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ASCO Preview: Five Top Late-Breakers To Watch For

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AstraZeneca plans to unveil multiple major data packages, while Servier reveals much-anticipated results in glioma, and ImmunoGen and Novartis will present key pivotal data in women's cancers.

The American Society of Clinical Oncology's (ASCO) 2023 annual meeting will kick off next week at Chicago's McCormick Place and will include a variety of important datasets across oncology, particularly in solid tumors, which will be presented from 2-6 June.

1. NATALEE Results Could Double Sales For Novartis's Kisqali

In April, Swiss drug maker *Novartis AG* announced as part of its first quarter earnings that it would cull its pipeline to streamline its R&D and commercial focus, removing among other agents its in-house PD-1 inhibitor spartalizumab. But one of the survivors of the culling was Kisqali (ribociclib), a CDK4/6 inhibitor for breast cancer. That should come as no surprise, given the announcement of successful results the month before from the pivotal Phase III NATALEE trial in patients with HR+/HER2- early breast cancer (EBC), including those with Stage IIA-III tumors regardless of nodal involvement, which analysts have forecast could double its peak sales potential to $8bn. (Also see "*Novartis Culls Pipeline As 'Pure-Play' Drive Progresses*" - Scrip, 25 Apr, 2023.)

Data from the trial showed that the drug administered at 400mg along with endocrine therapy met the invasive disease-free survival (iDFS) primary endpoint compared with endocrine therapy alone in patients at both high and intermediate risk of recurrence, which led NATALEE's independent data monitoring committee to recommend stopping the trial. (Also see "*Novartis's Kisqali Strikes Gold In Adjuvant Early Breast Cancer Setting*" - Scrip, 27 Mar, 2023.)

The positive results for a broader patient population could give the drug a market advantage over its competitor, *Eli Lilly and Company*'s CDK4/6 inhibitor, Verzenio (abemaciclib), which has FDA

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approval in combination with endocrine therapy for HR+/HER2- EBC, but only among patients at high risk of recurrence.

However, SVB Securities analysts Andrew Berens and Christopher Liu pointed to a potential market disadvantage for Kisqali, namely that it carries ECG safety monitoring requirements, while Verzenio does not, which could thus limit the Novartis drug's adoption in the adjuvant setting.

2. DESTINY-PanTumor02 Data May Give Clarity On Potential Usage

AstraZeneca plc and *Daiichi Sankyo Co., Ltd.* have found significant success with Enhertu (fam-trastuzumab deruxtecan-nxki), their HER2-targeting antibody-drug conjugate (ADC), which in 2022 reached blockbuster sales of $1.17bn, up from the prior year's $426m. That's just in the four indications – two in breast cancer, one in non-small cell lung cancer (NSCLC) and one in gastric and gastroesophageal junction cancer – in which it has approval. With the DESTINY-PanTumor02 study, the British and Japanese drug makers are now looking to expand Enhertu's use into additional cancer indications.

The 268-participant Phase II study has completed enrollment of patients with HER2-expressing urothelial bladder cancer, biliary tract cancer, cervical cancer, endometrial cancer, ovarian cancer, pancreatic cancer and rare tumors, according to clinicaltrials.gov.

So far, the study is off to a decent start. In March, AstraZeneca said the trial met the prespecified target for objective response rate (ORR) and duration of response (DOR) across multiple tumor types in heavily pretreated patients, although it did not announce numerical data. (Also see "*AstraZeneca/Daiichi Sankyo Line Up More Enhertu Indications*" - Scrip, 6 Mar, 2023.)

In a 22 May primer for the ASCO meeting, SVB's Berens and Liu said the interim efficacy and safety data that AstraZeneca and Daiichi Sankyo are presenting may suggest additional tumor indications in which the ADC could find usage.

Enhertu was the subject of a deal worth $1.35bn up front and up to $6.9bn in total, and analysts have forecast that it could reach peak sales of up to $6bn. The drug is a major competitor to *Gilead Sciences, Inc.*'s Trodelvy (sacituzumab govitecan-hziy), particularly in breast cancer, despite having a different mechanism of action.

3. Data For Servier IDH Inhibitor In Glioma Generate Analyst Buzz

Another oncology buyout that has paid off so far is *Les Laboratoires Servier*'s acquisition of *Agios Pharmaceuticals, Inc.*'s cancer drug portfolio in 2020 for $1.8bn, including the IDH inhibitor vorasidenib, which the French drug maker is developing in low-grade glioma carrying an IDH1 or IDH2 mutation, both of which the drug blocks. In March, Servier said the Phase III INDIGO trial testing vorasidenib at 40mg met its primary endpoint of progression-free survival over a 30-

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month timeframe. (Also see "*Servier's Oncology Strategy Pays Off As Vorasidenib Hits Bullseye In Pivotal Glioma Trial*" - Scrip, 15 Mar, 2023.)

Gliomas have proven to be a challenging area for drug development, with a long litany of failures, so the interim results from INDIGO provide a rare example of potential promise.

It's also good news for Servier, which had previously told *Scrip* that it regards vorasidenib as the "little brother" of Tibsovo (ivosidenib), its IDH1 inhibitor approved for acute myeloid leukemia. In a September 2022 interview, Servier's global head of oncology research and development Walid Kamoun told *Scrip* that the company was determined to get past the long track record of failure in glioma.

At ASCO, Servier will present results of INDIGO at a plenary session, which SVB's Berens and Liu said suggests that the data are "relevant and strongly positive," which thereby also suggests a strong likelihood of regulatory approval for the drug. The company would be able to receive a future milestone payment of $200m, as well as 15% royalties on US net sales for the drug.

4. ImmunoGen To Present Full Data From 'Home Run' MIRASOL

ImmunoGen, Inc. is poised to expand the reach of Elahere (mirvetuximab soravtansine-gynx) in folate receptor alpha (FRα)-positive platinum chemotherapy-resistant ovarian cancer with data from the Phase III MIRASOL trial that the company called a "home run" when it announced them earlier this month. (Also see "*ImmunoGen's Elahere Wins Big In Confirmatory Ovarian Cancer Trial*" - Scrip, 3 May, 2023.) The company plans to present full data from the trial at ASCO, and Guggenheim Partners analyst Michael Schmidt said the MIRASOL data were among the highlights of late-breaking data presentations at the meeting.

The company won accelerated approval from the US Food and Drug Administration for Elahere in November 2022 for patients with FRα-positive platinum-resistant epithelial ovarian, fallopian tube and primary peritoneal cancer who had received one to three prior lines of therapy, based on ORR and DOR data from the Phase III SORAYA study, making it a first-in-class ADC. (Also see "*ImmunoGen Transitions To Commercial Stage With Elahere Launch*" - Scrip, 15 Nov, 2022.) The approval was more than three decades in the making, with the company first raising venture capital funding in 1988.

At the time it announced the MIRASOL results, ImmunoGen said it plans to file a supplemental biologics license application with the FDA, as well as an application with the European Medicines Agency, which the data – showing statistically significant improvements in overall survival (OS) and progression-free survival (PFS) – put it in a position to do. ImmunoGen is additionally testing the drug in a Phase II study as a monotherapy for patients with third-line disease, in another Phase II trial in second-line disease combined with carboplatin chemotherapy, and in a Phase III study combined with *Roche Holding AG*'s Avastin (bevacizumab) as a maintenance

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treatment.

5. AstraZeneca Aims For First-Mover Advantage With DUO-O Data

In newly diagnosed ovarian cancer, AstraZeneca plans to present data from its Phase III DUO-O trial of the combination of its PARP inhibitor Lynparza (olaparib), partnered with *Merck & Co., Inc.*, and PD-L1 inhibitor Imfinzi (durvalumab), together with Roche's Avastin as maintenance therapy, among patients with advanced high-grade epithelial ovarian cancer without tumor BRCA mutations.

DUO-O was the first trial to report out on the combination of a PARP inhibitor and a checkpoint inhibitor, in an area where PARP inhibitors already play a dominant role, in addition to Avastin and platinum-based chemotherapy. AstraZeneca's hope is that moving Lynparza into the first-line BRCA wild-type setting will increase its treatable patient population. (Also see "*AstraZeneca Takes First Step For Lynparza/Imfinzi Combo In Ovarian Cancer*" - Scrip, 5 Apr, 2023.)

The data could put Lynparza on a stronger competitive footing against the other approved PARP inhibitors that dominate the market, *GSK plc*'s Zejula (niraparib) and *Pfizer Inc.*'s Talzenna (talazoparib). They could also give it a first-mover advantage over additional checkpoint inhibitor/PARP inhibitor combinations coming down the pike in the first-line ovarian cancer setting, such as Merck's own study combining its PD-1 inhibitor Keytruda (pembrolizumab) with Lynparza, and GSK's study combining Zejula with its Jemperli (dostarlimab).

SVB's Berens and Liu said DUO-O is noteworthy "in that PARP inhibitors have recently been questioned for their risk benefit in non-BRCA patients."

"We look for details in the non-BRCA population, given these concerns, as well as evidence of PARPi and anti-PD1 synergy, which has also been generally lackluster thus far," they said.

Additionally, AstraZeneca will present OS data at a plenary session for the Phase III ADAURA trial of Tagrisso (osimertinib) in patients with resected, EGFR-mutated Stage IB-IIIA NSCLC. Compelling OS results in the setting may continue to fuel growth for the drug, the analysts noted.

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