PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrTRODELVY®

sacituzumab govitecan

180 mg lyophilized powder for solution for injection, for intravenous use

Manufacturer's Standard

Antineoplastic Agent

Gilead Sciences Canada, Inc.

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

TRODELVY (sacituzumab govitecan) is 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 therapies, at least one of them for metastatic disease.

1.1 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (≥65 years of age): Evidence from clinical studies and experience suggests use in the geriatric population is not associated with differences in safety or effectiveness.

2 CONTRAINDICATIONS

Sacituzumab govitecan is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- **Severe or life-threatening neutropenia may occur.** Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Complete blood counts should be monitored prior to initiation of TRODELVY and prior to each dose, and as clinically indicated. Based on the severity of neutropenia, TRODELVY may require dose interruption or reduction [see 4.2 Recommended Dose and Dosage Adjustment]. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay [see 7 WARNINGS AND PRECAUTIONS].
- **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 [see 7 Warnings and Precautions]. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤ Grade 1 and reduce subsequent doses [see 4.2 Recommended Dose and Dosage Adjustment].

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Do NOT substitute TRODELVY for or use with other drugs containing irinotecan or its active metabolite SN-38.
- 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 when treated with TRODELVY [see 7. WARNINGS AND PRECAUTIONS, 10. Clinical Pharmacology].

- For intravenous infusion only. Do not administer as an intravenous push or bolus.
- The recommended dose is 10 mg/kg once weekly on Days 1 and 8 of continuous 21-day treatment cycles until disease progression or unacceptable toxicity [see 4.2 Recommended Dose and Dosage Adjustment].
- Premedication for prevention of infusion reactions is recommended [see 4.2 Recommended Dose and Dosage Adjustment, 7 WARNINGS AND PRECAUTIONS]. Have medications and emergency equipment to treat infusion-related reactions, including anaphylaxis, available for immediate use when administering TRODELVY.
- Premedication for prevention of chemotherapy-induced nausea and vomiting is recommended [see 4.2 Recommended Dose and Dosage Adjustment].
- Monitor patients during the infusion and for at least 30 minutes after completion of infusion. Treatment interruption and/or dose reduction may be needed to manage adverse reactions [see 4.2 Recommended Dose and Dosage Adjustment].

4.2 Recommended Dose and Dosage Adjustment

The recommended dose of TRODELVY is 10 mg/kg administered as an intravenous infusion once weekly on Days 1 and 8 of 21-day treatment cycles. Continue treatment until disease progression or unacceptable toxicity. Do not administer TRODELVY at doses greater than 10 mg/kg.

Administer TRODELVY as an intravenous infusion only. Do not administer as an intravenous push or bolus.

First infusion: Administer infusion over 3 hours. Observe patients during the infusion, and for at least 30 minutes following the initial dose, for signs or symptoms of infusion-related reactions [see 7 WARNINGS AND PRECAUTIONS].

Subsequent infusions: Administer infusion over 1 to 2 hours if prior infusions were tolerated. Observe patients during the infusion and for at least 30 minutes after infusion.

Premedication

Prior to each dose of TRODELVY, premedication for prevention of infusion reactions and prevention of chemotherapy-induced nausea and vomiting (CINV) is recommended.

- Premedicate with antipyretics and H1 and H2 blockers prior to infusion; corticosteroids may be used for patients who had prior infusion reactions.
- 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).

Infusion-related Reactions

Slow or interrupt the infusion rate of TRODELVY if the patient develops an infusion-related reaction. Permanently discontinue TRODELVY for life-threatening infusion-related reactions [see 7 WARNINGS AND PRECAUTIONS].

Dose Modifications for Adverse Reactions

Withhold or discontinue TRODELVY to manage adverse reactions as described in Table 1. Do not re-escalate the TRODELVY dose after a dose reduction for adverse reactions has been made.

Table 1: Dose Modifications for Adverse Reactions

Adverse Reaction	Occurrence	Dose Modification
Severe Neutropenia [see 7 WARNINGS AND PRECAUTIONS]		
Grade 4 neutropenia ≥7 days, OR Grade 3 febrile neutropenia (absolute neutrophil 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	25% dose reduction and administer granulocyte-colony stimulating factor (G-CSF)
	Second	50% dose reduction
	Third	Discontinue treatment
At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing beyond 3 weeks for recovery to ≤ Grade 1	First	Discontinue treatment
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 anti-diarrheal agents [see 7 WARNINGS AND PRECAUTIONS], 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	25% dose reduction
	Second	50% dose reduction
	Third	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	Discontinue treatment

Pediatrics (<18 years of age): Health Canada has not authorized an indication for pediatric use [see 1 INDICATIONS, 1.1 Pediatrics].

Geriatrics (≥65 years of age): No dose adjustment is necessary in older patients [see 7 WARNINGS AND PRECAUTIONS, 7.1.4 Geriatrics].

Renal Impairment: There are no data on the use of sacituzumab govitecan in patients with moderate or severe renal impairment or end-stage renal disease (creatinine clearance [CLcr] ≤ 15 mL/min).

Hepatic Impairment: No dose adjustment is necessary in patients with mild hepatic impairment [see 10.3 Pharmacokinetics]. The safety of TRODELVY in patients with moderate or severe hepatic impairment has not been established.

4.3 Reconstitution

Parenteral Products:

Table 2: Reconstitution

Vial Size	Volume of Diluent to be Added to Vial	Approximate Available Volume	Concentration per mL
180 mg	20 mL	20 mL	10 mg/mL

Reconstitution

- TRODELVY is a cytotoxic drug.
- Follow applicable special handling and disposal procedures.
- Calculate the required dose (mg) of TRODELVY based on the patient's body weight at the beginning of each treatment cycle (or more frequently if the patient's body weight changed by more than 10% since the previous administration) [see 4.2 Recommended Dose and Dosage Adjustment].
- Allow the required number of vials to warm to room temperature.
- Using a sterile syringe, slowly inject 20 mL of 0.9% Sodium Chloride Injection, USP, into each 180 mg TRODELVY vial. The resulting concentration will be 10 mg/mL.
- Gently swirl vials and allow to dissolve for up to 15 minutes. Do not shake. Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit. The solution should be free of visible particulates, clear, and yellow. Do not use the reconstituted solution if it is cloudy or discoloured.
- Use immediately to prepare a diluted TRODELVY infusion solution.

Dilution

- Calculate the required volume of the reconstituted TRODELVY solution needed to obtain the appropriate dose according to patient's body weight. Withdraw this amount from the vial(s) using a syringe. Discard any unused portion remaining in the vial(s).
- Adjust the volume in the infusion bag as needed with 0.9% Sodium Chloride Injection, USP, to obtain a concentration of 1.1 mg/mL to 3.4 mg/mL (total volume should not exceed 500 mL). For patients whose body weight exceeds 170 kg, divide the total dosage of TRODELVY equally between two 500 mL infusion bags and infuse sequentially via slow infusion.

- Slowly inject the required volume of reconstituted TRODELVY solution into a polyvinyl chloride, polypropylene, or polypropylene copolymer infusion bag to minimize foaming. Do not shake the contents.
- Only 0.9% Sodium Chloride Injection, USP should be used since the stability of the reconstituted product has not been determined with other infusion-based solutions. Use the diluted solution in the infusion bag immediately. If not used immediately, the infusion bag containing TRODELVY solution can be stored refrigerated at 2°C to 8°C for up to 4 hours. After refrigeration, administer diluted solution within 4 hours (including infusion time).

Do not freeze or shake. Protect from light [see 11 STORAGE, STABILITY AND DISPOSAL].

4.4 Administration

- Administer TRODELVY as an intravenous infusion [see 4.2 Recommended Dose and Dosage Adjustment]. Protect infusion bag from light.
- An infusion pump may be used.
- Do not mix TRODELVY, or administer as an infusion, with other medicinal products.
- Upon completion of the infusion, flush the intravenous line with 20 mL 0.9% Sodium Chloride Injection, USP.

5 OVERDOSAGE

In a clinical trial, planned doses of up to 18 mg/kg (approximately 1.8 times the maximum recommended dose of 10 mg/kg) of TRODELVY were administered. In these patients, a higher incidence of severe neutropenia was observed.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 3: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous	Lyophilized powder for solution for injection: 180 mg/vial	Powder: 2-(N-morpholino) ethane sulfonic acid, polysorbate 80, trehalose dihydrate Solvent: sodium chloride, water

TRODELVY is supplied as a sterile, preservative-free, off-white to yellowish lyophilized powder for intravenous use in a 50 mL clear glass single-dose vial, with a rubber stopper and crimp-sealed with an aluminum flip-off cap.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

Driving and Operating Machinery

TRODELVY has minor influence on the ability to drive and use machines. Dizziness has been reported. Advise patients to use caution when driving or using machines.

Endocrine and Metabolism

Genetic Polymorphism

Individuals who are homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are potentially at increased risk for neutropenia, febrile neutropenia, and anemia and may be at increased risk for other adverse reactions following initiation of TRODELVY treatment.

Eighty-nine percent (586/660) of patients who received TRODELVY (up to 10 mg/kg on Days 1 and 8 of a 21-day cycle) had retrospective UGT1A1 genotype results available. The incidence of Grade 3 to 4 neutropenia was 57% (40/70) in patients homozygous for the UGT1A1*28 allele, 47% (115/246) in patients heterozygous for the UGT1A1*28 allele, and 45% (117/261) in patients homozygous for the wild-type allele [see 10 CLINICAL PHARMACOLOGY].

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 enzyme activity [see 4.2 Recommended Dose and Dosage Adjustment].

Gastrointestinal

Diarrhea

TRODELVY can cause severe diarrhea. Diarrhea occurred in 63% (419/660) of all patients treated with TRODELVY. Grade 3 diarrhea occurred in 10% (68/660) of all patients treated with TRODELVY. No Grade 4 events were reported. Neutropenic colitis occurred in 0.5% of patients. In another clinical trial with Trodelvy, one patient had intestinal perforation following diarrhea.

Withhold TRODELVY for Grade 3 to 4 diarrhea at the time of scheduled treatment administration and resume when resolved to ≤ Grade 1 [see 3. Serious Warnings and Precautions, 4.2 Recommended Dose and Dosage Adjustment].

At the onset of diarrhea, 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 with TRODELVY (e.g., abdominal cramping, diarrhea, salivation, etc.) can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Nausea and Vomiting

TRODELVY is emetogenic. Nausea occurred in 67% (440/660) of all patients treated with TRODELVY. Grade 3-4 nausea occurred in 4% (29/660) of all patients treated with TRODELVY.

Vomiting occurred in 40% (263/660) of all patients treated with TRODELVY. Grade 3 and 4 vomiting occurred in 3% (18/660) and 0.2% (1/660) of all patients treated with TRODELVY.

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 to 4 vomiting at the time of scheduled treatment administration and resume with additional supportive measures when resolved to ≤ Grade 1 [see 4.2 Recommended Dose and Dosage Adjustment].

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.

Hematologic

Neutropenia

TRODELVY can cause severe, life-threatening or fatal neutropenia. Neutropenia occurred in 62% (409/660) of patients treated with TRODELVY. Grade 3 to 4 neutropenia occurred in 47% (312/660) of patients. Febrile neutropenia occurred in 6% (38/660) of patients.

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. Dose modifications may be required due to neutropenia [see 4.2 Recommended Dose and Dosage Adjustment].

Immune

Hypersensitivity

Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY treatment. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions [see 2 CONTRAINDICATIONS].

Hypersensitivity reactions within 24 hours of dosing occurred in 37% (243/660) of patients treated with TRODELVY. Grade 3 to 4 hypersensitivity occurred in 2% (10/660) of patients treated with TRODELVY. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.3% (2/660).

Premedication for patients receiving TRODELVY is recommended. Observe patients closely for infusion-related reactions during each TRODELVY infusion and for at least 30 minutes after completion of each infusion [see 4 DOSAGE AND ADMINISTRATION]. Have medications and emergency equipment to treat infusion-related reactions, including anaphylaxis, available for immediate use when administering TRODELVY.

Reproductive Health: Female and Male Potential

- **Fertility**

  Based on findings in animals, TRODELVY may impair fertility in females of reproductive potential [see 16 NON-CLINICAL TOXICOLOGY].

- **Teratogenic Risk**

  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 [see 10 CLINICAL PHARMACOLOGY and 16 NON-CLINICAL TOXICOLOGY]. 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 [see 7.1 Special Populations].

7.1 Special Populations

7.1.1 Pregnant Women

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 is toxic to rapidly dividing cells [see 10 CLINICAL PHARMACOLOGY and 16 NON-CLINICAL TOXICOLOGY]. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

Verify the pregnancy status of females of reproductive potential prior to the initiation of TRODELVY.

Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose.

Because of the potential for genotoxicity, 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.

7.1.2 Breast-feeding

It is unknown if TRODELVY is excreted in human milk.

Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment and for 1 month after the last dose of TRODELVY.

7.1.3 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Geriatrics (≥65 years): Of the patients who received TRODELVY, 68/366 (18.6%) of patients with mTNBC and 185/660 (28%) of all patients were ≥65 years old. Safety and efficacy were similar between these patients and younger patients.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The data described in the WARNINGS AND PRECAUTIONS section reflect exposure to TRODELVY as a single agent in 660 patients from two studies, IMMU-132-01 (single-arm trial) and IMMU-132-05 (randomized, active-controlled trial) which included 366 patients with mTNBC who had received prior systemic chemotherapy for advanced disease. TRODELVY was administered as an intravenous infusion

once weekly on Days 1 and 8 of 21-day treatment cycles at doses of 10 mg/kg until disease progression or unacceptable toxicity.

The data described below reflect exposure to TRODELVY as a single agent in 258 patients with mTNBC who had received prior systemic chemotherapy for advanced disease from pivotal Study IMMU-132-05 (ASCENT) [see 14 CLINICAL TRIALS]. The median duration of treatment was 4.4 months (range: 0 to 23 months).

Serious adverse reactions occurred in 26.9% of patients receiving TRODELVY. Serious adverse reactions in >1% of patients receiving TRODELVY were febrile neutropenia (5.0%), diarrhea (3.5%), neutropenia (2.7%), pneumonia (2.7%), anemia (1.2%), and abdominal pain (1.2%). Fatal adverse reactions occurred in 0.8% of patients who received TRODELVY, including respiratory failure (0.4%).

Adverse reactions leading to permanent discontinuation of TRODELVY occurred in 4.7% of patients. The most frequent adverse reactions leading to permanent discontinuation in patients who received TRODELVY were pneumonia (0.8%) and fatigue (0.8%).

Adverse reactions leading to a dose reduction of TRODELVY occurred in 21.7% of patients. The most frequent (≥1%) adverse reaction leading to a dose reduction was neutropenia (8.9%), diarrhea (4.7%), febrile neutropenia (2.7%), nausea (1.9%), fatigue (1.9%), anemia (1.2%). Adverse reactions leading to a treatment interruption of TRODELVY occurred in 63% of patients. The most frequent (≥4%) adverse reactions leading to a treatment interruption were neutropenia (46.1%), leukopenia (5.0%), and diarrhea (5.4%). Granulocyte-colony stimulating factor (G-CSF) was used in 47% (122/258) of patients who received TRODELVY.

The most common adverse reactions (incidence >25%) reported in patients receiving TRODELVY were: neutropenia (64.0%), diarrhea (65.1%), nausea (62.4%), fatigue (51.6%), alopecia (46.9%), anemia (39.5%), constipation (37.2%), vomiting (33.3%), and decreased appetite (27.5%).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC)

The following group of patients were excluded from both clinical studies: known history of Gilbert's disease or bone-only disease, unstable angina, myocardial infarction, or congestive heart failure present within 6 months of randomization or a clinically significant cardiac arrhythmia (other than stable atrial fibrillation) requiring anti-arrhythmia therapy, active infection requiring IV antibiotic use within 1 week of treatment initiation, Human immunodeficiency virus (HIV), hepatitis B, or hepatitis C positive, active chronic inflammatory bowel disease (ulcerative colitis, Crohn's disease), clinically significant bleeding, intestinal obstruction, or gastrointestinal perforation within 6 months of randomization, and clinically significant active chronic obstructive pulmonary disease or other moderate-to-severe chronic respiratory illness present within 6 months of randomization.

Table 4 lists Treatment Emergent Adverse Reactions (TEAR) from the pivotal ASCENT (IMMU-132-05) study, with incidences regardless of investigator assessment of causality, reported in this patient population.

Table 4: Adverse Reactions Reported in ≥1% of Patients with Metastatic Triple-negative Breast Cancer (mTNBC) in Study IMMU-132-05 (ASCENT)

Adverse Reaction	TRODELVY (n=258)			Treatment of Physician's Choice (n=224)		
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)
Blood and lymphatic system disorders						
Neutropenia	165 (64)	90 (35)	44 (17)	98 (44)	46 (21)	30 (13)
Anemia	102 (40)	24 (9)	0	62 (28)	13 (6)	0
Leukopenia	43 (17)	24 (9)	3 (1)	27 (12)	11 (5)	2 (1)
Lymphopenia	25 (10)	4 (2)	1 (0.4)	13 (6)	5 (2)	0
Thrombocytopenia	16 (6)	2 (1)	2 (1)	28 (13)	5 (2)	0
Febrile neutropenia	15 (6)	12 (5)	3 (1)	6 (3)	5 (2)	1 (0.4)
Cardiac disorders						
Palpitations	5 (2)	0	0	2 (1)	0	0
Eye disorders						
Dry eye	10 (4)	0	0	1 (0.4)	0	0
Vision blurred	8 (3)	0	0	1 (0.4)	0	0
Gastrointestinal disorders						
Diarrhea	168 (65)	29 (11)	0	38 (17)	2 (1)	0
Nausea	161 (62)	7 (3)	1 (0.4)	68 (30)	1 (0.4)	0
Constipation	96 (37)	1 (0.4)	0	52 (23)	0	0
Vomiting	86 (33)	3 (1)	1 (0.4)	36 (16)	3 (1)	0
Abdominal pain	55 (21)	7 (3)	0	18 (8)	3 (1)	0
Stomatitis	26 (10)	2 (1)	0	14 (6)	0	0
Abdominal pain upper	24 (9)	1 (0.4)	0	8 (4)	0	0
Gastroesophageal reflux disease	14 (5)	0	0	7 (3)	0	0
Abdominal distension	12 (5)	0	0	7 (3)	0	0
Dyspepsia	11 (4)	0	0	8 (4)	1 (0.4)	0
Colitis	4 (2)	1 (0.4)	0	0	0	0
Salivary hypersecretion	4 (2)	0	0	0	0	0
General disorders and administration site conditions						

Adverse Reaction	TRODELVY (n=258)			Treatment of Physician's Choice (n=224)		
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)
Fatigue	133 (52)	11 (4)	0	89 (40)	19 (8)	0
Asthenia	40 (16)	4 (2)	0	29 (13)	3 (1)	0
Pyrexia	38 (15)	1 (0.4)	0	32 (14)	5 (2)	0
Edema peripheral	24 (9)	0	0	24 (11)	2 (1)	0
Mucosal inflammation	20 (8)	2 (1)	0	14 (6)	3 (1)	0
Pain	19 (7)	2 (1)	0	11 (5)	2 (1)	0
Chills	14 (5)	0	0	6 (3)	0	0
Immune System Disorders						
Hypersensitivity[1]	88 (34)	3 (1)	0	46 (21)	3 (1)	0
Infections and infestations						
Urinary tract infection	33 (13)	1 (0.4)	0	18 (8)	1 (0.4)	0
Upper respiratory tract infection	31 (12)	0	0	7 (3)	0	0
Nasopharyngitis	18 (7)	0	0	5 (2)	0	0
Pneumonia	13 (5)	9 (3)	0	11 (5)	4 (2)	2 (1)
Rash pustular	3 (1)	0	0	0	0	0
Investigations						
Weight decreased	22 (9)	0	0	15 (7)	0	0
Aspartate aminotransferase increased	29 (11)	7 (3)	0	27 (12)	6 (3)	0
Alanine aminotransferase increased	27 (10)	3 (1)	0	22 (10)	2 (1)	1 (0.4)
Blood alkaline phosphatase increased	19 (7)	3 (1)	0	12 (5)	2 (1)	0
Electrocardiogram QT prolonged	12 (5)	1 (0.4)	0	3 (1)	0	1 (0.4)
Blood creatinine increased	7 (3)	1 (0.4)	0	0	0	0
Metabolism and nutrition disorders						
Decreased appetite	71 (28)	4 (2)	0	46 (21)	2 (1)	0
Hypokalaemia	41 (16)	7 (3)	0	29 (13)	1 (0.4)	0

Adverse Reaction	TRODELVY (n=258)			Treatment of Physician's Choice (n=224)		
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)
Hypomagnesemia	32 (12)	0	0	13 (6)	0	0
Hypophosphatemia	15 (6)	7 (3)	2 (1)	9 (4)	3 (1)	0
Hyperglycaemia	17 (7)	2 (1)	0	12 (5)	3 (1)	0
Hypocalcaemia	17 (7)	3 (1)	0	5 (2)	1 (0.4)	0
Dehydration	11 (4)	1 (0.4)	0	11 (5)	0	0
Hyponatraemia	8 (3)	2 (1)	1 (0.4)	6 (3)	0	0
Musculoskeletal and connective tissue disorders						
Back pain	42 (16)	3 (1)	0	31 (14)	4 (2)	0
Arthralgia	32 (12)	1 (0.4)	0	16 (7)	0	0
Bone pain	21 (8)	1 (0.4)	0	15 (7)	0	0
Pain in the extremity	20 (8)	6 (2)	0	17 (8)	2 (1)	0
Muscle spasms	12 (5)	0	0	5 (2)	0	0
Nervous system disorders						
Headache	46 (18)	2 (1)	0	28 (13)	1 (0.4)	0
Dizziness	26 (10)	0	0	16 (7)	0	0
Dysgeusia	22 (9)	0	0	6 (3)	0	0
Paraesthesia	10 (4)	0	0	6 (3)	0	0
Hypoaesthesia	8 (3)	0	0	3 (1)	0	0
Taste disorder	4 (2)	0	0	2 (1)	0	0
Tremor	4 (2)	0	0	1 (0.4)	0	0
Psychiatric disorders						
Insomnia	29 (11)	0	0	11 (5)	0	0
Respiratory, thoracic and mediastinal disorders						
Cough	61 (24)	0	0	40 (18)	1 (0.4)	0
Dyspnea[2]	54 (21)	9 (3)	1 (0.4)	50 (22)	11 (5)	1 (0.4)
Epistaxis	13 (5)	0	0	1 (0.4)	0	0
Nasal dryness	3 (1)	0	0	0	0	0
Skin and subcutaneous tissue disorders						

Adverse Reaction	TRODELVY (n=258)			Treatment of Physician's Choice (n=224)		
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)
Alopecia	121 (47)	0	0	36 (16)	0	0
Rash	32 (12)	1 (0.4)	0	12 (5)	1 (0.4)	0
Pruritus	26 (10)	0	0	7 (3)	0	0
Rash maculo-papular	18 (7)	0	0	3 (1)	0	0
Dry skin	17 (7)	0	0	3 (1)	0	0
Nail discolouration	4 (2)	0	0	0	0	0
Dermatitis acneiform	3 (1)	0	0	0	0	0
Vascular disorder						
Hypotension	11 (4)	0	0	9 (4)	2 (1)	0
Hot flush	6 (2)	0	0	6 (3)	0	0

Treatment of physician's choice included one of the following single agents: eribulin (n=139), capecitabine (n=33), gemcitabine (n=38), or vinorelbine (except if patient had ≥ Grade 2 neuropathy, n=52).

Adverse events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 23.0.

'Neutrophil count decreased', 'Lymphocyte count decreased', 'Platelet count decreased', 'White blood cell count decreased', 'Hemoglobin decreased', and 'Red blood cell count decreased' have been re-coded to Neutropenia, Lymphopenia, Thrombocytopenia, Leukopenia, and Anemia, correspondingly, for summary purposes.

1: Hypersensitivity events reported up to the end of the day after treatment was administered. Includes events coded to the following preferred terms: Cough; dyspnea; rash; pruritus; stomatitis; hypotension; rash maculopapular; flushing; erythema; chest discomfort; hypersensitivity; rhinitis allergic; wheezing; localized edema; dermatitis acneiform; conjunctivitis; rash pruritic; edema; rash macular; rash pustular; swelling; swelling face; urticaria; anaphylactic reaction; asthma; bronchospasm; conjunctivitis allergic; dermatitis; dermatitis contact; eye pruritus; mouth ulceration; periorbital edema; rash erythematous; scrotal edema; seasonal allergy; skin exfoliation; swollen tongue; tachypnoea; throat tightness; Type IV hypersensitivity reaction; choking.

2: Includes dyspnea exertional

8.3 Less Common Clinical Trial Adverse Reactions

Less common clinical trial adverse reactions (<1%) in metastatic triple-negative breast cancer patients treated with TRODELVY included:

Ear and labyrinth disorders: ear pain, vertigo
Gastrointestinal disorders: neutropenic colitis, retching, glossodynia
General disorders and administration site conditions: chest pain, non-cardiac chest pain, xerosis
Immune system disorders: anaphylactic reaction

Infections and infestations: bronchitis, oral herpes, sepsis, diverticulitis, genital herpes
Injury, poisoning and procedural complications: infusion related reaction
Investigations: activated partial thromboplastin time prolonged, blood lactate dehydrogenase increased, weight increased
Metabolism and nutrition disorders: appetite disorder
Musculoskeletal and connective tissue disorders: musculoskeletal pain, neck pain, muscle fatigue
Psychiatric disorders: anxiety
Renal and urinary disorders: proteinuria
Reproductive system and breast disorders: vulvovaginal dryness
Respiratory, thoracic and mediastinal disorders: hypoxia, nasal congestion, rhinorrhea
Skin and subcutaneous tissue disorders: dermatitis, night sweats, skin discolouration, urticaria, eczema, macule, onychoclasis, skin hyperpigmentation
Vascular disorders: flushing, hypertension

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

Table 5: Most Common Hematologic Laboratory Abnormalities in ASCENT Study (≥10% in Either Group) in Patients with Metastatic Triple-negative Breast Cancer

Hematologic Laboratory Abnormality	TRODELVY (n=258)			Treatment of Physician's Choice (n=224)		
	All Grades (%)	Grade 3 (%)	Grade 4 (%)	All Grades (%)	Grade 3 (%)	Grade 4 (%)
Decreased hemoglobin	93.8	8.9	0	84.3	5.8	0
Decreased leukocytes	87.6	35.3	5.8	70.1	20.1	5.4
Decreased lymphocytes	78.3	27.5	3.9	67.9	22.3	1.8
Decreased neutrophils	77.9	31.8	17.1	59.8	21.0	14.7
Decreased platelets	22.5	0.8	0.4	32.1	2.2	0.4

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No drug-drug interaction studies were conducted with sacituzumab govitecan or its components. Inhibitors or inducers of UGT1A1 are expected to increase or decrease SN-38 exposure, respectively.

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 [see 7 WARNINGS AND PRECAUTIONS and 10 CLINICAL PHARMACOLOGY]. Exercise caution when administering UGT1A1 inhibitors with TRODELVY.

Exposure to SN-38 may be substantially reduced in patients concomitantly receiving UGT1A1 enzyme inducers [see 7 WARNINGS AND PRECAUTIONS and 10 CLINICAL PHARMACOLOGY]. Exercise caution when administering UGT1A1 inducers with TRODELVY.

9.3 Drug-Behavioural Interactions

Interactions with behavioural factors have not been established.

9.4 Drug-Drug Interactions

The drugs listed in Table 6 are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 6: Potential Drug-Drug Interactions

Proper/Common name	Source of Evidence	Effect	Clinical comment
UGT1A1 inhibitors	Theoretical	Increased SN-38 exposure	Exercise caution when administering UGT1A1 inhibitors (e.g. propofol, ketoconazole, EGFR tyrosine kinase inhibitors) with TRODELVY
UGT1A1 inducers	Theoretical	Decreased SN-38 exposure	Exercise caution when administering UGT1A1 inducers (e.g. carbamazepine, phenytoin, rifampicin, protease inhibitors) with TRODELVY

SN-38 = the small molecule moiety of sacituzumab govitecan; UGT1A1 = uridine diphosphate-glucuronosyl transferase 1A1

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

TRODELVY (sacituzumab govitecan) is a Trop-2-directed antibody-drug conjugate (ADC) composed of three components: 1) sacituzumab is a humanized antibody that recognizes Trop-2, covalently linked to 2) a topoisomerase I inhibitor, SN-38, via 3) a hydrolysable linker (CL2A).

Pharmacology data suggest that sacituzumab govitecan binds to Trop-2-expressing cancer cells and is internalized with the subsequent release of SN-38 via hydrolysis of the linker. SN-38 interacts with topoisomerase I and prevents re-ligation of topoisomerase I-induced single strand breaks. The resulting DNA damage leads to apoptosis and cell death. Sacituzumab govitecan decreased tumor growth in mouse xenograft models of triple-negative breast cancer.

10.2 Pharmacodynamics

Cardiac electrophysiology

The effect of TRODELVY on QTc interval prolongation was studied in Phase 3 ASCENT substudy (Study IMMU-132-05, n=29). Study participants were administered IV infusion of 10 mg/kg on Days 1 and 8 of a 21-day cycle. TRODELVY was associated with QTcF prolongation at 1 day post-dosing, with a maximum mean change of 9.7 ms (90% CI 2.7, 16.8 ms). A positive exposure-response relationship between change from baseline QTcF and exposure of SN-38 was observed.

10.3 Pharmacokinetics

The serum pharmacokinetics of sacituzumab govitecan and SN-38 were evaluated in study IMMU-132-05 in a population of mTNBC patients who received sacituzumab govitecan as a single agent at a dose of 10 mg/kg. The pharmacokinetic parameters of sacituzumab govitecan and free SN-38 are presented in Table 7.

Table 7: Summary of Mean PK Parameters (CV%) of Sacituzumab Govitecan and Free SN-38 in mTNBC patients

	Sacituzumab govitecan	Free SN-38
C_{max}[ng/mL]	240000 (22.2%)	90.6 (65.0%)
AUC_{0-168}[ng*h/mL]	5340000 (23.7%)	2730 (41.1%)

Cmax: maximum plasma concentration
AUC_{0-168}: area under plasma concentration curve through 168 hours

Distribution:

The apparent mean volume of distribution at steady state for sacituzumab govitecan was 2.45 L.

Metabolism:

No metabolism studies with sacituzumab govitecan have been conducted. SN-38 (the small molecule moiety of sacituzumab govitecan) is metabolized via UGT1A1. The glucuronide metabolite of SN-38 (SN-38G) was detectable in the serum of patients.

Elimination

The mean half-life of sacituzumab govitecan and free SN-38 was 15.3 and 19.7 hours, respectively. The clearance of the sacituzumab govitecan was 0.14L/h.

Special Populations and Conditions

- **Pediatrics:** Sacituzumab govitecan was not studied in patients under 18 years of age.
- **Genetic Polymorphism:** SN-38 is metabolized via UGT1A1. Genetic variants of the UGT1A1 gene such as the UGT1A1*28 allele lead to reduced UGT1A1 enzyme activity. Individuals who are homozygous for the UGT1A1*28 allele are potentially at increased risk for neutropenia, febrile neutropenia, and anemia from TRODELVY [see 7 WARNINGS AND PRECAUTIONS]. Approximately 20% of the Black or African American population, 10% of the White population, and 2% of the East Asian population are homozygous for the UGT1A1*28 allele. Decreased function alleles other than UGT1A1*28 may be present in certain populations.
- **Hepatic Insufficiency:** The exposure of sacituzumab govitecan is similar in patients with mild hepatic impairment (bilirubin ≤ ULN and AST > ULN, or bilirubin >1.0 to <1.5× ULN and AST of

any level; n=59) to patients with normal hepatic function (bilirubin or AST < ULN; n=191).

No dedicated moderate or severe hepatic impairment study was conducted.

SN-38 exposure may be elevated in such patients due to decreased hepatic UGT1A1 activity.

- **Renal Insufficiency:** No dedicated moderate or severe renal impairment study was conducted.

11 STORAGE, STABILITY AND DISPOSAL

TRODELVY (sacituzumab govitecan) for injection is a sterile, off-white to yellowish lyophilized powder in a single-dose vial. Each TRODELVY vial is individually boxed in a carton containing one 180 mg vial.

Store vials in a refrigerator at 2°C to 8°C in the original carton to protect from light until time of reconstitution. Do not freeze.

12 SPECIAL HANDLING INSTRUCTIONS

TRODELVY is a cytotoxic drug. Follow applicable special handling and disposal procedures.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

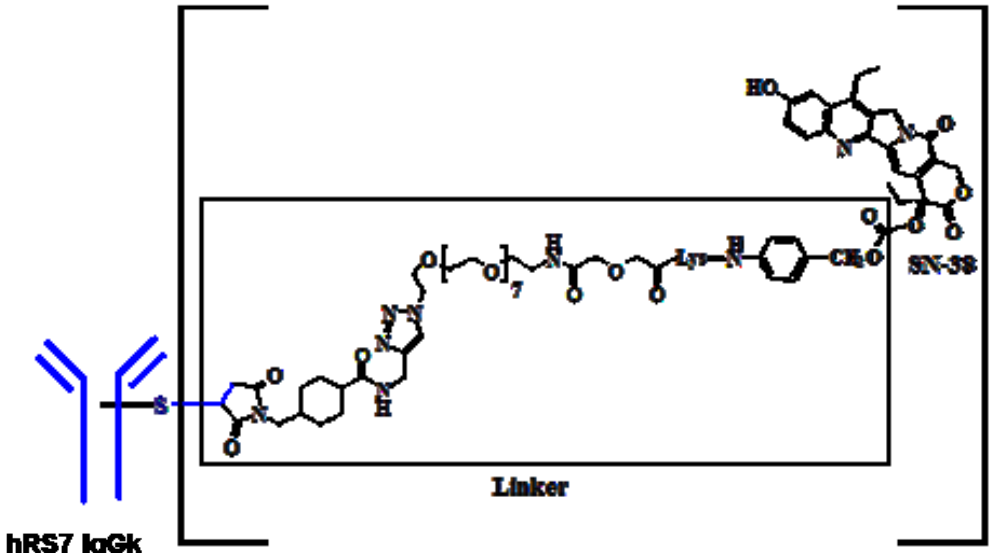
Proper name: Sacituzumab govitecan

Chemical name: Sacituzumab govitecan is a Trop-2 directed antibody and topoisomerase inhibitor conjugate, composed of the following three components:

- The humanized monoclonal antibody, hRS7 IgG1κ (also called sacituzumab), which binds to Trop-2 (the trophoblast cell-surface antigen-2);
- The drug SN-38, a topoisomerase inhibitor; and
- A hydrolysable linker (called CL2A), which links the humanized monoclonal antibody to SN-38.

Molecular formula and molecular mass: approximately 160 kilodaltons

Structural formula: Sacituzumab govitecan contains on average 7 to 8 molecules of SN-38 per antibody molecule. Sacituzumab govitecan has the following chemical structure:



Physicochemical properties: TRODELVY (sacituzumab govitecan) for injection is a sterile, preservative-free, off-white to yellowish lyophilized powder.

Pharmaceutical standard: Manufacturer's Standard

Product Characteristics:

The recombinant monoclonal antibody is produced by mammalian (murine myeloma) cells, while the small molecule components SN-38 and CL2A are produced by chemical synthesis.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Unresectable Locally Advanced or Metastatic Triple-Negative Breast Cancer (mTNBC)

The efficacy assessment of TRODELVY in the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received at least two prior therapies was based on the pivotal ASCENT (IMMU-132-05) study. Table 8 summarizes the patient demographics for the ASCENT (IMMU-132-05) study.

Table 8: Summary of Patient Demographics for Clinical Trials in Metastatic Triple-negative Breast Cancer

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Median age (Range)	Sex
ASCENT (IMMU-132-05)	Phase 3, multicentre, open-label, randomized trial	10 mg/kg IV on Days 1 and 8 of a 21-day cycle TRODELVY or Treatment of Physician's Choice (TPC) of single agent chemotherapy	Total: 529 TRODELVY:267 TPC:262	54 (27-82)	527 female 2 male

ASCENT study was conducted in 529 patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who had relapsed after at least two prior chemotherapies for breast cancer (one of which could be in the neoadjuvant or adjuvant setting provided progression occurred within a 12 month period). All patients received previous taxane treatment in either the adjuvant, neoadjuvant, or advanced stage unless they had a contraindication or were intolerant to taxanes during or at the end of the first taxane cycle. Poly-ADP ribose polymerase (PARP) inhibitors were allowed as one of the two prior chemotherapies for patients with a documented germ-line BRCA1/BRCA2 mutation.

The median age of patients in the full population (n = 529) was 54 years (range: 27–82 years); 99.6% were female; 79% were White, 12% were Black/African American; and 81% of patients were < 65 years of age. All patients had an ECOG performance status of 0 (43%) or 1 (57%). Forty-two percent of patients had hepatic metastases, 8% were BRCA1/BRCA2 mutational status positive, and 70% were TNBC at diagnosis.

Overall, 29% of patients had received prior PD-1/PD-L1 therapy. Thirteen percent of patients in the TRODELVY group in the full population received only 1 prior line of systemic therapy in the metastatic setting.

Patients with stable brain metastases were eligible. Magnetic resonance imaging (MRI) to determine brain metastases was required prior to enrollment for patients with known or suspected brain

metastases. The study included a pre-defined maximum of 15% for patients with brain metastases. Twelve percent had baseline brain metastases previously treated and stable (n=61; 32 on TRODELVY arm and 29 on single agent chemotherapy arm).

The following group of patients were excluded from clinical study: known history of Gilbert's disease or bone-only disease, unstable angina, myocardial infarction, or congestive heart failure present within 6 months of randomization or a clinically significant cardiac arrhythmia (other than stable atrial fibrillation) requiring anti-arrhythmia therapy, active infection requiring IV antibiotic use within 1 week of treatment initiation, Human immunodeficiency virus (HIV), hepatitis B, or hepatitis C positive, active chronic inflammatory bowel disease (ulcerative colitis, Crohn's disease), clinically significant bleeding, intestinal obstruction, or gastrointestinal perforation within 6 months of randomization, and clinically significant active chronic obstructive pulmonary disease or other moderate-to-severe chronic respiratory illness present within 6 months of randomization.

Patients were randomized 1:1 to receive TRODELVY 10 mg/kg as an intravenous infusion on Days 1 and 8 of a 21-day (n=267) or TPC single agent chemotherapy per the authorised labeling (n=262). TPC was determined by the investigator before randomization from one of the following single-agent choices: eribulin (n=139), capecitabine (n=33), gemcitabine (n=38), or vinorelbine (except if patient had ≥ Grade 2 neuropathy, n=52).

Patients were treated until disease progression or unacceptable toxicity. The major efficacy outcome was progression-free survival (PFS) as measured by a blinded, independent, centralized group of radiology experts using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria. Major secondary outcomes included overall survival (OS), objective response rate (ORR), and duration of response (DOR). Results are shown in Table 9, Figure 1 and Figure 2.

Table 9: Efficacy Results from ASCENT (all randomized patients, ITT population)

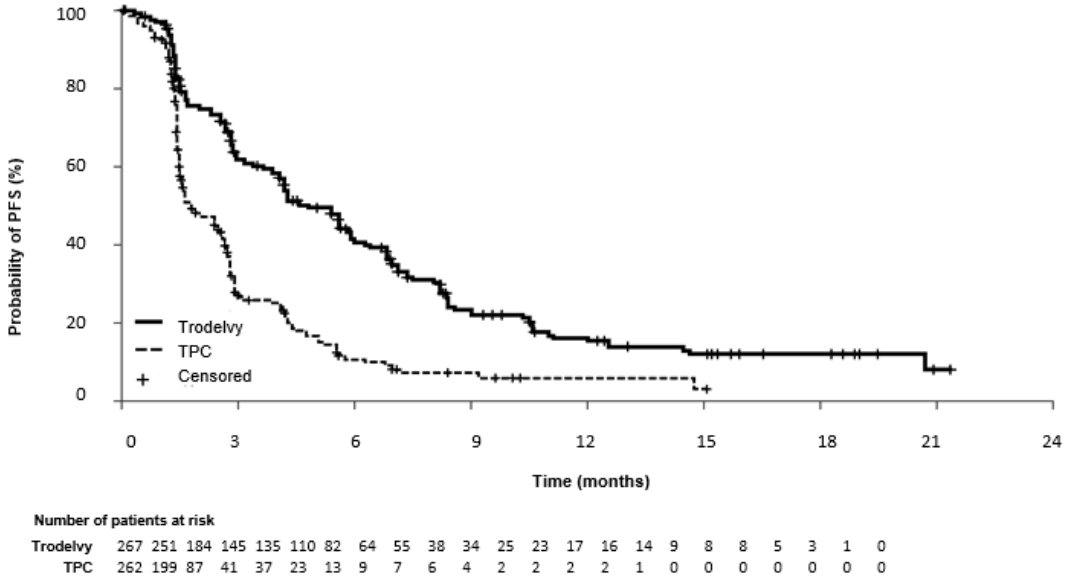
	Trodelvy n=267	**Treatment of physician's choice (TPC) n=262**
Progression-free survival[1]		
Number of events (%)	190 (71.2)	171 (65.3)
Median PFS in months (95% CI)	4.8 (4.1, 5.8)	1.7 (1.5, 2.5)
Hazard ratio (95% CI)	0.43 (0.35, 0.54)	
p-value[2]	<0.0001	
Overall Survival		
Number of deaths (%)	179 (67.0)	206 (78.6)
Median OS in months (95% CI)	11.8 (10.5, 13.8)	6.9 (5.9, 7.7)
Hazard ratio (95% CI)	0.51 (0.41, 0.62)	
p-value[2]	<0.0001	

1 PFS is defined as the time from the date of randomization to the date of the first radiological disease progression or death due to any cause, whichever comes first.

2 Stratified log-rank test adjusted for stratification factors: number of prior chemotherapies, presence of known brain metastases at study entry, and region.

CI = Confidence Interval

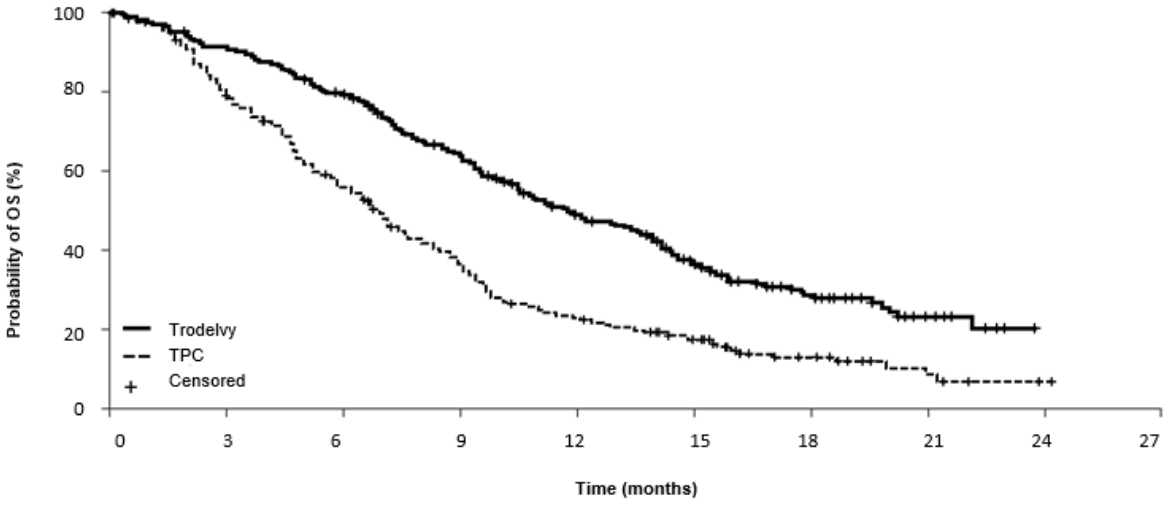
Figure 1: Progression free survival (all randomized patients, ITT population) by BICR



Number of patients at risk

Trodelvy	267	251	184	145	135	110	82	64	55	38	34	25	23	17	16	14	9	8	8	5	3	1	0
TPC	262	199	87	41	37	23	13	9	7	6	4	2	2	2	2	1	0	0	0	0	0	0	0

Figure 2: Overall survival (all randomized patients, ITT population)



Number of patients at risk

Trodelvy	267	260	250	242	232	219	208	189	174	164	145	127	116	109	98	76	56	46	39	31	21	13	8	1	0	0
TPC	262	239	222	192	174	150	132	113	97	84	64	58	52	46	42	34	24	17	14	9	6	5	3	2	1	0

For the ITT population, the number of responders was 83 (31%) in the TRODELVY arm and 11 (4%) in the control arm. The median duration of response was 6.3 months in the treatment arm and 3.6 months in the control arm.

In the BMNeg population (n=468), the median PFS in the TRODELVY arm was 5.6 months (95% CI: 4.3, 6.3) with an estimated HR of 0.41 (95% CI: 0.32, 0.52). In the brain metastases positive population

(BMPos) (n=61), the median PFS in the TRODELVY arm was 2.8 months (95% CI: 1.5, 3.9) with an estimated HR of 0.65 (95% CI: 0.35, 1.22).

In the BMNeg population (n=468), the median OS in the TRODELVY arm was 12.1 months (95% CI: 10.7, 14.0) with an estimated HR of 0.48 (95% CI: 0.38, 0.59). In the BMPos population (n=61), the median OS in the TRODELVY arm was 6.8 months (95% CI: 4.7, 14.1) with an estimated HR of 0.87 (95% CI: 0.47, 1.63).

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology

Cynomolgus Monkeys

In Cynomolgus monkeys, sacituzumab govitecan administered up to 50 mg/kg/dose for four treatment cycles (days 1 and 8 of a 21-day cycle) was considered a NOAEL, and 120 mg/kg/dose administered 3 days apart was associated with lethality. Lethality was considered due to bone marrow suppression and gastrointestinal disturbances. Across studies, target organs also included the female reproductive tract, skin, kidney, and/or lymphoid organs.

Carcinogenicity and Mutagenicity

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential of TRODELVY.

SN-38 was clastogenic in an in vitro mammalian cell micronucleus test in Chinese hamster ovary cells and was not mutagenic in an in vitro bacterial reverse mutation (Ames) assay.

Genotoxicity: The genotoxic potential of sacituzumab govitecan has not been fully evaluated. Sacituzumab govitecan contains the genotoxic topoisomerase I inhibitor component, SN-38, and is toxic to rapidly dividing cells, suggesting the potential for embryotoxicity and teratogenicity.

Reproductive and Developmental Toxicology

Impairment of Fertility

Dedicated fertility studies have not been conducted with sacituzumab govitecan. In a repeat-dose toxicity study in cynomolgus monkeys, intravenous administration of sacituzumab govitecan on Day 1 and Day 4 resulted in endometrial atrophy, uterine hemorrhage, increased follicular atresia of the ovary, and atrophy of vaginal epithelial cells at doses ≥60 mg/kg (≥6 times the human recommended dose of 10 mg/kg based on body weight).

Developmental Toxicity

There were no animal reproductive or developmental toxicity studies conducted with sacituzumab govitecan.

Juvenile Animal Studies

No juvenile toxicity studies have been conducted.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

TRODELVY®

Sacituzumab govitecan powder for solution for injection

Read this carefully before you start taking **Trodelvy**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Trodelvy**.

Serious Warnings and Precautions

- **Low white blood cell count (neutropenia).** Low white blood cell counts are common with **Trodelvy** and can sometimes be severe and lead to infections that can be life-threatening. Your healthcare provider should check your blood cell counts prior to treatment with TRODELVY and prior to each dose. If your white blood cell count is too low, your healthcare provider may need to lower your dose of **Trodelvy**, or in some cases may stop **Trodelvy**. Your healthcare provider may need to give you antibiotic medicines if you develop fever while your white blood cell count is low.
  Call your healthcare provider right away if you develop any of the following signs of infection during treatment with Trodelvy:
  - fever
  - chills
  - cough
  - shortness of breath
  - burning or pain when you urinate

- **Severe diarrhea.** Diarrhea is common with **Trodelvy** and can also be severe. Your healthcare provider should monitor you for diarrhea and give you medicine as needed to help control your diarrhea. If you lose too much body fluids (dehydration) your healthcare provider may need to give you fluids and electrolytes to replace body salts. Your healthcare provider may decrease your dose or stop **Trodelvy** if your diarrhea is severe and cannot be controlled with anti-diarrheal medicines.
  Call your healthcare provider right away:
  - the first time that you get diarrhea during treatment with **Trodelvy**
  - if you have black or bloody stools
  - if you have symptoms of losing too much body fluid (dehydration) and body salts, such as lightheadedness, dizziness or faintness
  - if you are unable to take fluids by mouth due to nausea or vomiting
  - if you are not able to get your diarrhea under control within 24 hours

What is Trodelvy used for?

Trodelvy is a prescription medicine used to treat adults 18 years or older with breast cancer that is:

- estrogen and progesterone hormone receptor (HR) negative, and human epidermal growth factor receptor 2 (HER2)-negative (also called triple-negative breast cancer), **and**
- that has spread to other parts of the body or cannot be removed by surgery (metastatic), **and**
- who previously received two or more prior therapies, at least one of them for metastatic disease.

How does Trodelvy work?

Trodelvy consists of a type of medicine called a “monoclonal antibody” linked to a type of medicine

called a “topoisomerase inhibitor”. Together, these medicines may slow down the growth and spread of your cancer.

What are the ingredients in Trodelvy?

Medicinal ingredients: sacituzumab govitecan

Non-medicinal ingredients: 2-(N-morpholino) ethane sulfonic acid, polysorbate 80, trehalose dihydrate

Trodelvy comes in the following dosage forms:

180 mg lyophilized powder in single-dose vials for solution for injection

- **Do not use Trodelvy if:** You are allergic to sacituzumab govitecan or any of the other ingredients in **Trodelvy**.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Trodelvy. Talk about any health conditions or problems you may have, including if you:

- Are pregnant or plan to become pregnant. **Trodelvy** can harm your unborn baby. Your healthcare provider should check to see if you are pregnant before you start receiving **Trodelvy**.
- Females who can become pregnant should use effective birth control during treatment and for 6 months after your last dose of **Trodelvy**. Talk to your healthcare provider about birth control choices that may be right for you during this time.
- Males with a female partner who can become pregnant should use effective birth control during treatment and for 3 months after your last dose of **Trodelvy**.
- Tell your healthcare provider right away if you or your partner become pregnant during treatment with **Trodelvy**.
- Are breastfeeding or plan to breastfeed. It is not known if **Trodelvy** passes into your breastmilk and can harm your baby. Do not breastfeed during treatment and for 1 month after your last dose of **Trodelvy**.
- Have been told that you carry a gene for uridine diphosphate-glucuronosyl transferase A1 (UGT1A1)*28. People who carry this gene have an increased risk of getting side effects with **Trodelvy**, especially low white blood cell counts.
- Have liver problems.
- Are younger than 18 years of age. It is not known if **Trodelvy** is safe and effective in children.

Other warnings you should know about:

- Nausea and vomiting may occur with **Trodelvy**. Your healthcare provider may decrease your dose or stop TRODELVY if your nausea or diarrhea are severe and cannot be controlled with medication.
- You should know that **Trodelvy** may affect your fertility. Talk to your healthcare practitioner if you are planning on having children.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements, or alternative medicines.

The following may interact with Trodelvy:

- UGT1A1 inhibitors such as atazanavir sulfate.
- UGT1A1 inducers such as efavirenz, fosamprenavir/ritonavir, tipranavir/ritonavir, rifampin.

How to take Trodelvy:

- Your healthcare provider will give you **Trodelvy** into your vein through an intravenous (IV) line.
- **Trodelvy** is given 1 time each week, on Day 1 and on Day 8 of a 21-day treatment cycle.
- You will receive the first dose of TRODELVY over 3 hours. If you tolerate the first dose well, future doses may be given over 1 to 2 hours.
- Before each dose of **Trodelvy**, you will receive medicines to help prevent infusion reactions, nausea, and vomiting.
- You will be monitored for side effects during and for at least 30 minutes after you receive each infusion of **Trodelvy**.
- Your healthcare provider may slow down or temporarily stop your infusion of **Trodelvy** if you have an infusion-related reaction, or permanently stop **Trodelvy** if you have a life-threatening infusion-related reaction.
- Your healthcare provider will decide how long you will continue to receive **Trodelvy**.

Usual dose:

10 mg/kg given 1 time each week, on Day 1 and on Day 8 of a 21-day treatment cycle.

Overdose:

If you think you, or a person you are caring for, have taken too much **Trodelvy**, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss any appointments, call your healthcare professional as soon as possible to reschedule your appointment.

What are possible side effects from using Trodelvy?

These are not all the possible side effects you may feel when taking **Trodelvy**. If you experience any side effects not listed here, contact your healthcare professional.

- Urinary tract infection which may cause frequent and painful urination
- Upper respiratory tract infection
- Severe infection throughout the body
- Hair loss
- Feeling tired
- Weight loss
- Decreased red blood cell count
- Decreased level of white blood cells
- Decreased number of a type of blood cell that helps to clot blood (platelet), causing bruising and/or bleeding
- Constipation
- Decreased appetite
- Stomach-area (abdominal) pain, swelling or discomfort
- Inflammation of the mouth and lips
- Indigestion
- Digestive disease in which stomach acid irritates the food pipe lining
- Inflammation of the lining of the large intestine

- Increased saliva
- Rash, general itching, dry skin, nail colour changes
- Small, raised, acne-like bumps usually on the face, scalp, chest, or upper back
- Feeling sick
- Hot flush
- Difficulty sleeping
- Low blood level of potassium, phosphate, magnesium, sodium or calcium
- High blood level of glucose
- Dehydration (when your body does not have as much water and fluid as it should)
- Headache
- Feeling dizzy
- Tremor
- Tingling, prickling or decreased sensation often in the arms, hands, legs, or feet
- Swelling or pain in the arms or legs
- Pain including bone pain, joint pain, or back pain
- Muscle spasms
- Dry eye or blurred vision
- Change in sense of taste
- Bleeding from the nose
- Shortness of breath, cough, sore throat, runny nose, dry nose, or sneezing
- Low blood pressure
- Palpitations
- Increased QT interval on electrocardiogram, which may be a sign of a heart problem
- Increase in an enzyme called alkaline phosphatase, which may be a sign of a bone or liver problem
- Increase in an enzyme called alanine aminotransferase or aspartate aminotransferase, which may be a sign of a liver problem
- Increase in blood creatinine, which may be a sign of a kidney problem

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional immediately**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Neutropenia: • Fever • Chills • Other signs of infection		✓	
Diarrhea: • The first time you experience diarrhea during treatment • Black or bloody stools • Symptoms of dehydration (feeling light-headed, dizzy, or faint) • Inability to take fluids by mouth		✓	

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional immediately**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
due to nausea or vomiting • Unable to get diarrhea under control within 24 hours			
Uncontrolled nausea or vomiting		✓	
Hypersensitivity (serious infusion reaction or anaphylaxis): • Swelling of your face, lips, tongue, or throat • Hives • Skin rash or flushing of your skin • Difficulty breathing or wheezing • Light-headedness, dizziness, feeling faint, or passing out • Chills or shaking chills (rigors) • Fever			✓
COMMON			
Pneumonia (an infection of the lungs): • Fever • Chills • Increase in sputum production, change in sputum colour • Cough or difficulty breathing		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store vials in a refrigerator at 2°C to 8°C. Do not freeze.
- Store in the original carton to protect from light until time of reconstitution.
- Keep out of reach and sight of children.

If you want more information about Trodelvy:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.gilead.ca, or by calling 1-866-207-4267.

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