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IN BRIEF

A New Breast Cancer Indication for Sacituzumab Govitecan *(Trodelvy)*

Sacituzumab govitecan-hziy (*Trodelvy* – Gilead) has been approved for treatment of unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer in adults who received prior endocrine therapy and ≥2 additional systemic therapies for metastatic disease. It was previously approved for treatment-refractory metastatic triple-negative breast cancer and for treatment of locally advanced or metastatic urothelial cancer in adults who received platinum-based chemotherapy and a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor.[1]

MECHANISM OF ACTION — *Trodelvy* contains the humanized monoclonal antibody sacituzumab conjugated to the topoisomerase I inhibitor SN-38 by a hydrolyzable linker. Sacituzumab binds to trophoblast cell-surface antigen-2 (Trop-2), a cell surface protein that stimulates cancer cell growth. SN-38, an active metabolite of irinotecan, prevents re-ligation of topoisomerase I-induced single strand breaks, resulting in apoptosis and cell death.

CLINICAL STUDIES — FDA approval of sacituzumab govitecan for the new indication was based on the results of an open label trial (TROPiCS-02) in 543 patients with unresectable locally advanced or metastatic HR-positive, HER2-negative breast cancer whose disease progressed following treatment with a CDK 4/6 inhibitor, endocrine therapy, and a taxane. Patients received at least two chemotherapy regimens in the metastatic setting (one of which could be in the neoadjuvant or adjuvant setting if recurrence occurred within 12 months). Patients were randomized to receive sacituzumab govitecan on days 1 and 8 of a 21-day cycle or investigator-selected chemotherapy (eribulin, vinorelbine, gemcitabine, or capecitabine) until disease progression or unacceptable toxicity occurred. Median progression-free survival (PFS) was statistically significantly longer with sacituzumab govitecan than with chemotherapy (5.5 vs 4.0 months). At 12 months, PFS was 21% with sacituzumab govitecan and 7% with chemotherapy. Median overall survival (OS) was 14.4 months for patients who received sacituzumab govitecan and 11.2 months for those who received chemotherapy.[2]

ADVERSE EFFECTS — The labeling of sacituzumab govitecan contains a boxed warning about severe or life-threatening neutropenia and severe diarrhea associated with its use. The most common adverse effects (frequency ≥25%) of sacituzumab govitecan in TROPiCS-02 were decreased leukocyte count (88%), decreased neutrophil count (83%), decreased hemoglobin levels (73%), decreased lymphocyte count (65%), diarrhea (62%), fatigue (60%), nausea (59%), alopecia (48%), hyperglycemia (37%), constipation (34%), and decreased albumin levels (32%).

DRUG INTERACTIONS — SN-38 is metabolized by uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1). Patients who are homozygous for the UGT1A1*28 allele have reduced enzyme activity and are at increased risk for neutropenia. Inhibitors of UGT1A1 can increase exposure and UGT1A1 inducers can reduce exposure to SN-38. Concomitant administration of *Trodelvy* with inducers or inhibitors of UGT1A1 should be avoided.

PREGNANCY AND LACTATION — SN-38 is teratogenic. Women of reproductive potential and their male partners should use effective contraception during treatment and for 6 months (females) or 3 months (males) after the last dose. There are no data on the presence of sacituzumab or SN-38 in human breast milk or on its effects on the breastfed infant or milk production.

DOSAGE, ADMINISTRATION, AND COST — The recommended dosage of *Trodelvy* is 10 mg/kg administered IV (over 3 hours for the first infusion and 1-2 hours for subsequent infusions) once weekly on days 1 and 8 of a 21-day treatment cycle until disease progression or unacceptable toxicity occurs. Patients should be monitored during and for at least 30 minutes after stopping the infusion. The labeling specifies a number of dosage adjustments that should be made if adverse effects occur. Premedication with antiemetic therapy is recommended. Administration of atropine for early-onset diarrhea and loperamide for severe diarrhea can be considered. One 180-mg vial of *Trodelvy* costs about $2290.[3]

CONCLUSION — In one clinical trial, the trophoblast cell-surface antigen-2 (Trop-2)-directed antibody and topoisomerase inhibitor conjugate sacituzumab govitecan-hziy *(Trodelvy)* prolonged median progression-free survival and overall survival more than investigator-selected chemotherapy in patients with endocrine-resistant, unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer. Myelotoxicity and severe diarrhea can occur. ■

1. Sacituzumab govitecan (Trodelvy) for metastatic triple-negative breast cancer. Med Lett Drugs Ther 2021; 63:e24.
2. HS Rugo et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer. J Clin Oncol 2022; 40:3365.
3. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. February 5, 2023. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/policies/drug-pricing-policy.