotoxic chemotherapy, and antineoplastic therapy, and improved ORR, PSA response, and investigator-assessed PFS2. Time to definitive clinically meaningful deterioration in global health status/quality of life (GHS/QoL) was significantly longer with TALA + ENZA vs PBO + ENZA (HR 0.69; 95% CI, 0.49–0.97; *P* = 0.03; median 27.1 vs 19.3 months).

Most Common Adverse Events

Per the abstract, grade (G) 3–4 treatment-emergent adverse events (TEAEs) were reported for 66.2% (TALA + ENZA) vs 37.2% (PBO + ENZA). There were more G≥3 hematologic TEAEs (anemia, neutropenia, thrombocytopenia, and leukopenia) with TALA + ENZA vs PBO + ENZA. TEAEs led to discontinuation of TALA in 10.1% vs PBO in 7.0%; discontinuation rates of ENZA were 7.6% (TALA + ENZA) vs 7.0% (PBO + ENZA).

Conclusion

Per the abstract, TALA + ENZA demonstrated a statistically significant and clinically meaningful improvement in rPFS over standard of care ENZA as 1L treatment for pts with mCRPC and HRR gene alterations, while delaying time to definitive

clinically meaningful deterioration in GHS/QoL. Toxicity was generally manageable and consistent with known safety profiles of TALA and ENZA.

Comment

Further data for the Talzenna-Xtandi combination in first-line mCRPC all-comers has been widely anticipated after the controversy of the Phase III PROpel trial of Lynparza and abiraterone in all-comer mCRPC patients, which recently ended in the FDA ruling to approve this combination in the restricted *BRCA*-mutated (*BRCA*m) population. These data have focused on the homologous recombination repair (HRR) population, which may be an attempt to solidify their case for a HRR-approval, in the likely case that the FDA are reluctant to grant an all-comers approval.

Talzenna has shown impressive efficacy in the HRR population, with an HR for rPFS by BICR being 0.20 in the *BRCA1/2* subgroup and 0.68 in those without a *BRCA1/2* alteration. No OS data has been presented yet, but after the controversy of Lynparza in an all-comer population, where it was found in non-HRD patients the OS HR was 1.06, it is likely the FDA will need detailed OS data across all subgroups for Talzenna and Xtandi in order to grant an approval.

Lynparza is approved in first-line mCRPC after demonstrating an impressive OS HR of 0.29 in the *BRCA*m subgroup, but the *BRCA*-restricted approval came after an initial fight and subsequent FDA advisory meeting in order to discuss its efficacy, or lack thereof, in patients without *BRCA* or homologous recombination repair deficient (HRD) mutations. Only approximately 20% of prostate cancers are HRD, with an even smaller <10% being *BRCA*m, severely restricting AstraZeneca's initial bid for approval in the total population. This means even if Talzenna fails to gain approval in the all-comer population, an approval in the larger HRD population over the relatively restricted *BRCA*m population will still give it access to a larger population and therefore an advantage over Lynparza.

Competing PARP inhibitor Zejula demonstrated efficacy in both the HRD and *BRCA*m populations in data released at ASCO GU 2022, leading to a European approval in April 2023 and an sNDA filing in March 2023. An earlier approval in Europe, and likely in the US due to early submission of an sNDA, will allow Zejula to gain physician familiarity and have somewhat of an advantage over Talzenna. Zejula plus abiraterone showed an rPFS of 19.5 months in the *BRCA*m subgroup, but Talzenna-Xtandi patients have not yet reached rPFS, with placebo rPFS being 21.9 months. Talzenna did not reach a median rPFS as of yet, compared to 13.8 months in the comparator subgroup. This makes it difficult to compare the two in terms of efficacy, as more data is needed. Talzenna will need to demonstrate a significant efficacy benefit in order to overcome the disadvantage of a later approval and gain an edge over Zejula.

Source:

Business Wire 05/25/2023 (PFE)
American Society of Clinical Oncology (ASCO) (Abstract 5004)
Citeline Analysis

Lenvima for Renal Cell Cancer (RCC)

Event Date:	05/25/2023
Event Type:	Trial Data - Updated Results (Clinical Analysis)
Trial Name:	Phase II - w/Pembrolizumab - KEYNOTE-B61
Market Group:	Oncology
Lead Company:	Eisai Co., Ltd. (4523:JP)
Partner Companies:	IQVIA (IQV) Knight Therapeutics (GUD) Merck (MRK) SFJ Pharmaceuticals
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

The abstract entitled "First-line lenvatinib + pembrolizumab treatment across non-clear cell renal cell carcinomas: Results of the phase 2 KEYNOTE-B61 study" will be presented at ASCO on June 2-6, 2023.

Data from this study were last seen in September 2022.

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

Adults with previously untreated advanced non-clear cell RCC and measurable disease per RECIST v1.1 received lenva 20 mg PO QD + pembro 400 mg IV Q6W for up to 18 cycles (~2 y). Histology was assessed by investigator (assessment by central review is planned).

Endpoints

The primary end point was ORR per RECIST v1.1 by blinded independent central review (BICR). Secondary end points included DOR, DCR, and PFS per RECIST v1.1 by BICR; OS; and safety.

Results

Of 158 treated pts, 93 (59%), 29 (18%), and 21 (13%) had papillary, chromophobe, and unclassified histology, respectively. Additionally, 6 pts (4%) had translocation and 9 (6%) had other histology. 70 pts (44%) had IMDC favorable risk and 88 (56%) had intermediate/poor risk. Median follow-up was 14.9 mo (range 8.7-19.7). ORR was 49% (95% CI, 41-57; 9 CRs [6%]; 69 PRs [44%]). DCR was 82% (95% CI, 75-88). Median DOR was not reached (NR; range, 1.5+ to 15.3+ mo). By Kaplan-Meier estimate, 75% of responders had a response for ≥12 mo. For the IMDC favorable risk group, ORR was 51% (95% CI, 39-64) and DCR was 87% (95% CI, 77-94). For the IMDC intermediate/poor risk group, ORR was 48% (95% CI, 37-59) and DCR was 78% (95% CI, 68-86). In all pts, median PFS and OS were 17.9 mo (95% CI,

13.5-NR) and NR (95% CI, NR-NR), respectively; 12-mo rates were 63% and 82%.

Most Common Adverse Events

Treatment-related AEs (TRAEs) occurred in 149 pts (94%) and were consistent with results from other studies. The most common (≥30%) TRAEs were hypertension (n=90; 57%), diarrhea (n=69; 44%), and hypothyroidism (n=58; 37%). Grade 3-4 TRAEs occurred in 81 pts (51%). Overall, 17 pts (11%) discontinued pembro, 14 (9%) discontinued lenva, and 5 (3%) discontinued both drugs because of TRAEs. No deaths occurred because of TRAEs.

Conclusion

In pts with advanced non-clear cell RCC enrolled in KEYNOTE-B61, lenva + pembro showed antitumor activity with no new safety signals. These data support the use of lenva + pembro as first-line treatment for pts with non-clear cell RCC, regardless of histology.

Comment

Non-clear cell RCC (non-cc RCC) is an understudied area of kidney cancer, with limited options. The combination of Lenvima and Keytruda, although still in earlier phases of investigation, has shed new light into the treatment algorithm through this undoubtedly positive data and will offer a strong treatment option for physicians, pending an approval.

The only preferred regimens for a metastatic patient with non-clear cell histology are Cabometyx, Sutent, and entering a clinical trial, as listed by the NCCN, although there are alternative options listed in the 'other recommended regimens' category. Cabometyx is the standard of care here, despite gaining approval based on trials primarily investigating clear-cell histology patients. In a meta-analysis, it was found that ORR in Cabometyx-treated non-cc RCC patients was 27% of patients, PFS was 7 months and OS was 12 months. The most common grade 3 events were skin toxicity (in 4% of patients) and hypertension (in 4% of patients). In a drastic comparison to these data, the Lenvima and Keytruda combination lead to a median PFS 17.9 months, whilst median OS was not reached at a median follow up of 14.9 months. Furthermore, the median ORR across all patients was 49%. This data is incredibly positive and given the high area of unmet need for non-cc RCC patients, it is highly likely that this combination will gain an approval.

Treatment-related adverse events (TRAEs) were higher in the Lenvima-Keytruda doublet, with 51% of patients experiencing a grade 3 or above TRAE. Although detailed grade 3 and above TRAE data was not disclosed, this less favorable safety profile is unlikely to affect physician's potential prescribing of the doublet due to the sheer size of the unmet need.

Approximately 25% of RCC cases are non-cc, so an approval here will be in a relatively restricted population. That said, there are limited treatment options for these patients, with those available lacking robust data backing their use in this patient segment. Lenvima and Keytruda would be able to dominate in this setting relatively unopposed, and provide a new treatment option for this oft-overlooked patient population. Keytruda and Lenvima are already approved as a combination regimen in for metastatic ccRCC patients; an additional approval for metastatic non-cc RCC will give the regimen ubiquity across the metastatic setting.

The Phase II KEYNOTE-B61 study included patients with papillary, chromophobe, translocation, unclassified, and 'other' histology. Most participants had the papillary histology, which is in line with real-world epidemiology patterns. The regimen was most effective in patients with the translocation histology, yielding an ORR of 67%, although this is likely skewed by the small patient population (n=6). The ORR was lowest in patients with chromophobe histology (28% with n=29), but due to lack of other options this is unlikely to curb prescribing of the Lenvima-Keytruda doublet in these patients, if approved. These results represent a step in the right direction for finding effective therapies for

non-cc RCC patients.

Source:

American Society of Clinical Oncology (ASCO) (Abstract 4518)
Citeline Analysis

Cabometyx / Cometriq for Renal Cell Cancer (RCC)

Event Date:	05/25/2023
Event Type:	Trial Data - Top-Line Results (Clinical Analysis)
Trial Name:	Phase II - w/Nivolumab + Ipilimumab - Non-Clear Cell RCC
Market Group:	Oncology
Lead Company:	Exelixis, Inc. (EXEL)
Partner Companies:	Bristol Myers Squibb (BMY) GSK (GSK) Ipsen (IPSEY) Swedish Orphan Biovitrum (SOBI) Takeda Pharmaceutical (TAK)
Former Companies:	N/A
Change to Likelihood of Approval:	0%
Likelihood of Approval:	100% (Same As Avg.)
Average Approval:	100%

The abstract entitled "Phase II study of cabozantinib (Cabo) with nivolumab (Nivo) and ipilimumab (Ipi) in advanced renal cell carcinoma with variant histologies (RCCvh)." will be presented at ASCO on June 2-6, 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

Eligible patients (pts) had metastatic RCCvh with ECOG performance status of 0-1 and may have received one line of prior therapy excluding immunotherapy or Cabo. Pts underwent a baseline biopsy and received treatment with Nivo 3 mg/kg and Ipi 1 mg/kg intravenously Q3 weeks (W) for 4 cycles followed by Nivo 480 mg IV Q4W. Cabo was given continuously at dose of 40 mg daily; reductions to 20 mg daily and 20 mg every other day were allowed.

Endpoints

The primary endpoint was objective response rate (ORR) by RECIST 1.1. Safety was a secondary endpoint.

Results

40 pts have been enrolled. At the time of data cut-off (Dec 9, 2022), 38 pts received at least 1 study drug. 11% (n=4) pts received prior systemic therapy. 45% (n=17) received all 4 doses of Nivo and Ipi; 18% (n=7) received 3 and 37% (n=14) received ≤ 2 doses. 61% (n=23) (15 of whom received 4 cycles Nivo/Ipi) received Nivo maintenance (median number of cycles, 5 (range, 1-21)). 71% (n=27) and 13% (n=5) required Cabo dose reduction to 20 mg and 20 mg every other day, respectively. Median follow-up was 8.4 (range, 2.1-23) months. Objective response was achieved in 8 pts (ORR 21%, two-sided 80% CI, 13%-32%). Median duration of response was not reached with 5 pts maintaining response > 6 months. Median progression-free survival was 8.9 (95% CI, 4.2-12.7) months.

Most Common Adverse Events

74% (n=28) developed treatment-related grade 3 or higher toxicities; 37% (n=14) developed ≥ grade 3 elevation in AST or ALT. 29% (n=11) required high dose steroids (prednisone ≥ 40 mg daily or equivalent). 13% (n=5) discontinued all study drugs due to toxicity. No grade 5 toxicity has been reported.

Conclusion

The study suggests activity for this combination in patients with RCCvh particularly among those without chromophobe histology. An additional cohort of 20 pts is enrolling with Cabo starting dose of 20 mg daily.

Comment

Non-clear cell RCC (non-cc RCC) is an area of kidney cancer with limited treatment options, having been often overlooked in clinical trials. The combination of Cabometyx, Opdivo, and Yervoy has shown moderate efficacy in these patients, although the Phase II trial only enrolled 40 patients. These data are positive, although are not largely different from currently approved therapies. Furthermore, data released for Lenvima-Keytruda combination therapy at ASCO 2023 overshadows these data, through more impressive efficacy.

Currently, preferred regimens for a metastatic patient with non-clear cell histology are Cabometyx, Sutent, and entering a clinical trial, as listed by the NCCN. Cabometyx has long reigned as the standard of care here, although its initial approval was based on trials primarily investigating clear-cell histology patients. In a meta-analysis, it was found that ORR in Cabometyx-treated non-cc RCC patients was 27% of patients, PFS was 7 months and OS was 12 months. For the triplet combination of Cabometyx-Opdivo-Yervoy, median PFS was 8.9 months, and no OS data was given. Median ORR was 21%; all data is similar to what was seen in Cabometyx-treated patients. Although this efficacy data is not negative, it is less impressive when compared to the data released for the Lenvima-Keytruda doublet (PFS: 17.9, ORR: 49%). Non-cc RCC patients do not have many treatment options, and so an approval for Cabometyx, Opdivo, and Yervoy may be granted to expand these, but it is likely that uptake will be low.

The most common grade 3 events for Cabometyx-treated patients were skin toxicity (in 4% of patients) and hypertension (in 4% of patients). In the Phase II Cabo-Opdivo-Yervoy trial, 74% of patients had a grade 3 treatment-related adverse event. This inflated rate of adverse events does not bode well for the triplet combination, and it is likely that its benefit-risk ratio will not justify its use in patients and lead to low uptake, particularly when Cabometyx monotherapy is a much more well-tolerated option with similar efficacy.

Source:

American Society of Clinical Oncology (ASCO) 05/25/2023 (Abstract 4520)
Citeline Analysis

BIOMEDTRACKER
CITELINE COMMERCIAL

List of Biomedtracker ASCO Abstract Night Events

Event Date	Drug	Lead Company	Ticker	Event Type	Trial Name	Link
Bladder Cancer						
05/25/2023	Padcev	Astellas Pharma, Inc.	4503:JP	Trial Data - Updated Results	Phase Ib/II - KEYNOTE-869	482166
Cancer						
05/25/2023	FLX475	RAPT Therapeutics, Inc.	RAPT	Trial Data - Updated Results	Phase I/II - +/-Pembrolizumab	482045
Chronic Heart Failure - Reduced Ejection Fraction (Chronic HFrEF)						
05/26/2023	Coreg	Cheplapharm Arzneimittel GmbH		Trial Data - Top-Line Results	Phase IIb - PREVENT-HF	482162
Chronic Lymphocytic Leukemia (CLL)/Small Cell Lymphocytic Lymphoma (SLL) - NHL						
05/25/2023	BGB-11417	BeiGene, Ltd.	BGNE	Trial Data - Updated Results	Phase I - Mature B-cell Malignancies (China)	482179
05/25/2023	Breyanzi	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase I/II - TRANSCEND-CLL-004	482035
05/25/2023	Venclexta	AbbVie Inc.	ABBV	Trial Data - Top-Line Results	Phase III - A041702 (w/Ibrutinib + Obinutuzumab; NCI)	482079
Colorectal Cancer (CRC)						
05/25/2023	Enhertu	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase II - DESTINY-CRC02	482084
05/25/2023	Tecentriq	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase II - AtezoTRIBE	482085
05/25/2023	Vectibix	Amgen, Inc.	AMGN	Trial Data - Final Results	Phase III - PARADIGM	482086
05/25/2023	ERAS-007	Erasca, Inc.	ERAS	Trial Data - Top-Line Results	Phase Ib/II - HERKULES-3 (w/encorafenib + cetuximab)	482120
Esophageal Cancer						
05/26/2023	HLX10	Shanghai Henlius Biotech Co. Ltd.	2696	Trial Data - Updated Results	Phase III - ASTRUM-007	482114
Follicular Lymphoma (FL)						
05/25/2023	Brukinsa	BeiGene, Ltd.	BGNE	Trial Data - Updated Results	Phase II - ROSEWOOD (w/Gazyva)	482031
Gastric Cancer						
05/25/2023	DKN-01	Leap Therapeutics, Inc.	LPTX	Trial Data - Updated Results	Phase IIa - DisTinGuish	482053
Gastrointestinal Stromal Tumor (GIST)						
05/25/2023	Qinlock	Deciphera Pharmaceuticals, Inc.	DCPH	Trial Data - Updated Results	Phase III - INTRIGUE	482050
05/25/2023	Olverembatinib	Ascentage Pharma Group Corporation	6855	Trial Data - Updated Results	Phase I - SJ-0003	482096
05/25/2023	THE-630	Theseus Pharmaceuticals, Inc.	THRX	Trial Data - Top-Line Results	Phase I/II - THE630-21-101	482138
Head and Neck Cancer						
05/26/2023	GX-188E	Genexine Inc.	095700	Trial Data - Top-Line Results	Phase II - w/GX-I7 + Keytruda (Yonsei University)	482133
05/26/2023	Eftilagimod Alpha	Immutep Ltd.	IMMP	Trial Data - Updated Results	Phase II - TACTI-002 (w/Pembrolizumab)	482106

05/25/2023	PDS0101	PDS Biotechnology Corporation	PDSB	Trial Data - Updated Results	Phase II - VERSATILE-002 (US/UK)	482044
05/25/2023	CUE-101	Cue Biopharma, Inc.	CUE	Trial Data - Updated Results	Phase I - First-in-Human (KEYNOTE-A78)	482036
Hematologic Cancer						
05/26/2023	IPH6101/SAR443579	Sanofi	SNY	Trial Data - Top-Line Results	Phase I/II - AML/ALL/MDS	482145
Hepatocellular (Liver) Cancer (HCC) (Including Secondary Metastases)						
05/26/2023	HBM4003	Harbour BioMed	2142	Trial Data - Top-Line Results	Phase Ib - w/Toripalimab (China)	482130
05/25/2023	Imfinzi	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - HIMALAYA (w/Tremelimumab)	482142
05/25/2023	Tislelizumab	BeiGene, Ltd.	BGNE	Trial Data - Updated Results	Phase III - RATIONALE 301	482030
05/25/2023	Imjudo	AstraZeneca PLC	AZN	Trial Data - Updated Results	Phase III - HIMALAYA	482082
05/25/2023	Avastin	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase III - IMbrave050	482083
05/25/2023	Tecentriq	Roche Holding AG	RHHBY	Trial Data - Updated Results	Phase III - IMbrave050	482078
HER2+ Breast Cancer						
05/25/2023	Patritumab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Top-Line Results	Phase II - BRE 354	482100
HR+/HER2- Breast Cancer						
05/25/2023	Pelareorep	Oncolytics Biotech, Inc.	ONC	Trial Data - Top-Line Results	Phase II - BRACELET-1	482103
05/25/2023	Trodelvy	Gilead Sciences, Inc.	GILD	Trial Data - Final Results	Phase III - TROPICS-02 (HR+/HER2- MBC)	482081
05/25/2023	Orserdu	The Menarini Group		Trial Data - Retrospective Analysis	Phase III - EMERALD (ER+/HER2-)	482048
Major Depressive Disorder (MDD)						
05/26/2023	COMP360	COMPASS Pathways	CMPS	Trial Data - Updated Results	Phase II - Patients w/Cancer	482153
Melanoma						
05/25/2023	EVX-01	Evaxion Biotech A/S	EVAX	Trial Data - Updated Results	Phase I/II - NeoPepVac	482123
05/25/2023	REGN-3767	Regeneron Pharmaceuticals, Inc.	REGN	Trial Data - Updated Results	Phase I - +/- Cemiplimab	482092
Multiple Myeloma (MM)						
05/26/2023	TASQ	Active Biotech AB	ACTI	Trial Data - Updated Results	Phase Ib/IIa - +/- IRd Chemotherapy (University of Pennsylvania)	482111
05/25/2023	REGN5458	Regeneron Pharmaceuticals, Inc.	REGN	Trial Data - Updated Results	Phase I/II - LINKER-MM1	482051
Myelodysplastic Syndrome (MDS)						
05/25/2023	Reblozyl	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase III - COMMANDS	482056
05/25/2023	Imetelstat	Geron Corporation	GERN	Trial Data - Updated Results	Phase II/III - IMerge (Transfusion-Dependent Subjects)	482039
Neuroendocrine Tumors (NET)						
05/26/2023	Danyelza	Y-mAbs Therapeutics Inc.	YMAB	Trial Data - Updated Results	Phase II - 201 (Osteomedullary Disease)	482176
Non-Hodgkin's Lymphoma (NHL)						

05/25/2023	AB-101 (Artiva)	Artiva Biotherapeutics, Inc.		Trial Data - Top-Line Results	Phase I/II - +/- Rituximab	482026
Non-Small Cell Lung Cancer (NSCLC)						
05/25/2023	Reqorsa	Genprex, Inc.	GNPX	Trial Data - Top-Line Results	Phase I/II - Acclaim-1 - w/Osimertinib	482037
05/25/2023	TJ4309	TRACON Pharmaceuticals Inc.	TCON	Trial Data - Updated Results	Phase Ib/II - +/- Toripalimab (China)	482043
05/25/2023	DZD9008	Dizal (Jiangsu) Pharmaceutical Co., Ltd.	688192	Trial Data - Updated Results	Phase II - WU-KONG6 (China)	482088
05/25/2023	APG-2449	Ascentage Pharma Group Corporation	6855	Trial Data - Updated Results	Phase I - XC101 (China)	482089
05/25/2023	CAN04	Cantargia AB	CANTA	Trial Data - Top-Line Results	Phase I/II - CESTAFOUR (EU)	482060
05/25/2023	Libtayo	Regeneron Pharmaceuticals, Inc.	REGN	Trial Data - Updated Results	Phase III - EMPOWER-Lung 1 (1st Line)	482069
05/25/2023	Datopotamab Deruxtecan	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase Ib - TROPION-Lung02 (w/Keytruda)	482071
Ovarian Cancer						
05/25/2023	ZN-c3	Zentalis Pharmaceuticals	ZNTL	Trial Data - Updated Results	Phase Ib - ZN-c3-002	482058
05/25/2023	SL-172154	Shattuck Labs, Inc.	STTK	Trial Data - Final Results	Phase I - SL03-OHD-101	482059
05/25/2023	VS-6766	Verastem, Inc.	VSTM	Trial Data - Updated Results	Phase II - RAMP 201	482047
Pancreatic Cancer						
05/25/2023	AVB-500	Aravive, Inc.	ARAV	Trial Data - Top-Line Results	Phase Ib/II - w/Gemcitabine and Nab-paclitaxel	482022
Prostate Cancer						
05/26/2023	MB-105	Mustang Bio Inc.	MBIO	Trial Data - Final Results	Phase I - City of Hope (NCI)	482165
05/25/2023	Talzenna	Pfizer Inc.	PFE	Trial Data - Updated Results	Phase III - TALAPRO-2	482055
05/25/2023	Xtandi	Astellas Pharma, Inc.	4503:JP	Trial Data - Top-Line Results	Phase II - ENACT	482076
Renal Cell Cancer (RCC)						
05/25/2023	Cabometyx / Cometriq	Exelixis, Inc.	EXEL	Trial Data - Top-Line Results	Phase II - w/Nivolumab + Ipilimumab - Non-Clear Cell RCC	482074
05/25/2023	Lenvima	Eisai Co., Ltd.	4523:JP	Trial Data - Updated Results	Phase II - w/Pembrolizumab - KEYNOTE-B61	482097
05/25/2023	Keytruda	Merck & Co., Inc.	MRK	Trial Data - Updated Results	Phase II - w/Lenvatinib - KEYNOTE-B61	482098
05/25/2023	Lenvima	Eisai Co., Ltd.	4523:JP	Trial Data - Final Results	Phase III - CLEAR (First Line)	482054
05/25/2023	AVB-500	Aravive, Inc.	ARAV	Trial Data - Updated Results	Phase Ib/II - RCC-003 (US)	482020
Sarcoma						
05/26/2023	Fyarro	AADi Bioscience, Inc.	AADI	Trial Data - Top-Line Results	Phase Ib/II - w/Pazopanib	482065
05/25/2023	Afami-cel	Adaptimmune Therapeutics plc	ADAP	Trial Data - Updated Results	Phase II - SPEARHEAD-1	482072
05/25/2023	TTI-621	Pfizer Inc.	PFE	Trial Data - Top-Line Results	Phase I/II - w/Doxorubicin	482062
Solid Tumors						
05/26/2023	Veyonda	Noxopharm Limited	NOX	Trial Data - Top-Line Results	Phase I - IONIC-1 (w/Opdivo)	482108

05/26/2023	HLX07	Shanghai Henlius Biotech Co. Ltd.	2696	Trial Data - Top-Line Results	Phase Ib/II - w/Chemotherapy (China)	482121
05/26/2023	HLX26	Shanghai Henlius Biotech Co. Ltd.	2696	Trial Data - Top-Line Results	Phase I - HLX26-001 (China)	482122
05/26/2023	FORE-8394	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase I/IIa - PLX120-03	482158
05/26/2023	FORE-8394	Daiichi Sankyo Co., Ltd.	4568	Trial Data - Updated Results	Phase I/IIa - PLX120-03	482163
05/25/2023	Vitrakvi	Bayer AG	BAYN	Trial Data - Top-Line Results	Phase II - ADVL1823	482146
05/25/2023	BAY2416964	Bayer AG	BAYN	Trial Data - Updated Results	Phase I - Safety	482119
05/25/2023	Sudocetaxel Zendusortide	Theratechnologies Inc.	THTX	Trial Data - Updated Results	Phase I - TH1902-CTR-0001	482124
05/25/2023	Zotatifin	eFFECTOR Therapeutics, Inc.	EFTR	Trial Data - Updated Results	Phase I/II - Advanced Solid Tumors	482109
05/25/2023	Non-Viral TCR Program (ZIOPHARM/Intrexon/NCI)	Alaunos Therapeutics, Inc.	TCRT	Trial Data - Updated Results	Phase I/II - Library TCR-T	482102
05/25/2023	AU-007	Aulos Bioscience, Inc.		Trial Data - Updated Results	Phase I/II - First-in-Human	482104
05/25/2023	SY-5609	Syros Pharmaceuticals, Inc.	SYRS	Trial Data - Updated Results	Phase I - SY-5609-101	482095
05/25/2023	TPST-1495	Tempest Therapeutics, Inc.	TPST	Trial Data - Top-Line Results	Phase Ia/Ib - TPST-1495-001 (w/Pembrolizumab)	482064
05/25/2023	MP0317	Molecular Partners AG	MOLN	Trial Data - Updated Results	Phase I - First-in-Human (Europe)	482077
05/25/2023	CBX-12	Cybrexa Therapeutics		Trial Data - Updated Results	Phase I/II - First-in-Human	482080
05/25/2023	Nirogacestat	SpringWorks Therapeutics Inc.	SWTX	Trial Data - Updated Results	Phase III - DeFi (Desmoid/Fibromatosis)	482087
05/25/2023	CLN-619	Cullinan Oncology, Inc.	CGEM	Trial Data - Top-Line Results	Phase I - +/- Pembrolizumab	482028
05/25/2023	BDC-1001	Bolt Biotherapeutics, Inc.	BOLT	Trial Data - Updated Results	Phase I/II - BBI-20201001	482029
05/25/2023	AFM24	Affimed N.V.	AFMD	Trial Data - Top-Line Results	Phase I/IIa - Dose Escalation w/ SNK-01	482024
05/25/2023	AL102	Ayala Pharmaceuticals, Inc.	ADXS	Trial Data - Updated Results	Phase II/III - RINGSIDE (Desmoid Tumors)	482025
05/25/2023	PY159	Pionyr Immunotherapeutics, Inc.		Trial Data - Top-Line Results	Phase Ia/Ib - w/Pembrolizumab	482038
05/25/2023	VT1021	Vigeo Therapeutics, Inc.		Trial Data - Updated Results	Phase Ib/II - Safety/Pharmacology (01)	482042
05/25/2023	BGB-A445	BeiGene, Ltd.	BGNE	Trial Data - Top-Line Results	Phase I - BGB-A317-A445-101	482032
05/25/2023	CTL-002	CatalYm GmbH		Trial Data - Updated Results	Phase I/IIa - GDFATHER	482033
05/25/2023	ATG-008	Bristol Myers Squibb Company	BMY	Trial Data - Updated Results	Phase I/II - TORCH-2	482057
05/25/2023	AFNT-211	Affini-T Therapeutics, Inc.		Trial Data - Preclinical Results	Preclinical Studies	482046
05/25/2023	RLY-4008	Relay Therapeutics, Inc.	RLAY	Trial Data - Updated Results	Phase I/II - ReFocus	482049
Thyroid Cancer						
05/25/2023	AIC100	AffyImmune Therapeutics, Inc.		Trial Data - Top-Line Results	Phase I - First-In-Human (Cornell University)	482023
Waldenstrom Macroglobulinemia (WM) / Lymphoplasmacytic Lymphoma (LPL) - NHL						
05/25/2023	APG-2575	Ascentage Pharma Group Corporation	6855	Trial Data - Top-Line Results	Phase Ib/II - MAPLE-1	482101

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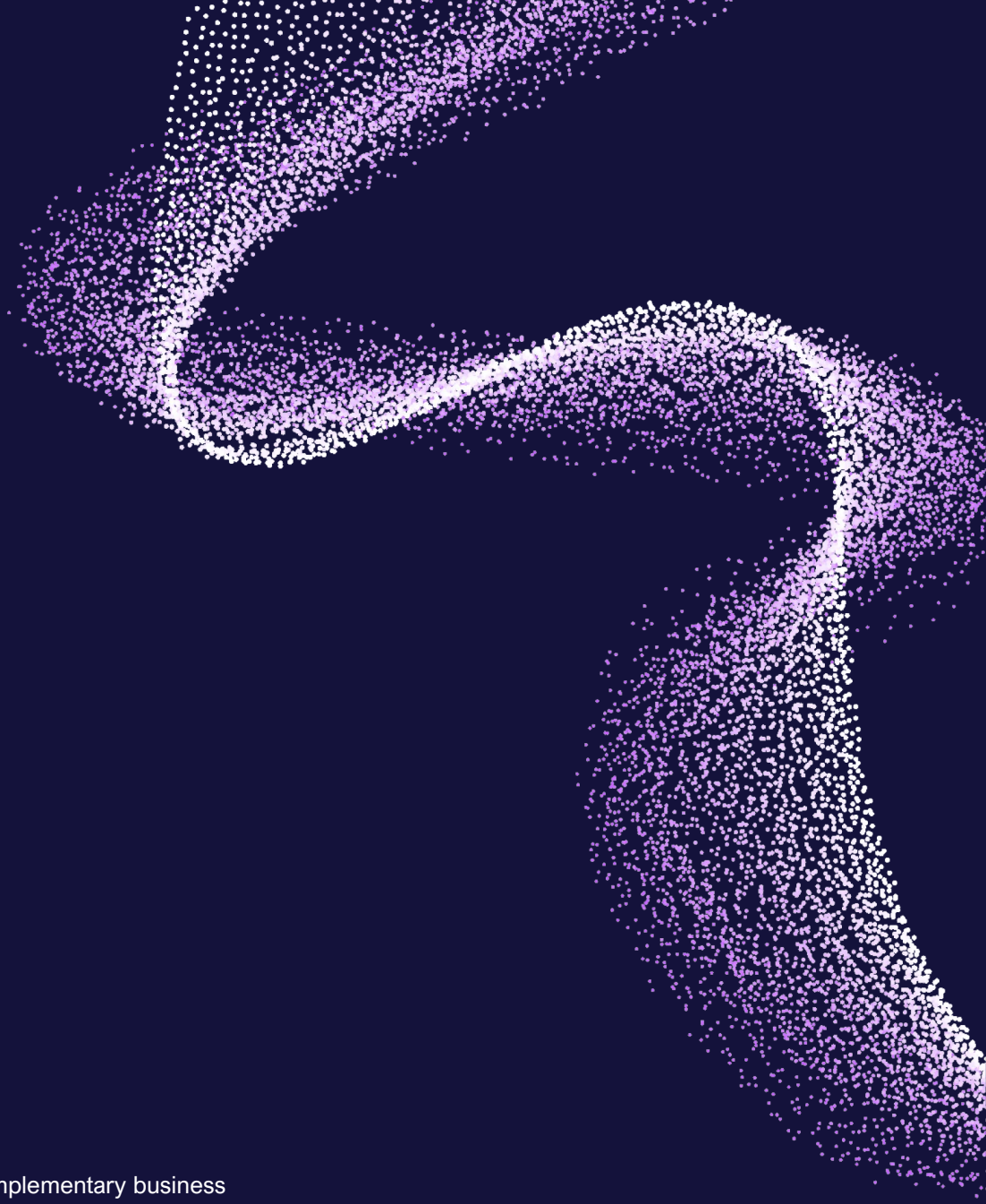

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