Trodelvy – Sacituzumab Govitecan (Breast)

Indication

Unresectable locally advanced or metastatic triple negative (ER/PR/HER2 negative) breast cancer previously treated with two or more prior lines of systemic therapy at least one of which was for advanced disease.

Previous systemic therapy must have included a taxane.

NICE TA819

ICD-10 codes

C50

Regimen details

Day	Drug	Dose	Route
1, 8	Trodelvy (sacituzumab govitecan)	10mg/kg	IV infusion

Cycle frequency

21 days

Number of cycles

Until disease progression or unacceptable toxicity.

Administration

Trodelvy is administered in sodium chloride 0.9% at a concentration between 1.1 – 3.4 mg/mL up to a maximum volume of 500mL. The first infusion should be administered over a period of 3 hours. Subsequent infusions may be administered over a period of 1 to 2 hours.

Patient should be observed during the infusion and for at least 30 minutes after each infusion for signs and symptoms of infusion related reactions.

If the patient develops an infusion related reaction the infusion should be slowed down or interrupted. If the patient experiences a life-threatening infusion-related reaction then Trodelvy should be permanently discontinued.

Pre-medication

The following pre-medication is required 30-60 minutes prior to infusion:
Paracetamol 1 g orally
Chlorphenamine 10mg IV slow bolus
Famotidine 20mg orally
Corticosteroids may be added if patients have previously had an infusion related reaction

Emetogenicity

This regimen has moderate emetic potential – refer to local policy

Additional supportive medication

Mouthwashes as per local policy
Proton pump inhibitor as required
Loperamide for cycle 1 then as required
Emollients as required

Extravasation

Trodelvy is an irritant (Group 3)

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT	14 days
Potassium	14 days
Magnesium	14 days
Calcium	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC*	96 hours
U+E (including creatinine)	7 days
LFT	7 days
Potassium	7 days
Magnesium	7 days
Calcium	7 days

* Additional FBC required within 24 hours of day 8

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	Day 1: ≥ 1.5 x 10^9/L Day 8: ≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Creatinine Clearance (CrCl)	>60 ml/min
Bilirubin	<1.5 x ULN*
ALT/AST	< 3 x ULN or < 5 x ULN if known liver metastases

*If high bilirubin linked to Gilbert syndrome this may be linked to UGT1A1*28 polymorphism and may be an indicator of increased risk of toxicity from the small molecule moiety of Trodelvy, SN38. Consider starting at a reduced dose (e.g. 75%) and monitor closely for toxicity then increase in future cycles if well tolerated.

Dose modifications

The Trodelvy dose should not be re-escalated after a dose reduction for an adverse reaction has been made.

- **Haematological toxicity**

Neutropenia	Occurrence	Dose adjustment
Grade 4 neutropenia (Neutrophils < 0.5 x 10^9/L) ≥ 7 days *OR* Grade 3 febrile neutropenia (Neutrophils < 1.0 x 10^9/L and fever ≥ 38.5°C) *OR* At time of scheduled treatment, Grade 3-4 neutropenia (Neutrophils < 1.0 x 10^9/L) which delays dosing by 2 or 3 weeks for recovery to ≤ Grade 1.	First	Reduce dose to 75% and add GCSF secondary prophylaxis
	Second	Reduce dose to 50%
	Third	Discontinue treatment
At time of scheduled treatment, Grade 3-4 neutropenia (Neutrophils < 1.0 x 10^9/L) which delays dosing beyond 3 weeks for recovery to ≤ Grade 1.	First	Discontinue treatment

Platelets	Occurrence	Dose adjustment
At time of scheduled treatment, Grade 3-4 thrombocytopenia (Platelets < 50 x 10^9/L) which delays dosing by 2 or 3 weeks for recovery to ≤ Grade 1.	First	Reduce dose to 75%
	Second	Reduce dose to 50%
	Third	Discontinue treatment
At time of scheduled treatment, Grade 3-4 thrombocytopenia (Platelets < 50 x 10^9/L) which delays dosing beyond 3 weeks for recovery to ≤ Grade 1.	First	Discontinue treatment

- **Renal impairment**

No dose adjustment is required in patients with mild renal impairment (CrCl=60-90mL/min). Trodelvy has not been studied in patients with moderate or severe renal impairment or in those with end-stage renal disease.

- **Hepatic impairment**

No adjustment to the starting dose is required in patients with mild hepatic impairment.

The safety of Trodelvy in patients with moderate or severe hepatic impairment has not been established. Trodelvy has not been studied and is therefore not recommended for use in patients with any of the following:

- Bilirubin > 1.5 x ULN
- AST/ALT > 3 x ULN in patients without liver metastases
- AST/ALT > 5 x ULN in patients with live metastases

- **Other toxicities**

Diarrhoea

Trodelvy can cause severe diarrhoea and should not be administered in case of ≥ Grade 2 diarrhoea at the time of scheduled treatment. Treatment should only be continued when resolved to ≤ Grade 1. Patients should be advised of the risk of diarrhoea, median time to onset of diarrhoea following start of first cycle was 13 days in trials. At the onset of diarrhoea, and if no infectious cause can be identified, promptly initiate loperamide 4mg initially followed by 2mg with every episode of diarrhoea for a maximum of 16 daily. Discontinue loperamide 12 hours after diarrhoea resolves. In patients with infectious diarrhoea, initiate anti-infective treatment as clinically indicated. Additional supportive measures (e.g. fluid and electrolyte substitution) may also be used as clinically indicated.

Patients who exhibit an excessive cholinergic response to treatment with Trodelvy (e.g. abdominal cramping, diarrhoea, salivation etc) can receive appropriate premedication (e.g. 250-300 micrograms atropine SC) for subsequent treatments.

Hypersensitivity
Anaphylactic reactions have been observed in clinical trials. Other hypersensitivity events observed during and within 24 hours of the infusion include dyspnoea, rash, pruritis, hypotension, wheezing, oedema including facial and tongue, urticaria and bronchospasm. Inform patients of the risk of serious infusion reactions and anaphylaxis and instruct patients to immediately report any of the above signs and symptoms.

Other toxicities

Definition	Occurrence	Dose adjustment
Grade 4 non-haematological toxicity which recovers to ≤ Grade 1 within 3 weeks *OR* Grade 3-4 nausea, vomiting or diarrhoea due to treatment that is not controlled with antiemetics or anti-diarrheal agents *OR* Other Grade 3-4 non-haematological toxicity persisting > 48 hours despite optimal medical management *OR* At time of scheduled treatment, Grade 3-4 non-neutropenic haematological or non-haematological toxicity, which delays dose by 2 or 3 weeks for recovery to ≤ Grade 1.	First	Reduce dose to 75%
	Second	Reduce dose to 50%
	Third	Discontinue treatment
In the event of Grade 3-4 non-neutropenic haematological or non-haematological toxicity, Grade 3 nausea or Grade 3-4 vomiting which does not recover to ≤ Grade 1 within 3 weeks	First	Discontinue treatment

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Anaphylaxis, hypersensitivity
Febrile neutropenia
Pneumonia

- **Frequently occurring side effects**

Diarrhoea
Nausea, vomiting
Neutropenia
Fatigue
Alopecia
Anaemia
Constipation
Decreased appetite
Cough
Abdominal pain
Urinary tract infections
Lymphopenia
Hypokalaemia
Hypomagnesaemia
Hyperglycaemia
Headache
Dizziness
Rash, pruritis

Pyrexia
Oedema
ALT increase

- **Other side effects**

Hypophosphataemia
Hypocalcaemia
Taste disturbance
Epistaxis
Stomatitis

Significant drug interactions – for full details consult product literature/ reference texts

UGT1A1 inhibitors e.g. propofol, ketoconazole, EGFR tyrosine kinase inhibitors: Concomitant administration of Trodelvy with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to a potential increase in exposure to SN-38 (small molecule moiety of Trodelvy). Use with caution and closely monitor for toxicity
UGT1A1 inducers e.g. carbamazepine, phenytoin, rifampicin, protease inhibitors: Exposure to SN-38 (small molecule moiety of Trodelvy) may be substantially reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Use with caution and monitor patients closely.

Additional comments

Patients with known reduced UGT1A1 activity should be closely monitored for adverse reactions. Gilbert syndrome is linked to UGT1A1*28 polymorphism so may be an indicator of increased risk of toxicity from the small molecule moiety of Trodelvy, SN38. In patients with Gilbert syndrome, consideration should be given to start treatment at a reduced dose (e.g. 75%) then increased on subsequent cycles if tolerated. Patients should be monitored closely for adverse reactions as they are likely to be at increased risk of severe neutropenia, diarrhoea and anaemia when treated with Trodelvy.

References

- Summary of Product Characteristics Trodelvy (Gilead) accessed 11th August 2022 via www.medicines.org.uk
- National Institute for Health and Care Excellence (TA819) accessed 17th August 2022 via www.nice.org.uk
- Bardia, A. *et al*. Sacituzumab govitecan in metastatic triple-negative breast cancer. N Engl J Med 2021;384:1529-1541

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