

The Use of Sacituzumab Govitecan in Triple-Negative Breast Cancer



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Sacituzumab govitecan-hziy (Trodely) has been a recent topic of conversation in the breast cancer space after updates showed positive results in terms of survival. Specifically, the phase 3 ASCENT trial (NCT02574455), which assessed sacituzumab vs chemotherapy or the standard of care (SOC), produced encouraging results.¹

A discussion during a *Between the Lines* program hosted by CancerNetwork®, experts in breast cancer discussed the ASCENT trial in depth, and the use of sacituzumab for patients with triple-negative breast cancer (TNBC).

The clinicians included **Aditya Bardia, MD, MPH**, a medical oncologist from Massachusetts General Hospital in Boston, and **Alison K. Conlin, MD**, a medical oncologist from Providence Cancer Institute in Portland, Oregon. Bardia and Conlin reviewed the trial results and discussed how they affect future research.

Overview of TNBC

To begin the conversation, Bardia asked his colleague to highlight the standard of care for patients with TNBC and how providers should go about treating this population. Conlin noted that patients who have metastatic disease are some of the hardest to treat. Specifically, she said, because these patients typically do not live longer than 1 to 2 years.

When asked about the typical treatment for metastatic TNBC, Conlin explained that clinicians will use a regimen with a backbone of taxane and anthracyclines.

“If we can, and there’s enough of a

disease-free survival interval, we’re starting with a taxane [therapy],” she said. “If not, gemcitabine and carboplatin have been [the] typical combination chemotherapy we’ve used. With the advent of immunotherapy, we are looking for our immunotherapy-sensitive patients, although again that’s not the majority of patients, so we’re hoping we find some sort of home run with that.”

Bardia acknowledged that he too follows this regimen. However, patients who have PD-L1–positive metastatic TNBC will respond for about 4 to 6 months and then have disease progression. Conlin agreed, which spurred the next part of the discussion regarding the targeting of Trop-2 in breast cancer.

Although other therapies have been considered, such as chemotherapy and paclitaxel, significant toxicities have been observed with these treatments. Recently, the use of antibody-drug conjugates (ADCs) has exploded, and these agents help target an overexpression of cancer cells. Trop-2 is often overexpressed in patients with TNBC and hormone receptor–positive cancers, and as a result, ADCs are being used to target Trop-2.

One of the ADCs includes sacituzumab govitecan. Regarding the recently reported results of the ASCENT trial, Bardia noted that patients treated with sacituzumab had better outcomes than those who received the SOC.

ASCENT trial

The ASCENT trial comprised 529 patients (median age, 54 years) with TNBC who were

randomly assigned 1:1 to receive either sacituzumab or SOC chemotherapy. At baseline, 61 patients had brain metastases. A total of 32 patients who were supposed to receive SOC did not receive it (n = 26) or withdrew their consent (n = 6). At data cutoff, 15 patients continued to receive sacituzumab, and 0 received the SOC.

The median follow-up was 17.7 months and the median progression-free survival (PFS), which was determined by central review, was 5.6 months (95% CI, 4.3-6.3) in the sacituzumab arm vs 1.7 months (95% CI, 1.5-2.6) in the SOC arm (HR, 0.41; 95% CI, 0.32-0.52; $P < .001$). The PFS benefit was observed across all subgroups. Patients had a median overall survival of 12.1 months (95% CI, 10.7-14.0) in the sacituzumab arm and 6.7 months (95% CI, 5.8-7.7) in the SOC arm (HR, 0.48; 95% CI, 0.38-0.59; $P < .001$).

In the sacituzumab arm, the objective response rate was 35% vs 5% in the SOC arm. Patients had a median duration of response of 6.3 months (95% CI, 5.5-9.0) in the sacituzumab arm and 3.6 months (95% CI, 2.8-not estimated) in the SOC arm (HR, 0.39; 95% CI, 0.14-1.07). Between both arms, patients had a median time to response of 1.5 months.

The most common treatment-related adverse effects (TRAEs) between the sacituzumab arm and the SOC arm were neutropenia (63% vs 43%), diarrhea (59% vs 12%), and nausea (57% vs 26%). The most frequent TRAEs of grade 3 or higher were neutropenia (51% vs 33%, respectively), leukopenia (10% vs 5%), and diarrhea (10% vs < 1%). Serious TRAEs occurred in 15% of patients in the sacituzumab arm vs 8% in the SOC arm, with dose reductions happening in 22% vs 26% of patients, respectively. Treatment discontinuation occurred in 5% in both arms.

Based on the results of this trial, the FDA granted regular approval to sacituzumab govitecan in April 2021 for patients with TNBC.²

In reference to the AEs observed,

the rates of diarrhea and nausea were relatively low grade when sacituzumab was given compared with those of other agents, noted Conlin. She asked Bardia to further explain the recent data relating to the research of Trop-2 expression on the tumor.

Bardia outlined 3 broad themes that were uncovered during this research. The first is that Trop-2 expression was correlated with response rates when patients received sacituzumab, specifically looking at PFS rates between high and low Trop-2 expression.

Second, clinicians looked at the *UGT1A1* gene because sacituzumab has SN-38 and is metabolized by the gene. They were curious to see whether AEs were correlated in patients who could not metabolize treatment well. Lastly, subgroup analyses were undertaken in patients older or younger than 65 years who had *BRCA* mutations or wild-type disease or who were originally estrogen receptor-positive but now had TNBC. A higher benefit was observed in ASCENT study participants when sacituzumab was given vs chemotherapy.

Conlin agreed with Bardia that Trop-2 is not a current SOC but may be in the future. She also pointed out that the subgroup included patients who had brain metastases, as that is often something they see in patients with TNBC. “Patients were included not as part of the primary end point, but there was a proportion of patients who had treated stable brain metastases.”

Patients in the subgroup also benefited from sacituzumab govitecan over other choices of chemotherapy.

“We’re considering our patients with brain metastases [as having] a very high unmet need and we do need more work on those patients with active progressing TNBC in the brain. [But] for now, we can feel good that if we locally treat our patients with TNBC that have brain metastases, this is still a great option for them to control the rest of their systemic disease,” Conlin said.

Looking Toward the Future

Both clinicians pondered what would be next for sacituzumab govitecan. Bardia discussed the phase 3 TROPiCS-02 trial (NCT03901339), which evaluated sacituzumab vs physician’s choice chemotherapy in patients with hormone receptor-positive or HER2-negative metastatic breast cancer.³ This study was designed to use sacituzumab as a third- or fourth-line therapy. Recent updated overall survival results of 14.4 months in the sacituzumab arm vs 11.2 months in the chemotherapy arm (HR, 0.79; 95% CI, 0.65-0.96; $P = .02$) showed a 3.2-month improvement in survival and a 21% reduction in the risk of death.⁴ The FDA has granted priority review to sacituzumab in this combination, with an expected decision in February 2023.⁵

In addition, Conlin added that the group of patients who need treatment are those who have not achieved a pathologic complete response. In the coming years, she said she hopes to see earlier-line treatment in combination with immunotherapy. A current unmet need in the space includes needing to find a way to better treat patients who have early-stage disease, specifically finding a way to reduce the use of quadruplet regimens. ■

References

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