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Jazz Hits High Note With Updated Zanidatamab Data In Biliary Tract Cancer At ASCO

by Alaric DeArment

The company said it is in talks with the US FDA for an accelerated approval filing of the HER2-directed bispecific antibody, which showed better ORR and PFS than the standard of care.

Jazz Pharmaceuticals plc has its eyes on becoming the first to receive US Food and Drug Administration approval for an agent in HER2-positive biliary tract cancer (BTC), with updated data at the American Society of Clinical Oncology (ASCO) annual meeting showing an extension of progression-free survival (PFS) among patients with the rare disease who received its HER2-directed bispecific antibody, zanidatamab.

The company presented updated safety and efficacy data from the 87-patient HERIZON-BTC-01 trial in an oral presentation at the meeting on 2 June. Jazz is developing the drug under a partnership with *Zymeworks, Inc.* that the two firms announced in October 2022.

BTC is overall rare, diagnosed in around 210,000 people every year, and it has seen relatively little in the way of drug development for HER2-overexpressing disease. On an analyst call to discuss the results, HERIZON-BTC-01 investigator Shubham Pant of The University of Texas MD Anderson Cancer Center said there were about 12,000 people living with HER2-positive cases of BTC in the US, Europe and Japan, with limited therapeutic benefit in patients with locally advanced, stage IV metastatic disease in the second line and beyond.

ClinicalTrials.gov lists a few commercial trials of HER2-directed therapies, mostly taking place in China – where Jazz's study also enrolled some of its patients – along with basket studies in HER2-positive solid tumors that include BTC and some academic trials in Korea with *Roche Holding AG*'s HER2-directed monoclonal antibody Herceptin (trastuzumab).

Data Show Win On PFS

Results presented at ASCO and published in *The Lancet Oncology* showed a confirmed overall response rate (cORR) of 41.3% and median duration of response of 12.9 months – similar to topline data that Zymeworks announced in December – along with median progression-free survival (PFS) of 5.5 months. (Also see "*Zymeworks' HER2 Antibody Hits Target In Pivotal Biliary Tract Cancer Trial*" - Scrip, 20 Dec, 2022.)

The complete response (CR) and partial response (PR) rates by central review were 1.3% and 40%, and 5% and 36.3% by investigator assessment. Sixteen patients had ongoing responses at the time of data cutoff.

Pant told the call that chemotherapy in the setting yields a 5%-15% ORR and median PFS of about four months. Jazz chief medical officer Kelvin Tan noted that the combination of Herceptin with a second HER2-directed monoclonal antibody from Roche, Perjeta (pertuzumab), is also used off-label, with similar levels of efficacy.

By contrast, zanidatamab is designed to bind to two domains of HER2 and has shown greater activity in preclinical studies than either Herceptin or Herceptin/Perjeta, Pant added.

"The prognosis is quite poor, and the chemotherapies are, I would say, somewhat poorly tolerated," Jazz executive vice president for research and development Robert Iannone told *Scrip*. "So there's a really substantial, high unmet need in patients with biliary tract cancer in general, especially those who have progressed after initial therapy."

Pant noted on the call that 96.6% of patients in the trial had treatment-emergent adverse events (TEAE), while 72.4% had treatment-related adverse events (TRAE), though only two patients discontinued treatment in relation to those, and the majority of TRAEs were grade 1-2; none were grade 4 or fatal. Diarrhea, infusion-related reaction, ejection fraction decrease, nausea and anemia were the most common side effects.

The company plans to take the results to the FDA in the hope of getting accelerated approval.

"We do believe that these data can be used to support accelerated approval in the United States and, potentially, conditional approval around the world in various places," Iannone said. "We are in dialogue with the FDA about finding the most appropriate and fastest path to approval in the US."