נובמבר 2026

הודעה על עדכון עלון:

TRODELVY®

Powder for concentrate for solution for infusion

(sacituzumab govitecan 200 mg/vial)

רופאים ורוקחים נכבדים,

חברת גיליאד סיאנסז ישראל בע"מ מבקשת להודיעכם כי חל עדכון בעלון לרופא של התכשיר בנדון.

ההתוויה הרשומה לתכשיר בישראל:

Trodelvy, in combination with pembrolizumab, is indicated for the first-line treatment of adult patients with unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 [Combined Positive Score (CPS ≥ 10)] as determined by an authorized test.

Trodelvy as a single agent is indicated for the first-line treatment of adult patients with unresectable locally advanced or metastatic triple negative breast cancer (TNBC) who are not candidates for PD-1 or PD-L1 inhibitor based therapy.

Trodelvy as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic triple negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease.

Trodelvy is indicated for the treatment of adult patients with 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.

השינויים מסומנים בעלון המצורף כאשר הטקסט המודגש באדום הוסף לעלון ואילו הטקסט המחוק ~~בקו חוצה~~ נגרע ממנו. העדכונים המשמעותיים ביותר מופיעים במכתב זה, קיימים עדכונים נוספים.

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בברכה,

ילנה קפלן

רוקחת ממונה

גיליאד סיאנסז ישראל בע"מ

העדכונים המהותיים בעלון לרופא:

4.1 Therapeutic indications

Triple-Negative Breast Cancer

First Line

Trodelvy as a single agent is indicated for the first-line treatment of adult patients with unresectable locally advanced or metastatic triple negative breast cancer (TNBC) who are not candidates for PD-1 or PD-L1 inhibitor based therapy.

Trodelvy, in combination with pembrolizumab is indicated for the first-line treatment of adult patients with unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 [Combined Positive Score (CPS ≥ 10)] as determined by an authorized test.

Second Line or Later

Trodelvy as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease (see section 5.1).

HR-Positive, HER2-Negative Breast Cancer

Trodelvy is indicated for the treatment of adult patients with 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.

4.2 Posology and method of administration

Trodelvy must only be prescribed and administered to patients by healthcare professionals experienced in the use of anti-cancer therapies and administered in an environment where full resuscitation facilities are available.

Select patients for treatment of unresectable locally advanced or metastatic TNBC with Trodelvy in combination with pembrolizumab, based on the tumor expression of PD-L1 [see Pharmacodynamic properties (5.1)].

Posology

The recommended dose of sacituzumab govitecan as a single agent or in combination with pembrolizumab is 10 mg/kg body weight administered as an intravenous infusion once weekly on Day 1 and Day 8 of 21-day treatment cycles. Treatment should be continued until disease progression or unacceptable toxicity.

When Trodelvy is administered in combination with pembrolizumab, discontinue pembrolizumab after approximately 24 months.

Refer to the Prescribing Information for pembrolizumab for the recommended dosing information.

Prevention treatment

Prior to each dose of sacituzumab govitecan, treatment for prevention of infusion-related reactions and prevention of chemotherapy-induced nausea and vomiting (CINV) is recommended (see section 4.4).

Prophylaxis for Neutropenia

Primary prophylaxis with granulocyte colony-stimulating factor (G-CSF) should be considered starting in the first cycle in patients at increased risk of febrile neutropenia (see section 4.4).

~~Dose modifications for infusion-related reactions~~

~~The infusion rate of sacituzumab govitecan should be slowed down or infusion interrupted if the patient develops an infusion-related reaction. Sacituzumab govitecan should be permanently discontinued if life-threatening infusion-related reactions occur (see section 4.4).~~

Dose modifications for adverse reactions for sacituzumab govitecan

Management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation of sacituzumab govitecan. The recommended dosage reduction schedule is presented in Table 1 and the recommended dosage modifications for adverse reactions are provided in Table 2. ~~Dose modifications to manage adverse reactions of sacituzumab govitecan are described in Table 1.~~ The sacituzumab govitecan dose should not be re-escalated after a dose reduction for adverse reactions has been made.

Table 1: Dosage Reduction Schedule

Dose Reduction Schedule	Dose Level
Recommended starting dose	10 mg/kg
First dose reduction	Reduce to 7.5 mg/kg
Second dose reduction	Reduce to 5 mg/kg
Requirement for further dose reduction	Discontinue treatment

Table ~~1~~ 2: Recommended dose modifications for adverse reactions

Adverse reactions	**Severity**	**Dose Modification**
Neutropenia	Grade 3-4 neutropenia (ANC<1000/mm^3) Grade 3-4 febrile neutropenia (ANC<1000/mm^3)	Withhold treatment until resolved to ≤ Grade 1 (ANC ≥ 1500/mm^3) for Day 1 dose or Grade 2 (ANC ≥ 1000/mm^3) for Day 8 Dose (see section 4.4). Administer G-CSF during treatment as clinically indicated. For subsequent Grade 3-4 febrile neutropenia events or subsequent prolonged Grade 3-4 neutropenia events, reduce one dose level with each recurrence or discontinue according to Table 1.
Nausea/Vomiting/ Diarrhoea	Grade 3-4 nausea, vomiting or diarrhoea due to treatment that is not controlled with antiemetics and anti-diarrheal agents	Withhold treatment until resolved to ≤ Grade 1 (see section 4.4). Reduce one dose level with each occurrence or discontinue according to Table 1.
Infusion-Related Reaction	Grade 1-3 infusion-related reactions	Slow or interrupt the infusion rate of sacituzumab govitecan
	Grade 4 infusion-related reactions	Discontinue treatment
Other Toxicities	Other Grade 3-4 toxicities of any duration despite optimal medical management	Withhold treatment until resolved to ≤ Grade 1. Reduce one dose level with each occurrence or discontinue according to Table 1.

Adverse reaction	Occurrence	Dose modification
Severe neutropenia		
Grade 4 neutropenia ≥ 7 days or less if clinically indicated, OR Grade 3-4 febrile neutropenia OR At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing by 2 or 3 weeks for recovery to ≤ Grade 1	First	Administer granulocyte colony stimulating factor (GCSF), as soon as clinically indicated
	Second	25% dose reduction: administer G-CSF as soon as clinically indicated
	Third	50% dose reduction: administer G-CSF as soon as clinically indicated
	Fourth	Discontinue treatment: administer G-CSF as soon as clinically indicated
At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing beyond 3 weeks for recovery to ≤ Grade 1	First	Discontinue treatment: administer G-CSF as soon as clinically indicated
Severe non-neutropenic toxicity		
Grade 4 non-hematologic toxicity of any duration, OR Any Grade 3-4 nausea, vomiting or diarrhoea due to treatment that is not controlled with antiemetics and anti-diarrhoeal agents, 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, Grade 3 nausea or Grade 3-4 vomiting, which does not recover to ≤ Grade 1 within 3 weeks	First	Discontinue treatment

Dosage Modifications for Adverse Reactions for Trodelvy in Combination with Pembrolizumab

Interrupt or discontinue one or both drugs of the combination or reduce the dose of Trodelvy to manage adverse reactions as appropriate. Refer to the prescribing information for pembrolizumab for recommendations on dosage interruption or discontinuation due to adverse reactions. For Trodelvy dosage modifications, refer to Table 2.

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4.4 Special warnings and precautions for use

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Neutropenia

Sacituzumab govitecan can cause severe or life-threatening neutropenia (see section 4.8). Fatal infections in the setting of neutropenia have been observed in clinical studies with sacituzumab govitecan, primarily in the first two cycles of treatment.

Primary prophylaxis with G-CSF should be considered starting in the first cycle of treatment in patients at increased risk of febrile neutropenia, e.g., older patients (in particular aged 65 years and older), patients with previous neutropenia, poor performance status, organ dysfunction (including renal, liver or cardiovascular dysfunction), or multiple comorbid conditions. Monitor ANC during treatment.

Sacituzumab govitecan should not be administered if the ~~absolute neutrophil count~~ ANC is below 1500/mm3 on Day 1 of any cycle or if the neutrophil count is below 1000/mm3 on Day 8 of any cycle. ~~Therefore, it is recommended that patients' blood counts are monitored as clinically indicated during treatment.~~ Sacituzumab govitecan should not be administered in case of neutropenic fever. ~~Treatment with granulocyte colony stimulating factor and d~~Dose modifications may be required due to neutropenia or febrile neutropenia. Treat neutropenia with G-CSF and consider prophylaxis in subsequent cycles as clinically indicated (see sections 4.2 and 4.8).

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Use in patients with reduced UGT1A1 activity

SN-38 (the small molecule moiety of sacituzumab govitecan) is metabolised via uridine diphosphate-glucuronosyl transferase (UGT1A1). Genetic variants of the UGT1A1 gene such as the UGT1A1*28 allele lead to reduced UGT1A1 enzyme activity. Individuals who are homozygous for UGT1A1*28 allele are at increased risk for neutropenia, febrile neutropenia, and anaemia and are at increased risk for other adverse reactions following initiation of sacituzumab govitecan treatment (see section 4.8). A higher incidence of Grade 3-4 neutropenia, febrile neutropenia, and anaemia was observed in patients homozygous for the UGT1A1*28 allele and patients heterozygous for the UGT1A1*6 allele compared to patients homozygous for the wild-type allele. Approximately 20% of the Black population, 10% of the White population, and 2% of the East Asian population are homozygous for the UGT1A1*28 allele. Approximately 0.2% of the Black population, 0.3% of the White population, and 27% of the East Asian population are heterozygous for the UGT1A1*6 allele. Variants in other alleles potentially associated with reduced UGT1A1 enzyme activities might be prevalent in certain populations ~~Decreased function alleles other than UGT1A1*28 may be present in certain populations~~. Patients with known reduced UGT1A1 activity should be closely monitored for adverse reactions. When unknown, no testing of UGT1A1 status is required as the management of adverse reactions including the recommended dose modifications will be the same for all patients.

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4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

UGT1A1 inhibitors

Concomitant administration of sacituzumab govitecan with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Sacituzumab

govitecan should be used with caution in patients receiving UGT1A1 inhibitors (e.g. propofol, ketoconazole, EGFR tyrosine kinase inhibitors).

UGT1A1 inducers

Exposure to SN-38 may be reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Sacituzumab govitecan should be used with caution in patients receiving UGT1A1 inducers (e.g. carbamazepine, phenytoin, rifampicin, ritonavir, tipranavir).

Based on the limited data available from patients who received UGT1A1 inhibitors (n=~~16~~15) or inducers (n=~~5~~7) while being treated with sacituzumab govitecan, free SN-38 exposures in these patients were comparable to those in patients who did not receive UGT1A1 inhibitor or inducer.

4.8 Undesirable effects

Summary of the safety profile

Sacituzumab govitecan as monotherapy

The most common adverse reactions reported in patients treated with sacituzumab govitecan were: neutropenia (67.~~6~~3%), nausea (62.~~6~~1%), diarrhoea (~~62.5~~59.9%), fatigue (~~61.5~~57.4%), alopecia (~~45.6~~48.3%), anaemia (40.~~7~~1%), constipation (36.~~2~~7%), vomiting (~~33.6~~31.3%), and decreased appetite (~~25.7~~23.3%).
The most common grade 3 or higher adverse reactions were neutropenia (~~50.7~~48.6%), diarrhoea (10.0%), leukopenia (~~10.5~~9.6%), ~~diarrhoea (10.3%),~~ anaemia (~~9.3~~7.7%), fatigue (~~6~~5.8%), febrile neutropenia (5.6%), and lymphopenia (3.1%).

The most frequently reported serious adverse reactions in patients treated with sacituzumab govitecan were febrile neutropenia (4.~~8~~5%), diarrhoea (3.~~9~~7%), neutropenia (2.~~6~~9%) and pneumonia (2.1%).

Sacituzumab govitecan in combination with pembrolizumab

Adverse reactions occurring in patients treated with sacituzumab govitecan in combination with pembrolizumab were generally similar to those observed with sacituzumab govitecan or pembrolizumab in breast cancer treatment. The most frequent adverse reactions in patients treated with sacituzumab govitecan in combination with pembrolizumab were diarrhoea (70.1%), nausea (67.9%), neutropenia (62.9%), fatigue (58.4%), alopecia (51.6%), constipation (40.7%), anaemia (36.7%) and vomiting (29.4%), and the most frequent grade 3 or higher adverse reactions were neutropenia (43.0%) and diarrhoea (10.0%).

The combination of sacituzumab govitecan with pembrolizumab did not increase the frequency or severity of pembrolizumab-associated immune-mediated adverse reactions.

When sacituzumab govitecan is administered in combination with pembrolizumab, refer to the PI for the respective combination therapy components prior to initiation of treatment. Adverse reactions known to occur with sacituzumab govitecan or combination therapy components given alone may occur during treatment with these medicinal products in combination, even if these reactions were not reported in clinical studies with combination therapy.

Tabulated list of adverse reactions

The frequencies of adverse reactions are based on pooled data from ~~three~~ four clinical studies involving ~~688~~ 963 patients who received sacituzumab govitecan 10 mg/kg body weight for the treatment of metastatic TNBC and HR+/HER2- breast cancer. The median exposure to sacituzumab govitecan in this data set was ~~4.63~~ 5.29 months.

The safety of sacituzumab govitecan in combination with pembrolizumab has also been evaluated in a clinical study of 221 patients with metastatic TNBC whose tumours express PD-L1 receiving sacituzumab govitecan 10 mg/kg on Days 1 and 8 and pembrolizumab 200 mg on Day 1 of a 21-day cycle. The median exposure of sacituzumab govitecan in the combination therapy data set was 8.9 months.

Adverse reactions observed in clinical studies of sacituzumab govitecan as monotherapy or in combination with pembrolizumab or reported from post-marketing use of sacituzumab govitecan are listed in Table 3. The adverse reaction frequencies are based on all-cause adverse event frequencies, where a proportion of the events for an adverse reaction may have other causes than sacituzumab govitecan, such as the disease, other medicinal products or unrelated causes. The severity of adverse drug reactions was assessed based on the Common Terminology Criteria for Adverse Events (CTCAE), defining grade 1 = mild, grade 2 = moderate, grade 3 = severe, grade 4 = life threatening, and 5 = death.

Adverse reactions are listed by System Organ Class and frequency category. Frequency categories are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000); and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table ~~2~~ 3: List of adverse reactions

System organ class (SOC)	**Frequency**	**~~Adverse reactions~~ Monotherapy**	**In combination with pembrolizumab**
Infections and infestations			
	Very common	Urinary tract infection Upper respiratory tract infection	Urinary tract infection Upper respiratory tract infection
	Common	Sepsis Pneumonia Influenza Bronchitis Nasopharyngitis Sinusitis Oral herpes	Sepsis Pneumonia Influenza Bronchitis Nasopharyngitis Sinusitis Oral herpes
Blood and lymphatic system disorders			
	Very common	Neutropenia[1] Anaemia[2] Leukopenia[3] Lymphopenia[4]	Neutropenia[1] Anaemia[2] Leukopenia[3]
	Common	Febrile neutropenia Thrombocytopenia[5]	Febrile neutropenia Lymphopenia[4] Thrombocytopenia[5]
Immune system disorders			
	Very common	Hypersensitivity[6]	Hypersensitivity[6]
Metabolism and nutrition disorders			
	Very common	Decreased appetite Hypokalaemia Hypomagnesaemia	Decreased appetite
	Common	Dehydration Hyperglycaemia Hypophosphataemia Hypocalcaemia	Dehydration Hyperglycaemia Hypokalaemia Hypomagnesaemia

		Hyponatraemia	Hypophosphataemia Hypocalcaemia Hyponatraemia
Psychiatric disorders			
	~~Very common~~ Common	Insomnia Anxiety	Insomnia Anxiety
Nervous system disorders			
	Very common	Headache Dizziness	Headache Dizziness
	Common	Dysgeusia	Dysgeusia
Vascular disorders			
	Common	Hypotension	Hypotension
Respiratory, thoracic and mediastinal disorders			
	Very common	Dyspnoea[7] Cough	Cough
	Common	Epistaxis Productive cough Rhinorrhoea Nasal congestion Upper airway cough syndrome	Dyspnoea[7] Epistaxis Productive cough Rhinorrhoea Nasal congestion
	Uncommon		Upper airway cough syndrome
Gastrointestinal disorders			
	Very common	Diarrhoea Vomiting ~~Nausea~~ Constipation Stomatitis Nausea Abdominal pain	Diarrhoea Vomiting Constipation Stomatitis Nausea Abdominal Pain
	Common	Neutropenic colitis[8] Colitis ~~Stomatitis~~ Abdominal pain upper Dyspepsia Gastrooesophageal reflux disease Abdominal distension	Colitis Abdominal pain upper Dyspepsia Gastrooesophageal reflux disease Abdominal distension
	Uncommon	Enteritis	Neutropenic colitis[8] Enteritis
Skin and subcutaneous tissue disorders			
	Very common	Alopecia Rash Pruritus	Alopecia Rash Pruritus
	Common	Rash maculopapular Skin hyperpigmentation Dermatitis acneiform Dry skin	Rash maculopapular Skin hyperpigmentation Dermatitis acneiform Dry skin
Musculoskeletal and connective tissue disorders			
	Very common	Back pain Arthralgia	Back pain Arthralgia
	Common	Musculoskeletal chest pain Muscle spasms	Musculoskeletal chest pain Muscle spasms
Renal and urinary disorders			
	Common	Haematuria Proteinuria	Haematuria Proteinuria

		Dysuria	Dysuria
General disorders and administration site conditions			
	Very common	Fatigue[9]	Fatigue[9]
	Common	Pain Chills	Pain Chills
Investigations			
	Very common	Blood alkaline phosphatase increased	Weight decreased Blood alkaline phosphatase increased
	Common	Weight decreased ~~Blood alkaline phosphatase increased~~ Activated partial thromboplastin time prolonged Blood lactate dehydrogenase increased	Blood lactate dehydrogenase increased
Injury, poisoning and procedural complications			
	~~Uncommon~~ Common	Infusion related reaction	Infusion related reaction

1: Includes the following preferred terms: neutropenia; neutrophil count decreased.
2: Includes the following preferred terms: anaemia; haemoglobin decreased; red blood cell count decreased.
3: Includes the following preferred terms: leukopenia; white blood cell count decreased.
4: Includes the following preferred terms: lymphopenia; lymphocyte count decreased.
5: Includes the following preferred terms: thrombocytopenia; platelet count decreased.
6: Hypersensitivity events reported up to the end of the day after treatment was administered. Includes events coded to the following preferred terms: rash, infusion related reaction, hypersensitivity, periorbital oedema, catheter site dermatitis, contrast media reaction, dermatitis allergic, dermatitis contact, eczema, rash erythematous, urticaria, anaphylactic reaction, bronchospasm, conjunctivitis allergic, dermatitis, dermatitis acneiform, dermatitis exfoliative generalised, drug hypersensitivity, infusion related hypersensitivity reaction, rash macular, rash maculo-papular, rash papular, rash pustular, rhinitis allergic, swelling face, swelling of eyelid, swollen tongue, Type IV hypersensitivity reaction, cough with pruritus, cough with rash, dyspnoea with pruritus, dyspnoea with rash, dyspnoea with wheezing and rash, hypotension with dyspnoea. ~~dyspnoea; hypotension; flushing; erythema; chest discomfort; rhinitis allergic; wheezing; oedema; urticaria; anaphylactic reaction; mouth ulceration; skin exfoliation; swollen tongue; throat tightness.~~
7: Includes the following preferred terms: dyspnoea; dyspnoea exertional
8: Includes the preferred term of neutropenic colitis and events reported as typhlitis
9: Includes the following preferred terms: fatigue, asthenia

Description of selected adverse reactions

The data below reflect information for significant adverse reactions for sacituzumab govitecan as monotherapy in clinical trials (see section 5.1). The management guidelines for these adverse reactions are described in sections 4.2 and 4.4.

Neutropenia
The median time to onset of neutropenia (including febrile neutropenia) following the start of the first treatment cycle was ~~16~~ 20 days. The median duration of neutropenia was ~~8~~ 10 days.

Neutropenia occurred in 67.6~~3~~% ~~(465/688)~~ of patients treated with sacituzumab govitecan, including Grade 3-4 neutropenia in 48.6~~50.7~~% of patients. Neutropenia was the reason for dose reduction in 14.2~~12.4~~% of patients. Neutropenic colitis was observed in 1.3% ~~(7/688)~~ of patients. Fatal infections secondary to neutropenia (including neutropenic colitis) occurred in 0.6% of patients.

Febrile neutropenia occurred in ~~6.1~~5.6% ~~(42/688)~~ of patients treated with sacituzumab govitecan. Febrile neutropenia was the reason for dose reduction in 2.~~9~~7% of patients.

Use in patients with reduced UGT1A1 activity
The incidence of Grade 3-4 neutropenia was ~~60~~59.6% ~~(43/71)~~ in patients homozygous for the UGT1A1*28 allele, ~~52~~50.9~~7~~% ~~(144/272)~~ in patients heterozygous for the UGT1A1*28 allele, and ~~49~~44.~~1~~9% ~~(140/285)~~ in patients homozygous for the wild-type allele. The incidence of Grade 3-4 febrile neutropenia was ~~14~~10.~~1~~6% ~~(10/71)~~ in patients homozygous for the UGT1A1*28 allele, 5.9% ~~(16/272)~~ in patients heterozygous for the UGT1A1*28 allele, and 4.~~6~~3% ~~(13/285)~~ in patients homozygous for the wild-type allele. The incidence of Grade 3-4 anaemia was ~~15~~10.~~5~~6% ~~(11/71)~~ in patients homozygous for the UGT1A1*28 allele, ~~7~~6.4% ~~(20/272)~~ in patients heterozygous for the UGT1A1*28 allele, and ~~8.1~~6.3% ~~(23/285)~~ in patients homozygous for the wild-type allele. For patients heterozygous for the UGT1A1*6 allele, the incidences of Grade 3-4 neutropenia, febrile neutropenia, and anaemia were 53.8%, 7.7%, and 7.7%, respectively.

Compared to patients homozygous for the wild-type allele, earlier median onset of neutropenia and anaemia was observed in patients homozygous for the UGT1A1*28 allele and in patients heterozygous for the UGT1A1*28 allele.

Diarrhoea
The median time to onset of diarrhoea following the start of the first treatment cycle was 13 days. The median duration of diarrhoea was ~~8~~ 7 days.

Diarrhoea occurred in ~~62.5~~59.9% ~~(430/688)~~ of patients treated with sacituzumab govitecan. Grade 3 events occurred in 10.~~3~~0% ~~(71/688)~~ of patients. Four ~~Three~~ of 963~~688~~ patients (< 1%) discontinued treatment because of diarrhoea.

Hypersensitivity
Hypersensitivity reactions reported up to the end of the day following dosing occurred in ~~33.0~~12.8% ~~(227/688)~~ of patients treated with sacituzumab govitecan. Grade 3 and above hypersensitivity occurred in 0.5~~1.7~~% ~~(12/688)~~ of patients treated with sacituzumab govitecan. The incidence of hypersensitivity reactions leading to permanent discontinuation of sacituzumab govitecan was 0.~~1~~2% ~~(1/688)~~.

Immunogenicity
Across clinical studies in patients treated with sacituzumab govitecan, ~~9~~ 13 (1.~~1~~2%) of ~~785~~ 1058 patients developed antibodies to sacituzumab govitecan following administration; ~~6~~ 10 of these patients (0.~~8~~9% of all patients treated with sacituzumab govitecan) had neutralizing antibodies against sacituzumab govitecan. In study ASCENT-04, no treatment-emergent antibodies against sacituzumab govitecan were observed in 207 patients who were evaluable for antibodies against sacituzumab govitecan and received sacituzumab govitecan 10 mg/kg in combination with pembrolizumab.

Special Populations
There was a higher discontinuation rate due to adverse reactions in patients aged 65 years or older (8%) compared with younger patients (4%) with metastatic breast cancer. ~~There was no difference in discontinuation rate due to adverse events in patients aged 65 years or older compared with younger patients with mTNBC. There was a higher discontinuation rate due to adverse reactions in patients aged 65 years or older (14%) compared with younger patients (3%) with HR+/HER2- metastatic breast cancer. There was a higher incidence rate of serious adverse events in patients aged 75 years or older (67%) compared to patients aged 65 years or older (43%) and patients younger than 65 years (24%) with HR+/HER2- metastatic breast cancer.~~ Higher incidence rates of febrile neutropenia and severe diarrhoea were observed in patients aged 65 years or older. A higher incidence rate of fatal infections was observed in patients aged 65 years or older. There was a higher incidence rate of serious adverse events in patients aged 75 years or older (52%) compared to patients aged 65 years or older (35%) and patients younger than 65 years (25%) with metastatic breast cancer.

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5.1 Pharmacodynamic properties

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Clinical efficacy and safety

Triple Negative Breast Cancer (TNBC)

In Combination with Pembrolizumab in Previously Untreated, Unresectable Locally Advanced or Metastatic TNBC whose tumours express PD-L1 (ASCENT-04)

The efficacy of sacituzumab govitecan in combination with pembrolizumab was evaluated in a multicentre, open-label, randomised study (ASCENT-04) conducted in 443 patients with unresectable locally advanced or metastatic TNBC who had not received prior systemic therapy for advanced disease and whose tumours express PD-L1 (defined using the PD-L1 IHC 22C3 assay as tumours with a CPS ≥ 10) at screening. Patients may have received chemotherapy with or without a PD-1 or PD-L1 inhibitor and/or radiotherapy in early-stage TNBC, however at least 6 months must have elapsed between the completion of curative systemic breast cancer therapy or surgery, whichever occurred last, and first local or distant recurrence. No prior treatment with topoisomerase 1 inhibitors or antibody drug conjugates containing a topoisomerase inhibitor was allowed.

Patients with active chronic inflammatory bowel disease or gastrointestinal (GI) perforation within 6 months of enrolment or with active serious infections requiring systemic antimicrobial therapy were excluded.

Randomisation was stratified by treatment-free interval (de novo versus disease recurrence within 6 to 12 months from completion of treatment in the curative setting versus disease recurrence > 12 months from completion of treatment in the curative setting), and by geographic region (United State/Canada/Western Europe versus Rest of World), and prior exposure to PD-1 or PD-L1 inhibitor (yes versus no).

Patients were randomised (1:1) to receive either:

Sacituzumab govitecan 10 mg/kg as an intravenous (IV) infusion on Days 1 and 8 of 21-day cycles and pembrolizumab 200 mg on Day 1 of 21-day cycles. Pembrolizumab was administered for a maximum of 35 cycles (approximately 24 months).

Pembrolizumab 200 mg on Day 1 of 21-day cycles in combination with nab-paclitaxel 100 mg/m2 on Days 1, 8 and 15 every 28 days, or paclitaxel 90 mg/m2 on Days 1, 8, and 15 every 28 days, or gemcitabine 1000 mg/m2 and carboplatin AUC 2 mg/mL/min on Days 1 and 8 every 21 days. Pembrolizumab was administered for a maximum of 35 cycles (approximately 24 months).

Patients were treated until blinded independent central review (BICR)-verified disease progression, unacceptable toxicity, death, or consent withdrawal. Tumour imaging was obtained every 8 weeks for the first 18 months followed by every 12 weeks thereafter. Following BICR-verified radiographic disease progression and study treatment discontinuation, patients who were randomised to treatment of physician's choice (TPC) and pembrolizumab were able to be enrolled in the crossover phase of this study to receive sacituzumab govitecan monotherapy.

The primary efficacy outcome was progression-free survival (PFS) by BICR per RECIST v1.1. Additional efficacy outcomes measures included overall survival (OS) and objective response rate (ORR).

The median age of patients in the study population was 55 years (range: 23-88 years), and 26% of patients were 65 years or over. All patients were female (100%). The majority of patients were White (58%) and Asian (24%); 6% were American Indian or Alaska Native, 5% were Black, and 3% were other race. Thirty-four percent of patients presented with de novo metastatic disease at screening, 18%

with recurrent disease within 6 to 12 months from completion of treatment in the curative setting and 48% with recurrent disease > 12 month from completion of treatment in the curative setting. One-point four percent (1.4%) of patients received a prior PD-1 or PD-L1 inhibitor. At study entry, all patients had an ECOG performance status of 0 (70%) or 1 (30%), 36% of patients were pre-menopausal and 64% were post-menopausal. The majority of patients (95%) had metastatic disease at screening, brain metastases were observed in 3% of patients. BRCA mutation analysis by Whole Exome Sequencing was available for 75% of participants, of which 21% of the participants had BRCA1 or BRCA2 mutated tumours.

Sacituzumab govitecan in combination with pembrolizumab demonstrated a statistically significant improvement in PFS versus TPC in combination with pembrolizumab as assessed by BICR. At the time of the interim analysis of OS, patients had a median follow-up of 22.5 months. The efficacy results are summarized in Table 4, Figure 1 and Figure 2.

Table 4: Efficacy endpoints (ASCENT-04)

	Sacituzumab govitecan 10 mg/kg in combination with Pembrolizumab n=221	**TPC in combination with Pembrolizumab n=222**
Progression-Free Survival by BICR[1]		
Number (%) of patients with events	109 (49%)	140 (63%)
Median PFS in months (95% CI)	11.2 (9.3, 16.7)	7.8 (7.3, 9.3)
Hazard ratio (95% CI)[2]	0.65 (0.51, 0.84)	
p-value[3]	0.0009	
Objective Response Rate by BICR[1]		
ORR (95% CI)[4]	60% (53, 66)	53% (46, 60)
Overall Survival[5]		
Number (%) of patients with events	97 (43.9%)	106 (47.7%)
Median OS in months (95% CI)	31.21 (25.56, NR)	28.39 (24.44, NR)
Hazard ratio (95% CI)[2]	0.915 (0.694, 1.206)	

[1] Based on PFS primary analysis with median follow-up time 14 months (data cut-off 3 March 2025)
[2] Hazard ratio based on the stratified Cox proportional hazard model
[3] Stratified log-rank test adjusted for stratification factors: treatment-free interval (de novo vs recurrent disease within 6 to 12 months vs recurrent disease occurring > 12 months from completion of treatment in the curative setting) and geographic region (US/Canada/Western Europe vs Rest of World
[4] Based on 2-sided 95% CIs using the Clopper-Pearson method
[5] Based on interim OS analysis (data cut-off 16 February 2026)
BICR = Blinded Independent Central Review; CI = Confidence Interval
NR= Not reached
TPC = nab-paclitaxel, paclitaxel, or gemcitabine

Figure 1: Progression free survival by BICR in ASCENT-04

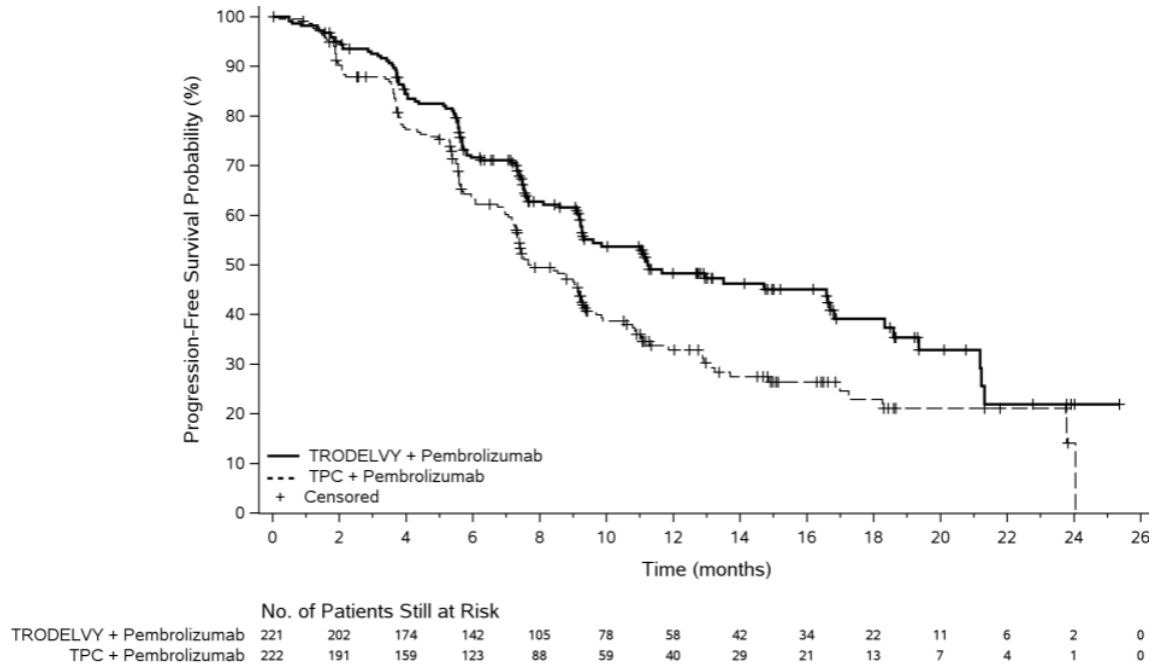
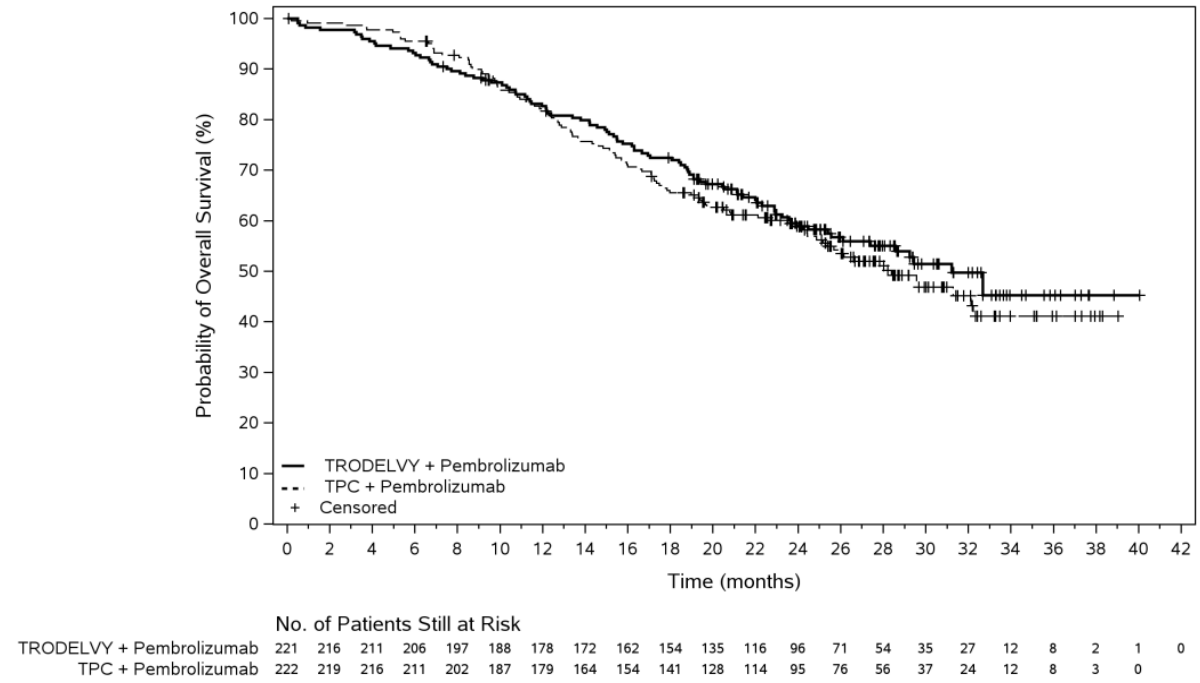


Figure 2: Overall survival in ASCENT-04



Previously Untreated, Unresectable Locally Advanced or Metastatic TNBC in patients who are not candidates for PD-1/PD-L1 inhibitor therapy (ASCENT-03)

The efficacy of sacituzumab govitecan was evaluated in a multicentre, open-label, randomised study (ASCENT-03) conducted in 558 patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who had not received previous systemic therapy for advanced disease and who were not candidates for PD-1 or PD-L1 inhibitor therapy. The study enrolled patients with tumours that are PD-L1 negative (defined as having a tumour CPS < 10 using the IHC 22C3 assay), and patients with tumours that are PD-L1 positive (defined as having a CPS ≥ 10 using the

IHC 22C3 assay) if they received a PD-1 or PD-L1 inhibitor in the (neo)adjuvant setting or if they had a comorbidity precluding treatment with PD-1 or PD-L1 inhibitor therapy.

Patients may have received chemotherapy with or without a PD-1 or PD-L1 inhibitor and/or radiotherapy in the early-stage of TNBC, however at least 6 months must have elapsed between the completion of systemic (neo) adjuvant breast cancer therapy or surgery, whichever occurred last, and first local or distant recurrence. No prior treatment with topoisomerase 1 inhibitors or antibody drug conjugates containing a topoisomerase inhibitor was allowed.

Patients were randomised (1:1) to receive sacituzumab govitecan 10 mg/kg as an intravenous infusion on Days 1 and 8 of a 21-day cycle (n=279) or Treatment of Physician's Choice (TPC) (n=279). TPC was determined by the investigator before randomisation from one of the following regimens: gemcitabine and carboplatin, paclitaxel or nab-paclitaxel. Randomisation was stratified by de novo vs recurrent disease within 6 to 12 months from completion of treatment in the curative setting versus recurrent disease > 12 months from completion of treatment in the curative setting, and by geographic region (United States, Canada, Western Europe vs. Rest of World).

Patients were treated until BICR-verified disease progression, unacceptable toxicity, death, or consent withdrawal. Tumour imaging was obtained every 6 weeks for the first year followed by every 12 weeks thereafter. Following BICR-verified objective disease progression and study treatment discontinuation, patients who were randomised to TPC chemotherapy were able to receive sacituzumab govitecan supplied on trial in the crossover phase of this study if eligible.

The primary efficacy outcome was progression-free survival (PFS) by BICR per RECIST v1.1. Additional efficacy outcomes measures included overall survival (OS) and objective response rate (ORR) by BICR.

The median age of the study population was 55 years (range: 23-86 years), and 26% of patients were 65 years or over; 99.5% of patients were female. The majority of patients were White (64%); 23% were Asian, 3% were Black, and 4% were other race. Thirty-one percent (31%) of patients had de novo disease, 21% of patients had recurrent disease with a disease-free interval (DFI) 6 to 12 months and 48% of patients with DFI > 12 months. Ninety-nine point five percent (99.5%) of patients enrolled had tumours that were PD-L1 negative and 0.5% of patients had tumours that were PD-L1 positive. At study entry, all patients had an ECOG performance status of 0 (66%) or 1 (34%). The majority of patients (97.8%) had metastatic disease at screening; brain metastases were observed in 5% of patients. BRCA 1/2 mutation status was known for 76% of participants, out of which 18% of tested study participants had positive BRCA mutations.

Sacituzumab govitecan demonstrated a statistically significant improvement in PFS versus TPC by BICR. At the time of the first interim OS analysis, patients had a median follow-up of 17.7 months. Efficacy results are summarized in Table 5, Figure 3 and Figure 4.

Table 5. Efficacy endpoints (ASCENT-03)

	Sacituzumab govitecan N=279	**TPC N=279**
Progression-Free Survival by BICR[1]		
Number (%) of patients with events	161 (58%)	188 (67%)
Median PFS in months (95% CI)	9.7 (8.1, 11.1)	6.9 (5.6, 8.2)
Hazard ratio (95% CI)[2]	0.62 (0.50, 0.77)	
p-value[3]	< 0.0001	
Objective Response Rate by BICR[1]		
ORR, (95% CI)[4]	48% (42%, 54%)	46% (40%, 52%)
Overall survival[5]		
Number (%) of patients with events	139 (50%)	144 (52%)
Median OS in months (95% CI)	21.5 (18.9, 26.5)	21.3 (18.7, 25.2)
Hazard ratio (95% CI)[2]	0.950.75, 1.20)	

[1] Based on PFS primary analysis (data cut-off 2 April 2025) with median follow-up time 13.2 months.

[2] Hazard ratio with 95% CIs based on the stratified Cox proportional hazards model adjusted for randomisation stratification factors: disease stratification (de novo vs recurrent disease within 6 to 12 months vs recurrent disease occurring > 12 months from completion of treatment in the curative setting) and geographic region (US/Canada/Western Europe vs rest of the world).

[3] 2-sided p-value based on log-rank test adjusted for randomisation stratification factors: disease stratification (de novo vs recurrent disease within 6 to 12 months vs recurrent disease occurring > 12 months from completion of treatment in the curative setting) and geographic region (US/Canada/Western Europe vs rest of the world)

[4] The 95% CI is based on the Clopper-Pearson exact method.

[5] Based on first interim OS analysis (data cut-off 27 October 2025) with median follow-up time 17.7 months

BICR = Blinded Independent Central Review; CI = Confidence Interval
TPC = gemcitabine and carboplatin, paclitaxel, or nab-paclitaxel

At OS IA1, in the BRCA1/2 mutated subgroup of patients (SG n=40; TPC n=37), defined by whole exome sequencing, median PFS was 12.5 months in the SG arm and 8.3 months in the TPC arm, corresponding to an HR of 0.60 (95% CI: 0.34, 1.07). The HR for OS at OS IA1 was 1.08 (95% CI: 0.55, 2.14).

Figure 3: Progression free survival by BICR in ASCENT-03 (data cut-off date 2 April 2025)

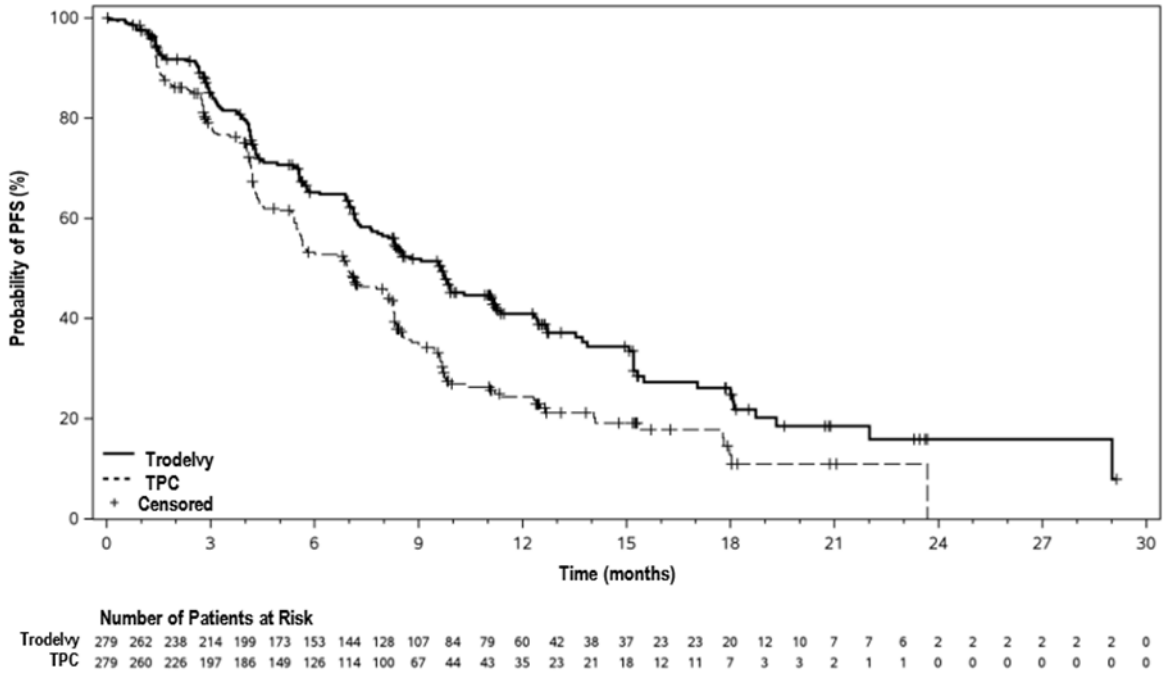
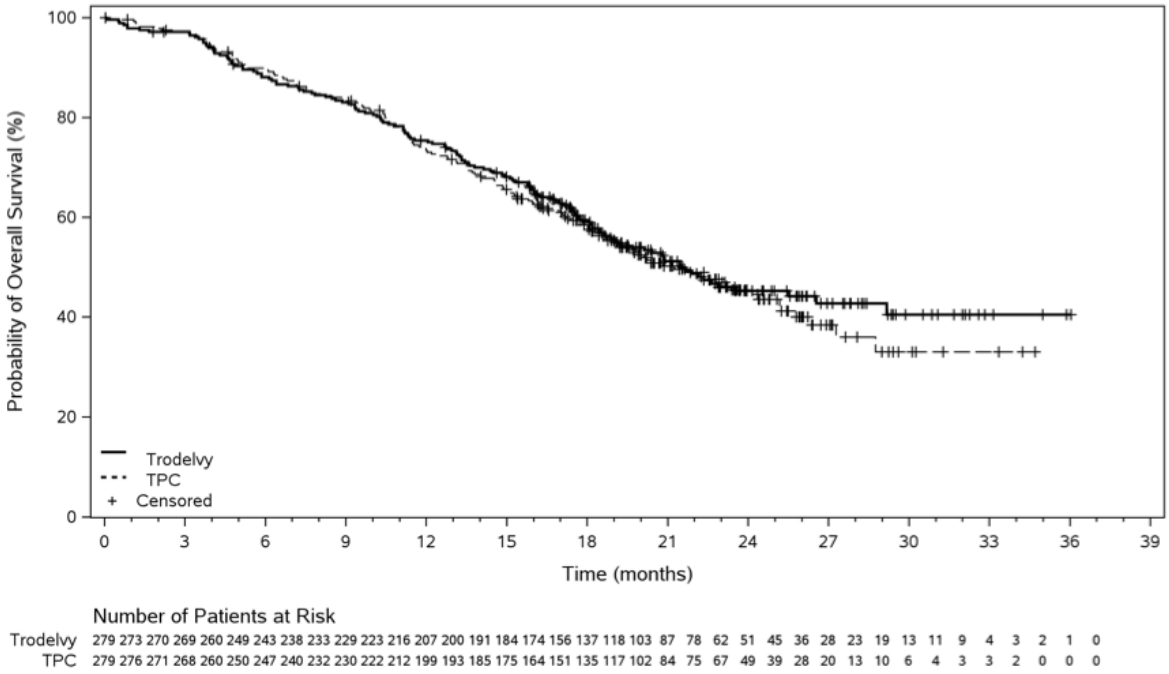


Figure 4: Overall survival in ASCENT-03 (data cut-off date 27 Oct 2025)



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5.2 Pharmacokinetic properties

The serum pharmacokinetics of sacituzumab govitecan and SN-38 were evaluated in ~~the ASCENT study in a population of mTNBC~~ patients with metastatic breast cancer (mBC) who received sacituzumab govitecan ~~as a single agent~~ at a dose of 10 mg/kg as monotherapy or in combination with pembrolizumab.~~body weight.~~ The pharmacokinetic parameters of sacituzumab govitecan and free SN-38 when administered as monotherapy or in combination with pembrolizumab are presented in Table ~~5~~8.

There was no impact of pembrolizumab coadministration on pharmacokinetics of sacituzumab govitecan or SN-38.

Table ~~5~~8: Summary of mean PK parameters (CV%) of sacituzumab govitecan and free SN-38

	Sacituzumab govitecan	**Free SN-38**
C_{max} [ng/mL]	258378~~242 000~~ (17~~22~~%)	97 ~~91~~ (41~~65~~%)
AUC_{0-168} [ng*h/mL]	12285980 ~~5 560 000~~ (19~~24~~%)	3120~~2 730~~ (62~~41~~%)

*Parameters estimated based on population PK analyses
C_{max}: maximum serum concentration from 0-168 hours after the first dose
AUC_{0-168}: area under serum concentration curve through 168 hours after the first dose

Distribution

Based on population pharmacokinetic analyses, the steady state volume of distribution of sacituzumab govitecan when administered as monotherapy or in combination with pembrolizumab was ~~3.58~~4.79 L.

Biotransformation

No metabolism studies with sacituzumab govitecan have been conducted.
SN-38 (the small molecule moiety of sacituzumab govitecan) is metabolised via UGT1A1.

Elimination

The median elimination half-life ($t_{1/2}$) of sacituzumab govitecan and free SN-38, based on population pharmacokinetic analysis, in patients who received sacituzumab govitecan as monotherapy or in combination with pembrolizumab, ~~with metastatic triple negative breast cancer~~ was ~~23.4~~170 and ~~17~~21.~~6 4~~ hours, respectively. ~~Based on population pharmacokinetic analyses,~~ The estimated mean (%CV) ~~the~~ clearance of sacituzumab govitecan is 0.~~128~~ 129 L/h (21%).

~~Metabolism~~

~~No metabolism studies with sacituzumab govitecan have been conducted.~~
~~SN-38 (the small molecule moiety of sacituzumab govitecan) is metabolised via UGT1A1.~~

Special populations

Pharmacokinetic analyses in patients treated with sacituzumab govitecan ~~(n = 789)~~ did not identify an effect of age, race, and mild or moderate renal impairment on the pharmacokinetics of sacituzumab govitecan.

Renal impairment
Renal elimination is known to contribute minimally to the excretion of SN-38, the small molecule moiety of sacituzumab govitecan. There are no data on the pharmacokinetics of sacituzumab govitecan in patients with severe renal impairment or end-stage renal disease (CrCl ≤ 15 mL/min).

Hepatic Impairment
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 = 257~~) to patients with normal hepatic function (bilirubin and AST ≤ ULN~~; n = 526~~).

There is limited data on ~~Sacituzumab~~ sacituzumab govitecan and free SN-38 exposures ~~are unknown~~ in patients with moderate or severe hepatic impairment.

6.6 Special precautions for disposal and other handling

Trodelvy is a cytotoxic medicinal product. Applicable special handling and disposal procedures have to be followed.

Reconstitution

- 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)~~.
- ~~Allow the required number of vials to warm to room temperature (20°C to 25°C).~~
- Using a sterile syringe, slowly inject 20 mL of sodium chloride 9 mg/mL (0.9%) solution for injection into each vial. The resulting concentration will be 10 mg/mL.
- Gently swirl vials and allow to dissolve for up to 15 minutes. Do not shake. The product should be inspected visually for particulate matter and discoloration prior to administration. 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 solution for infusion.

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