TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection

TRODELVY Mechanism of Action

How TRODELVY Is Thought to Work

INDICATIONS

TRODELVY® (sacituzumab govitecan-hziy) is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with:

- Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.
- Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: NEUTROPENIA AND DIARRHEA

- **Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay.**
- **Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤Grade 1 and reduce subsequent doses.**

CONTRAINDICATIONS

- Severe hypersensitivity reaction to TRODELVY.

WARNINGS AND PRECAUTIONS

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur and may require dose modification. Neutropenia occurred in 64% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6%. Neutropenic colitis occurred in 1.4%. Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 on Day 1 of any cycle or neutrophil count below 1000/mm^3 on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Administer G-CSF as clinically indicated or indicated in Table 1 of USPI.

Diarrhea: Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 11% of patients. One patient had intestinal perforation following diarrhea. Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all patients. Withhold TRODELVY for Grade 3-4 diarrhea and resume when resolved to ≤Grade 1. At onset, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Please see full Important Safety Information throughout, and click to see full Prescribing Information, including BOXED WARNING.

TRODELVY is designed to work differently than traditional chemotherapy[1,2]

The proposed mechanism of action is based on preclinical data, which may not correlate with clinical outcomes.

TRODELVY is a Trop-2–directed ADC.[1]

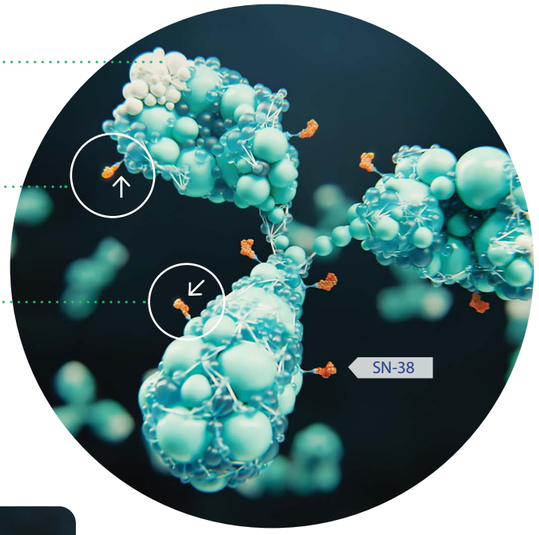
ADCs contain a cytotoxic agent and antibody component that can recognize a target.[3]

TRODELVY was intentionally designed with a unique pH-sensitive, hydrolysable linker (CL2A) and a topoisomerase inhibitor payload that could deliver powerful activity against Trop-2–expressing cells.[4,5]

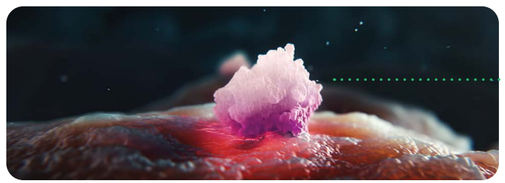
Humanized monoclonal antibody
Binds to Trop-2[1]

Hydrolysable linker
SN-38, a topoisomerase I inhibitor, is covalently attached to the antibody, sacituzumab, by the linker[1]

Cytotoxic agent
SN-38 interacts with topoisomerase I and prevents religation of topoisomerase I-induced single-strand breaks, leading to apoptosis and cell death[1]



What is Trop-2?



Trop-2 is expressed in >80% of breast cancer and overexpressed in many other solid tumors.[6-9]

TRODELVY has a high drug-to-antibody ratio, with an average of ~8 molecules of the cytotoxic agent SN-38 per antibody molecule.[1,4]

Abbreviations: ADC, antibody-drug conjugate; Trop-2, trophoblast cell surface antigen 2

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hypersensitivity and Infusion-Related Reactions: Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 35% of patients. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.2%. The incidence of anaphylactic reactions was 0.2%. Pre-infusion medication is recommended. Have medications and emergency equipment to treat such reactions available for immediate use. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

Please see full Important Safety Information throughout, and click to see full Prescribing Information, including BOXED WARNING.

How TRODELVY is designed to work

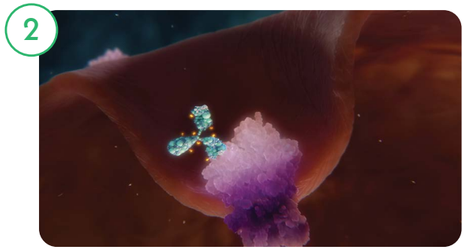
TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection

Pharmacology data suggest TRODELVY binds to the antigen Trop-2 and delivers and concentrates a potent cytotoxic agent into the cell and surrounding cells.[1,10]

1

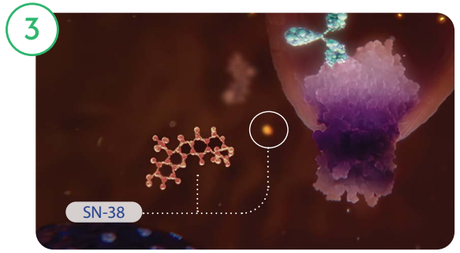
Binds
The antibody component of TRODELVY binds to Trop-2.[1,4,9]

2



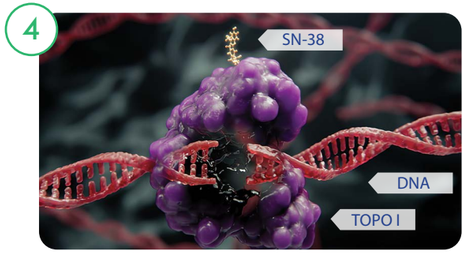
Internalizes
Trop-2 and TRODELVY enter the cell.[1,4]

3



Releases
Once inside the tumor cell, the linker connecting the antibody to the cytotoxic payload is hydrolyzed, releasing the active SN-38.[1,4,9]

4



Damages DNA
SN-38 is a TOPO I inhibitor that prevents religation of TOPO I-induced single-strand breaks. The resulting DNA damage leads to apoptosis and cell death.[1,4,9]

Bystander effect
Preclinical data suggest that the topoisomerase inhibitor payload can act both on the target Trop-2–overexpressing cells and on surrounding cells following intracellular release, enabling the bystander effect.[4,5,11,12]

This unique design delivers potent cytotoxic activity to Trop-2–overexpressing cells, including cancer cells, and the surrounding microenvironment.[4,5,11,12]

Abbreviations: DNA, deoxyribonucleic acid; TOPO I, topoisomerase I; Trop-2, trophoblast cell surface antigen 2

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Nausea and Vomiting: Nausea occurred in 64% of all patients treated with TRODELVY and Grade 3-4 nausea occurred in 3% of these patients. Vomiting occurred in 35% of patients and Grade 3-4 vomiting occurred in 2% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist as well as other drugs as indicated) for prevention of chemotherapy-induced nausea and vomiting (CINV). Withhold TRODELVY doses for Grade 3 nausea or Grade 3-4 vomiting and resume with additional supportive measures when resolved to Grade ≤1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity: Patients homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia and may be at increased risk for other adverse reactions with TRODELVY. The incidence of Grade 3-4 neutropenia was 58% in patients homozygous for the UGT1A1*28, 49% in patients heterozygous for the UGT1A1*28 allele, and 43% in patients homozygous for the wild-type allele. The incidence of Grade 3-4 anemia was 21% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 9% in patients homozygous for the wild-type allele. Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY based on clinical assessment of the onset, duration and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 function.

Embryo-Fetal Toxicity: Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. TRODELVY contains a genotoxic component, SN-38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.

ADVERSE REACTIONS

In the pooled safety population, the most common (≥ 25%) adverse reactions including laboratory abnormalities were decreased leukocyte count (84%), decreased neutrophil count (75%), decreased hemoglobin (69%), diarrhea (64%), nausea (64%), decreased lymphocyte count (63%), fatigue (51%), alopecia (45%), constipation (37%), increased glucose (37%), decreased albumin (35%), vomiting (35%), decreased appetite (30%), decreased creatinine clearance (28%), increased alkaline phosphatase (28%), decreased magnesium (27%), decreased potassium (26%), and decreased sodium (26%).

In the ASCENT study (locally advanced or metastatic triple-negative breast cancer), the most common adverse reactions (incidence ≥25%) were fatigue, diarrhea, nausea, alopecia, constipation, vomiting, abdominal pain, and decreased appetite. The most frequent serious adverse reactions (SAR) (>1%) were neutropenia (7%), diarrhea (4%), and pneumonia (3%). SAR were reported in 27% of patients, and 5% discontinued therapy due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the ASCENT study were reduced neutrophils, leukocytes, and lymphocytes.

In the TROPiCS-02 study (locally advanced or metastatic HR-positive, HER2-negative breast cancer), the most common adverse reactions (incidence ≥25%) were diarrhea, fatigue, nausea, alopecia, and constipation. The most frequent serious adverse reactions (SAR) (>1%) were diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%). SAR were reported in 28% of patients, and 6% discontinued therapy due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the TROPiCS-02 study were reduced neutrophils and leukocytes.

DRUG INTERACTIONS

UGT1A1 Inhibitors: Concomitant administration of TRODELVY with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Avoid administering UGT1A1 inhibitors with TRODELVY.

UGT1A1 Inducers: Exposure to SN-38 may be reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.

Please see full Important Safety Information throughout, and click to see full Prescribing Information, including BOXED WARNING.

References: 1. Trodelvy. Package insert. Gilead Sciences, Inc; February 2023. **2.** Peters C, Brown S. Antibody-drug conjugates as novel anti-cancer chemotherapeutics. *Biosci Rep.* 2015;35(4):1-20. doi:10.1042/BSR20150089 **3.** Hafeez U, Parakh S, Gan HK, Scott AM. Antibody-drug conjugates for cancer therapy. *Molecules.* 2020;25(20):4764. doi:10.3390/molecules25204764 **4.** Goldenberg DM, Cardillo TM, Govindan SV, Rossi EA, Sharkey RM. Trop-2 is a novel target for solid cancer therapy with sacituzumab govitecan (IMMU-132), an antibody-drug conjugate (ADC). *Oncotarget.* 2015;6(26):22496-22512. doi:10.18632/oncotarget.4318 **5.** Kopp A, Hofsess S, Cardillo TM, Govindan SV, Donnell J, Thurber GM. Antibody drug conjugate sacituzumab govitecan drives efficient tissue penetration and rapid intracellular drug release. *Mol Cancer Ther.* 2023;22(1):102-111. doi: 10.1158/1535-7163.MCT-22-0375 **6.** Bardia A, Hurvitz SA, Tolaney, SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med.* 2021;384(16):1529-1541. doi:10.1056/NEJMoa2028485 **7.** Shvartsur A, Bonavida B. Trop2 and its overexpression in cancers: regulation and clinical/therapeutic implications. *Genes Cancer.* 2015;6(3-4):84-105. doi:10.18632/genesandcancer.40 **8.** Trerotola M, Cantanelli P, Guerra E, et al. Upregulation of Trop-2 quantitatively stimulates human cancer growth. *Oncogene.* 2013;32(2):222- 233. doi:10.1038/onc.2012.36 **9.** Stepan LP, Trueblood ES, Hale K, Babcook J, Borges L, Sutherland CL. Expression of Trop2 cell surface glycoprotein in normal and tumor tissues: potential implications as a cancer therapeutic target. *J Histochem Cytochem.* 2011;59(7):701-710. doi:10.1369/0022155411410430 **10.** Goldenberg DM, Sharkey RM. Antibody-drug conjugates targeting TROP-2 and incorporating SN-38: a case study of anti-TROP-2 sacituzumab govitecan. *MAbs.* 2019;11(6):987-995. doi:10.1080/19420862.2019.1632115 **11.** Lopez S, Perrone E, Bellone S, et al. Preclinical activity of sacituzumab govitecan (IMMU-132) in uterine and ovarian carcinosarcomas. *Oncotarget.* 2020;11(5):560-570. doi:10.18632/oncotarget.27342 **12.** Perrone E, Manara P, Lopez S, et al. Sacituzumab govitecan, an antibody-drug conjugate targeting trophoblast cell-surface antigen 2, shows cytotoxic activity against poorly differentiated endometrial adenocarcinomas in vitro and in vivo. *Mol Oncol.* 2020;14(3):645-656. doi:10.1002/1878-0261.12627

GILEAD

US-TROP-0995 08/23

TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection