Chemotherapy Protocol

Breast Cancer

SACITUZUMAB GOVITECAN

Regimen

- Breast – Sacituzumab Govitecan

Indication

- The patient has a histologically or cytologically - confirmed diagnosis of breast cancer
- The patient has unresectable locally advanced or metastatic breast cancer
- The patient's breast cancer has had receptor analysis performed and this is negatived for the following: HER2 receptor, oestrogen receptor and progesterone receptor (i.e. triple negative disease)
- The patient has had 2 or more prior lines of systemic therapy specifically for the unresectable locally advanced or metastatic breast cancer indication or the patient has only had 1 line of systemic therapy specifically for the unresectable locally advanced or metastatic breast cancer indication and has also previously received adjuvant or neoadjuvant systemic therapy.
- The patient's breast cancer has been tested for PD-L1 expression and if positive and according the NICE recommendations, either the patient has been treated with first line atezolizumab or pembrolizumab or the patient was technically eligible for 1st line atezolizumab or pembrolizumab but use of immunotherapy was contraindicated.
- The patient has been previously been treated with taxane chemotherapy in the adjuvant, neoadjuvant or advanced disease setting unless the patient has a clear and documented contraindication to chemotherapy with a taxane.
- The patient has had no prior treatment with Sacituzumab Govitecan for locally advanced or metastatic disease unless this was received for this indication via the Gilead early access scheme and all other treatment criteria are fulfilled.
- The patient will continue with treatment with Sacituzumab Govitecan until disease progression or unacceptable toxicity or withdrawal of patient consent, whichever occurs first.
- The patient has an ECOG performance status of 0 or 1
- The patient has no symptomatically active brain metastases or leptomeningeal metastases.
- The prescriber is aware that Sacituzumab Govitecan can cause the following:
    - Can cause severe diarrhoea and life-threatening neutropenia
    - Patients known to be homozygous for uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1) 28 allele are at increased risk of toxicity.
    - Sacituzumab Govitecan has drug interactions with UGT1A1 inhibitors and inducers as outlined in the summary of product characteristics.

Toxicity

Drug	Adverse Effect
Sacituzumab Govitecan	Diarrhoea, nausea, vomiting, neutropenia, fatigue, anaemia, alopecia, constipation, decreased appetite, cough, abdominal pain, pneumonia, hypersensitivity

The adverse effects listed are not exhaustive. Please refer to the relevant summary of product characteristics for further details.

Monitoring

- FBC prior to day 1 and 8 of the cycle
- U&E, LFTs and magnesium prior to day 1 of each cycle.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L).

Proceed on day 1 of the cycle if neutrophils are ≥1.5x10^9/L and platelets are ≥100x10^9/L. If these criteria are not met delay cycle until count recovery.

Proceed on day 8 of the cycle if neutrophils are ≥1.0x10^9/L and platelets are ≥100x10^9/L. On day 8 of the cycle if blood results do not meet the above criteria, the patient will miss that dose and proceed to the next cycle.

Adverse Reaction	Occurrence	Dosage Modification
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

Hepatic Impairment

No adjustment to the starting dose is required when administering Sacituzumab Govitecan to patients with mild hepatic impairment.

The safety of Sacituzumab Govitecan in patients with moderate or severe hepatic impairment has not been established. Sacituzumab Govitecan has not been studied in patients with any of the following:

- Serum bilirubin > 1.5xULN
- AST or ALT >3xULN in patients without liver metastases
- AST or ALT >5xULN in patients with metastases

The use of Sacituzumab Govitecan in these patients is not recommended.

Renal Impairment

No adjustment to the starting dose is required in patients with mild renal impairment. Sacituzumab Govitecan has not been studied in patients with moderate renal impairment, severe renal impairment or end stage renal impairment.

Other toxicities

Grade 4 non-haematological toxicity which recovers to ≤ grade 1 within 3 weeks OR Any 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 >48hours despite optimal medical management OR At time of scheduled treatment, grade 3-4 non-neutropenic hematologic or non-hematologic toxicity which delays dose by 2 or 3 weeks for recovery to ≤ grade 1	First occurrence	25% dose reduction
	Second occurrence	50% dose reduction
	Third occurrence	Discontinue treatment
In the event of grade 3-4 non-neutropenic hematologic or non-	First occurrence	Discontinue treatment

hematologic toxicity, grade 3 nausea or grade 3-4 vomiting, which does not recover to ≤ grade 1 within 3 weeks		

Diarrhoea

Sacituzumab Govitecan can cause severe diarrhoea. Sacituzumab Govitecan should not be administered in case of Grade 3-4 diarrhoea at the time of scheduled treatment and treatment should only be continued when resolved to ≤ Grade 1.

Patients should be advised of the risk of diarrhoea and be closely monitored. Instruct patients to immediately contact their healthcare provider if they experience diarrhoea for the first-time during treatment. Instruct patients to immediately contact their healthcare provider if they experience melena, haematochezia, dehydration, an inability to tolerate oral fluids or an inability to manage diarrhoea within 24 hours.

At the onset of diarrhoea, and if no infectious cause can be identified, promptly initiate loperamide 4 mg initially followed by 2 mg with every episode of diarrhoea up to a maximum of 16 mg 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 employed as clinically indicated.

Instruct patients to immediately contact their healthcare provider if they experience melena, haematochezia, dehydration, an inability to tolerate oral fluids or an inability to manage diarrhoea within 24 hours.

Patients who exhibit an excessive cholinergic response to treatment with Sacituzumab Govitecan (e.g. abdominal cramping, diarrhoea, salivation, etc.) can receive appropriate premedication (e.g. atropine) for subsequent treatments.

Increased risk of adverse reactions in patients with reduced UGT1A1 activity

Individuals who are homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk of severe neutropenia, severe diarrhoea, febrile neutropenia, and anaemia and may be at increased risk for other adverse reactions following initiation of Sacituzumab Govitecan treatment. Patients with known reduced UGT1A1 activity should be closely monitored for adverse reactions. Withhold or permanently discontinue Sacituzumab Govitecan 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 activity.

Regimen

21 day cycle until disease progression or intolerance (6 cycles will be set in ARIA)

Drug	Dose	Days	Administration
Sacituzumab govitecan	10mg/kg	1 and 8	Intravenous infusion in 500ml Sodium Chloride 0.9% over 180 for the first infusion. If this is well tolerated subsequent infusions may be given over 60-120 minutes.

Dose Information

- For any patients over 170kg the dose will need to be divided into two separate infusions.

- Sacituzumab govitecan will be dose banded in accordance with the national dose bands (Sacituzumab govitecan 10mg/ml)

Administration Information

- 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.

- The first infusion should be administered over 180 minutes (3 hours). Subsequent infusions should be administered over a period of 1 to 2 hours (60-120 minutes) if prior infusions were tolerated.

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

- Sacituzumab govitecan can cause severe and life-threatening hypersensitivity. Other hypersensitivity events observed during and within 24 hours following the infusion included dyspnoea; rash; pruritus; hypotension; wheezing; oedema including facial and tongue; urticaria; and bronchospasm. Inform patients of the risk of serious infusion reactions and anaphylaxis. Instruct patients to immediately contact their healthcare provider if they experience these signs and symptoms. Medication to treat life-threatening hypersensitivity, as well as emergency equipment, should be available for immediate use.

Additional Therapy

- Antiemetics

  Premedication 30 minutes prior to Sacituzumab govitecan

  - Aprepitant 125mg oral
  - Ondansetron 8mg oral or intravenous

  As take home medication

  - Metoclopramide 10mg three times a day when required oral
  - Dexamethasone 4mg daily for 3 days oral
  - Ondansetron 8mg twice a day for 3 days oral
  - Aprepitant 80mg once a day for 2 days

- Loperamide 4mg oral after the first loose stool, then 2mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours)

- Premedication 30 minutes prior to Sacituzumab govitecan to reduce the risk of hypersensitivity reactions:
    - Chlorphenamine 10mg intravenous
    - Dexamethasone 8mg oral or intravenous
    - H_2 antagonist according to local formulary choice and availability
    - Paracetamol 1000mg oral

Additional Information

- There are many drug interactions associated with Sacituzumab govitecan. Always check for drug interactions.

References

1. Gilead Sciences Ltd. Trodelvy 180mg powder for concentrate for solution for infusion summary of product characteristics. Available from http://www.medicines.org.uk/emc/product/12880. Last updated 1/7/2022. Accessed 24/11/2022.
2. NEJM 2021; 384:1529-1541 Bardia et al, Sacituzumab govitecan in metastatic triple negative breast cancer

REGIMEN SUMMARY

Sacituzumab Govitecan

Day 1

1. Chlorphenamine 10mg intravenous
Administration Instructions:
Administer 30 minutes prior to SACT

2. Dexamethasone 8mg Oral
Administration Instructions:
Administer 30 minutes prior to SACT. This may be given as dexamethasone 8mg IV stat or equivalent dose as required.

3. Paracetamol 1000mg Oral
Administration Instructions:
Administer 30 minutes prior to SACT. Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses.

4. H2 antagonist according to formulary choice and availability
Administration Instructions:
Administer according to local formulary choice and availability one of the following 30 minutes prior to SACT:
   a. Ranitidine 50mg intravenous once only
   b. Famotidine 20mg oral once only
   c. Nizatidine 150mg oral once only
   d. Ranitidine 150mg oral once only

5. Aprepitant 125mg oral
Administration instructions:
Administer 30 minutes prior to SACT

6. Ondansetron 8mg oral
Administration instructions:
Administer 30 minutes prior to treatment. This may be given as ondansetron 8mg IV stat if required.

7. Sacituzumab Govitecan 10mg/kg in 250ml Sodium Chloride 0.9% over 180 minutes
Administration instructions:
The first infusion of Sacituzumab Govitecan must be administered over 180 minutes. If this is well tolerated administer subsequent infusions over 60 to 120 minutes.

Patients should be observed for 30 minutes after infusion.

Take home medicines

8. Aprepitant 80mg daily for 2 days
Administration instructions:
Starting on day 2 of the cycle

6. Dexamethasone 4mg daily for 3 days oral
Administration instructions:
Take with or after food, starting on day 2 of the cycle.

7. Metoclopramide 10mg three times a day when required oral
Administration instructions:
When required for the relief of nausea. Please supply 10 days or an original pack as appropriate.

8. Loperamide 4mg oral after the first loose stool, then 2mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours)

Day 8

1. Chlorphenamine 10mg intravenous
Administration Instructions:
Administer 30 minutes prior to SACT

2. Dexamethasone 8mg Oral
Administration Instructions:
Administer 30 minutes prior to SACT. This may be given as dexamethasone 8mg IV stat or equivalent dose as required.

3. Paracetamol 1000mg Oral
Administration Instructions:
Administer 30 minutes prior to SACT. Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses.

4. H2 antagonist according to formulary choice and availability
Administration Instructions:
Administer according to local formulary choice and availability one of the following 30 minutes prior to SACT:

a. Ranitidine 50mg intravenous once only
b. Famotidine 20mg oral once only
c. Nizatidine 150mg oral once only
d. Ranitidine 150mg oral once only

5. Aprepitant 125mg oral
Administration instructions:
Administer 30 minutes prior to SACT

6. Ondansetron 8mg oral
Administration instructions:
Administer 30 minutes prior to treatment. This may be given as ondansetron 8mg IV stat if required.

7. Sacituzumab Govitecan 10mg/kg in 250ml Sodium Chloride 0.9% over 180 minutes
Administration instructions:
The first infusion of Sacituzumab govitecan must be administered over 180 minutes. If this is well tolerated administer subsequent infusions over 60 to 120 minutes.

Patients should be observed for 30 minutes after infusion.

Take home medicines

8. Aprepitant 80mg daily for 2 days
Administration instructions:
Starting on day 9 of the cycle

6. Dexamethasone 4mg daily for 3 days oral
Administration instructions:
Take with or after food, starting on day 9 of the cycle.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	November 2022	None	Alexandra Pritchard Pharmacist	Dr Jenny Bradbury Consultant Oncologist
2	May 2024	Sacituzumab volume changed from 500ml to 250ml	Stuart Martin	N/A

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.