Trodelvy (sacituzumab govitecan-hziy)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Trodelvy
- **Generic name:** Sacituzumab govitecan-hziy
- **Pharmacologic class:** Trop-2-directed antibody and topoisomerase inhibitor conjugate
- **Strength and Formulation:** 180mg; per vial; lyophilized powder for IV infusion after reconstitution and dilution; preservative-free
- **Manufacturer:** Immunomedics
- **How supplied:** Single-dose vial—1
- **Legal Classification:** Rx

Trodelvy

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Indication

- For the treatment of adult patients with **metastatic triple-negative breast cancer** (mTNBC) who have received at least 2 prior therapies for metastatic disease
  - Indication is approved under accelerated approval based on tumor response rate and duration of response
  - Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials

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Dosage and Administration

- Premedicate with antipyretics, H_1 and H_2 blockers prior to infusion; may use corticosteroids for those with prior infusion reactions
- Also, can premedicate with a 2 or 3 drug combination regimen (eg, dexamethasone with either a 5-HT_3 or NK_1 receptor antagonist)
- Give by IV infusion over 3 hours for 1st infusion, then over 1–2 hours for subsequent infusions if tolerated
- **10mg/kg (max dose) once weekly on Days 1 and 8 of 21-day cycles**
- Continue until disease progression or unacceptable toxicity

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Dose Modification for Adverse Reactions

Severe Neutropenia

- Grade 4 neutropenia ≥7 days, **or** Grade 3 febrile neutropenia (absolute neutropenia count <1000/mm^3 and fever ≥38.5°C, **or** at time of scheduled treatment, Grade 3-4 neutropenia which delays dosing by 2 or 3 weeks for recovery to ≤ Grade 1
  - *First occurrence*: 25% dose reduction and administer granulocyte-colony stimulating factor
  - *Second occurrence*: 50% dose reduction
  - *Third occurrence*: Discontinue treatment

- At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing beyond 3 weeks for recovery to ≤ Grade 1
  - *First occurrence*: Discontinue treatment

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Dose Modification for Adverse Reactions

Severe Non-Neutropenic Toxicity

- Grade 4 non-hematologic toxicity of any duration, **or** any Grade 3-4 nausea, vomiting or diarrhea due to treatment that is not controlled with antiemetics and antidiarrheals, **or** other Grade 3-4 non-hematologic toxicity persisting >48 hours despite optimal medical management, **or** at time of scheduled treatment, Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which delays dose by 2 or 3 weeks for recovery to ≤ Grade 1
  - *First occurrence*: 25% dose reduction
  - *Second occurrence*: 50% dose reduction
  - *Third occurrence*: Discontinue treatment

- In the event of Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which does not recover to ≤ Grade 1 within 3 weeks
  - *First occurrence*: Discontinue treatment

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Considerations for Special Populations

- **Pregnancy:** can cause teratogenicity and/or embryo-fetal lethality
- **Nursing mothers**: not recommended during treatment and for 1 month after last dose
- **Pediatric**: not established
- **Geriatrics**: no overall differences in safety or effectiveness observed
- **Hepatic impairment**: safety in patients with moderate or severe impairment not established; has not been tested in patients with serum bilirubin >1.5 ULN, or AST and ALT >3 ULN, or AST and ALT >5 ULN and associated with liver metastases

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Boxed Warnings

- **Severe neutropenia may occur**
  - Withhold 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 and give fluid and electrolytes as needed
  - Administer atropine, if not contraindicated, for early diarrhea of any severity
  - At the onset of late diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide
  - If severe diarrhea occurs, withhold until resolved to ≤ Grade 1 and reduce subsequent doses

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Warnings/Precautions

- Do not substitute Trodelvy for or use with other drugs containing irinotecan or its active metabolite SN-38
- Monitor closely for infusion-related reactions during and for at least 30mins after each infusion
- Permanently discontinue if life-threatening infusion-related reactions occur
- Patients homozygous for UGT1A1*28 allele
- Monitor closely in those with reduced UGT1A1 activity for severe neutropenia
- Effective contraception should be used during and for 6 months in females or 3 months in males with female partners after the last dose

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Interactions

- May be potentiated by UGT1A1 inhibitors; avoid
- May be antagonized by UGT1A1 inducers; avoid

Adverse Reactions

- **Most frequent** (≥25%): nausea, neutropenia, diarrhea, fatigue, anemia, vomiting, alopecia, constipation, rash, decreased appetite, and abdominal pain
- **Others:** lab abnormalities, hypersensitivity reactions

Mechanism of Action

- Sacituzumab govitecan-hziy is a Trop-2-directed antibody and topoisomerase inhibitor drug conjugate that binds to Trop-2-expressing cancer cells and is internalized with the subsequent release of SN-38, the active metabolite of irinotecan
- The resulting DNA damage leads to apoptosis and cell death

Pharmacogenomics

- SN-38 is metabolized via UGT1A1
- Genetic variants of the UGT1A1 gene such as the UGT1A1*28 allele lead to reduced UGT1A1 enzyme activity
- Patients who are homozygous for the UGT1A1*28 allele are at increased risk for neutropenia from Trodelvy

Clinical Trials

- Efficacy of Trodelvy was evaluated in a single-arm trial (IMMU-132-01) that included 108 patients with mTNBC who had received at least 2 prior treatments for metastatic disease
- Patients received Trodelvy 10mg/kg intravenously on Days 1 and 8 of a 21-day cycle until disease progression or intolerance to therapy
- Primary efficacy outcome: overall response rate (ORR) using RECIST 1.1 and duration of response (DoR)

Clinical Trials

- **Patient demographics**
  - Median age: 55 years; 87% were younger than 65 years
  - 99% female; 76% White
  - ECOG performance status of 0 (29%) or 1 (71%)
  - 76% had visceral disease; 42% had hepatic metastases; 56% had lung/pleura metastases; 2% had brain metastases
  - 11% had Stage IV disease at the time of initial diagnosis
  - Median number of prior systemic therapies: 3 (range 2-10)
  - Prior therapies included: carboplatin or cisplatin (69%), gemcitabine (55%), paclitaxel or docetaxel (53%), capecitabine (51%), eribulin (45%), doxorubicin (24%), vinorelbine (16%), cyclophosphamide (19%), and ixabepilone (8%)

Clinical Trials

- Results showed an ORR of 33.3% (95% CI, 24.6-43.1) with 2.8% of patients achieving a complete response and 30.6% having a partial response
- Among the 36 responders, the median DoR was 7.7 months (95% CI, 4.9-10.8); 55.6% of these patients maintained response for ≥6 months, while 16.7% maintained response for ≥12 months

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/trodelvy/