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SAN ANTONIO – Patients with hormone receptor (HR)-positive, HER2-negative advanced breast cancers had similar progression-free survival (PFS) whether they were treated with sacituzumab govitecan-hziy (Trodelvy) or standard-of-care chemotherapy as the first treatment after endocrine therapy, according to results from the Phase III ASCENT-07 clinical trial presented at the San Antonio Breast Cancer Symposium (SABCS), held December 9-12, 2025.

“HR-positive, HER2-negative breast cancers are typically treated with first-line endocrine therapy, but treatment resistance is common,” said Komal Jhaveri, MD, the Patricia and James Cayne chair for junior faculty; associate attending, Breast Medicine and Early Drug Development Services; and section head of the Endocrine Therapy Research Program at Memorial Sloan Kettering Cancer Center.

“In cases where HR-positive, HER2-negative, metastatic breast cancer has become refractory to endocrine therapy, chemotherapy remains a common standard,” she explained. “Chemotherapy agents have shown marginal survival benefit but are associated with numerous toxicities that can be severe and long-lasting. Therefore, there remains a high unmet need in this setting for additional effective treatments.”

Sacituzumab govitecan-hziy is an antibody-drug conjugate that targets the TROP-2 protein found on the surface of most breast cancer cells to deliver a cytotoxic agent to these cells, as well as to neighboring cells within the tumor microenvironment.

One of the therapeutic’s approved indications is for patients with HR-positive, HER2-negative

advanced breast cancers that have progressed on or after endocrine therapy and chemotherapy.

The approval was based on statistically significant and clinically meaningful PFS and overall survival (OS) data from the Phase III TROPiCS-02 clinical trial, said Jhaveri. In that study, patients treated with sacituzumab govitecan-hziy after two or more lines of chemotherapy had a 34% lower risk of disease progression or death and a 3.2-month improvement in OS compared with those treated with another line of chemotherapy.

Those results led Jhaveri and colleagues to ask whether sacituzumab govitecan-hziy would also be beneficial earlier in the treatment course—for patients who had received endocrine therapy but who had not yet been treated with chemotherapy.

To test this, they conducted the ASCENT-07 trial, which enrolled 690 patients with HR-positive, HER2-negative advanced breast cancers who had received prior endocrine therapy and who were candidates for first chemotherapy. Patients were randomly assigned (2:1) to receive either sacituzumab govitecan-hziy or standard-of-care chemotherapy.

The ASCENT-07 trial did not meet its primary endpoint of improved PFS by blinded independent central review. After a median follow-up of 15.4 months, the median PFS was 8.3 months in both arms with a hazard ratio of 0.85.

While data on OS were not mature at the time of this primary analysis, Jhaveri noted that preliminary results suggest a potentially lower risk of death among patients treated with sacituzumab govitecan-hziy. “It will be critical that we continue to follow patients for overall survival to better understand the potential long-term impact of sacituzumab govitecan-hziy in this treatment setting,” she added.

The rates of treatment response were similar between the arms, but numerically higher for patients treated with sacituzumab govitecan-hziy, with 37% of patients experiencing responses to sacituzumab govitecan-hziy and 33% to chemotherapy. The median duration of response was numerically longer with sacituzumab govitecan-hziy than with chemotherapy (12.1 months vs. 9.3 months).

According to Jhaveri, the toxicities associated with sacituzumab govitecan-hziy in this trial were consistent with those observed in previous breast cancer studies. In both arms, the most common grade 3 or higher treatment-related adverse events were neutropenia and leukopenia, with both of these occurring at higher rates among patients treated with sacituzumab govitecan-hziy. Treatment-related adverse events that led to treatment discontinuation were observed in approximately 3% of patients in the sacituzumab govitecan-hziy and 7% in the chemotherapy arm.

“While our study did not meet its primary endpoint of PFS for patients who have not yet received chemotherapy, sacituzumab govitecan-hziy remains a standard of care for HR-positive, HER2-negative metastatic breast cancers after prior endocrine therapy and chemotherapy based on the PFS and overall survival results seen in the TROPiCS-02 study,” said Jhaveri.

“HR-positive, HER2-negative metastatic breast cancer is a highly heterogeneous disease, and this complexity makes it particularly challenging to manage, especially in patients whose disease has already progressed on multiple lines of endocrine therapy,” she added.

The study did not compare the efficacy of sacituzumab govitecan-hziy with trastuzumab deruxtecan (T-DXd; Enhertu), a HER2-targeted antibody-drug conjugate that is now approved for some HR-positive, HER2-negative breast cancers that express enough HER2 to be considered “HER2-low” or “HER2-ultralow.” T-DXd was not approved to treat HER2-low and -ultralow breast cancers in the chemotherapy-naive setting until after enrollment for the ASCENT-07 trial had closed.

“The ASCENT-07 study design and choice of comparator was aligned with treatment guidelines for this line of treatment and disease setting at the time of study planning and conduct,” Jhaveri noted.

The study was sponsored by Gilead Sciences.

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