SCRIP
CITELINE COMMERCIAL

04 Jun 2023 | **News**

# ImmunoGen's Elahere Data In Avastin-Naïve Ovarian Cancer Prompt Discussion About Earlier Use

by Alaric DeArment

The presenter on the MIRASOL study called the data "practice changing," while the discussant cited Sutro's STRO-002 as a potential option for patients with low folate receptor alpha expression.

Data presented at the American Society of Clinical Oncology annual meeting seem likely to shake up the ovarian cancer market. *ImmunoGen, Inc.*'s Phase III confirmatory MIRASOL trial of its antibody-drug conjugate Elahere (mirvetuximab soravtansine-gynx) supports a shift in treatment paradigms for patients with ovarian cancer resistant to platinum chemotherapy. Meanwhile, *Sutro Biopharma, Inc.*'s luveltamab tazevibulin presents a potential option for patients with levels of folate receptor alpha (FRα) expression too low to make them eligible for treatment with Elahere.

The MIRASOL trial, presented 4 June at ASCO, showed a statistically significant improvement on the primary endpoint of progression-free survival (PFS) as well as an overall survival benefit. Differences in OS based on whether patients have previously received *Roche Holding AG*'s anti-VEGF drug Avastin (bevacizumab) have prompted discussion about potentially bringing Elahere into earlier lines of treatment.

"Until this day, no Phase III study has ever demonstrated an improvement in overall survival in the platinum-resistant ovarian cancer space," principal investigator Kathleen Moore, associate director of clinical research at the University of Oklahoma's Stephenson Cancer Center, said in the presentation of the late-breaking abstract, calling the data "practice changing."

MIRASOL is the confirmatory trial for Elahere, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC) that won accelerated approval from the US Food and Drug Administration

in November 2022 for patients with one to three prior lines of therapy, based on overall response rate (ORR) data from the Phase III SORAYA trial. The presentation followed the announcement of the MIRASOL data in early May, with ImmunoGen calling the results a "home run." (Also see "*ImmunoGen's Elahere Wins Big In Confirmatory Ovarian Cancer Trial*" - Scrip, 3 May, 2023.)

## Data Prompt Discussion On Earlier Use

As the company stated in May, data showed a median PFS by investigator assessment of 5.62 months for patients receiving Elahere, versus 3.98 months for those receiving chemotherapy (HR 0.65, p<0.0001). On OS, the median was 16.46 months for the Elahere arm and 12.75 months for the chemotherapy arm (HR 0.67, p=0.0046).

***ImmunoGen Transitions To Commercial Stage With Elahere Launch***

By Jessica Merrill

15 Nov 2022
The antibody-drug conjugate was approved by the US FDA for the treatment of FRα-positive, platinum-resistant epithelial ovarian cancer.

*Read the full article here*

Among the 453 patients included in the study, the majority – 281 – had previously received Avastin, while the remaining 172 were Avastin-naïve. Prior maintenance with Avastin as well as PARP inhibitors was allowed and considered under MIRASOL's inclusion criteria to count as a prior line of therapy.

When stratifying patients according to Avastin exposure, the PFS HR remained mostly consistent and also statistically significant – 0.66 and p=0.0210 in the Avastin-naïve population and 0.64 and p=0.0011 in the Avastin-pretreated population.

For OS, the HR for Avastin-naïve patients was 0.51 and reached statistical significance (p=0.0099), but for Avastin-pretreated patients it was 0.74 and did not reach statistical significance (p=0.0789).

"Based on the data presented by Dr. Moore, I wonder, should we be considering moving the treatment a little bit earlier in the disease course," Memorial Sloan Kettering Cancer Center gynecologic oncologist Roisin O'Cearbhaill, the discussant for the session, said after Moore's presentation. "Bearing in mind that these patients had received up to three prior lines of therapy, it is interesting to note that patients who have not received prior bevacizumab appear to derive more substantial benefit from mirvetuximab."

In December, ImmunoGen launched the Phase III GLORIOSA trial of Elahere/Avastin versus Avastin alone in maintenance treatment of platinum-sensitive ovarian cancer, which is designed to enroll 418 patients and has primary and study completion dates in 2027 and 2029, respectively.

In terms of adverse events, hematological toxicities were significantly lower in the Elahere group compared with patients receiving investigator's choice of chemotherapy, which included paclitaxel, pegylated liposomal doxorubicin and topotecan.

On the other hand, some toxicities occurred at rates similar to those of paclitaxel, including diarrhea (29% Elahere vs. 32% paclitaxel), nausea (27% vs. 26%) and peripheral neuropathy (22% vs. 29%), while ocular toxicities were all significantly higher in the Elahere-treated group versus chemotherapy, including blurred vision (41%, 8% grade 3+), keratopathy (32%, 9% grade 3+) and dry eye (28%, 3% grade 3+).

O'Cearbhaill said the gastrointestinal toxicities could be managed with patient education and working with the clinical team "from the get-go." For managing the drug's "unique" eye toxicities, it will make working with eye specialists particularly important, she added.

## FRα Expression Levels Could Help Determine Drug Choice

Coming up behind Elahere is Sutro's luveltamab tazevibulin, or STRO-002, which is also an FRα-targeting ADC. Phase I data were presented at ASCO on 3 June. Sutro's candidate is designed for patients with lower FRα expression levels, and the study enrolled patients with tumor proportion scores (TPS) of greater than 25% irrespective of staining intensity, which according to Sutro represents about 80% of the advanced ovarian cancer population. MIRASOL enrolled patients with high FRα expression, and participants had to have FRα detected via immunohistochemistry with PS2+ intensity among 75% or more of viable tumor cells.

The data from Sutro's study at ASCO were consistent with a prior announcement in January and showed a 37.5% ORR, median duration of response (DOR) of 5.5 months and a 6.1-month PFS. At a higher starting dose, the ORR was 43.8%, DOR was 5.4 months and PFS was 6.6 months. The company noted that the responses were in patients "who may not be eligible for other approved therapies targeting" FRα.

"It's very clear that we now have a new biomarker that we need to investigate and also check whether our patients have expression on this biomarker, folate receptor alpha," O'Ceabhaill said.

That, she said, would mean figuring out how to enrich for the expression of biomarkers like FRα "because we have seen that progression-free survival outcomes can be improved when we enrich for the target." The level of target expression could be a factor in determining the choice of drug, she added, citing the luveltamab tazevibulin study as an example of a subset of patients who could still benefit from target therapy despite lower levels of FRα expression.