PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

SACITUZUMAB GOVITECEN
Metastatic Triple Negative Breast Cancer (TNBC)

PROTOCOL REF: MPHASGBC
(Version No.: 1.1)

Approved for use in:

- Unresectable locally advanced or metastatic triple negative breast cancer in patients who have received two or more prior lines of treatment, with at least one given in the palliative setting.
- NOTE: one of these prior lines of treatment CAN be in the neoadjuvant / adjuvant setting.
- PS 0 or 1

****BLUETEQ REQUIRED****

Dosage:

Drug	Dose	Route	Frequency
Sacituzumab govitecan	**10mg/kg**	IV infusion	Day 1 and 8 of a 21 day cycle

Treatment is given until disease progression or unacceptable toxicity

Administration:

First infusion is to be given over 3 hours, followed by **observation period of at least 30 minutes** after completion of the infusion to monitor for signs of infusion related reactions.

Subsequent infusions can be reduced to 1 to 2 hours if tolerated, with 30 minute observation after completion of the infusion.

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

Emetogenic risk:

Moderately emetogenic.

Supportive treatments:

Dexamethasone 12mg orally, 30 minutes prior to chemotherapy

Ondansetron 16mg orally, 30 minutes prior to chemotherapy

Dexamethasone 4mg orally twice daily for 3 days

Metoclopramide 10mg tablets, to be taken up to three times a day as required for nausea and vomiting for maximum 5 consecutive days

Loperamide 4mg orally after initial diarrhoea, followed by 2mg after each episode up to maximum of 16mg in 24 hours

Filgrastim injections – >70kg 480micrograms daily for 5 days from day 9

< 70kg 300 micrograms daily for 5 days from day 9

Premedication is required to reduce risk of infusion reactions: famotidine 40mg orally, paracetamol 1000mg orally, chlorphenamine 10mg IV

Extravasation risk:

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Dosing in renal and hepatic impairment:

Renal	No adjustment needed for mild renal impairment. Not studied in patients with moderate or severe impairment and therefore not recommended Baseline creatinine clearance needs to be above 60mL/min.

Hepatic	No adjustment required in mild hepatic impairment. It is not recommended in patients with bilirubin > 1.5 times ULN or AST/ALT above 3 times ULN in patients without liver metastases. In patients with liver metastases the limit is AST/ALT 5 times ULN

Interactions:

Concomitant administration with inhibitors of UGT1A1 may increase the incidence of adverse reactions e.g. propofol, ketoconazole, EGFR tyrosine kinase inhibitors, and patients should be closely monitored.

Exposure may be substantially reduced in patients concomitantly receiving UGT1A1 enzyme inducers e.g. carbamazepine, phenytoin, rifampicin, protease inhibitors, and patients should be closely monitored.

Please refer to SPC for further details:
https://www.medicines.org.uk/emc/product/12880/smpc#gref

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	Famotidine	40mg	PO	60 minutes before chemotherapy
	Dexamethasone	12mg	PO	30 minutes before chemotherapy
	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Chlorphenamine	10mg	IV	30 minutes before chemotherapy
	Sacituzumab govitecan	**10mg/kg**	**IV**	Sodium Chloride 0.9% 500mL over 60 minutes*
8	Famotidine	40mg	PO	60 minutes before chemotherapy
	Dexamethasone	12mg	PO	30 minutes before chemotherapy
	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Chlorphenamine	10mg	IV	30 minutes before chemotherapy
	Sacituzumab govitecan	**10mg/kg**	**IV**	Sodium Chloride 0.9% 500mL over 60 minutes
9 to 13	Filgrastim injections	300 or 480 micrograms	S/C	Daily for 5 days starting on day 9 of cycle

*First dose to be administered over 3 hours, if well tolerated then dose 2 can be given over 2 hours and then subsequently over 60 minutes

Filgrastim dose:

For patients under 70kg: 300 micrograms subcutaneous injection daily

For patients 70kg and above: 480 micrograms subcutaneous injection daily

Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, fatigue

Alopecia occurred in almost half of patients in the clinical trial.

Sacituzumab Govitecan	
Neutropenia	See dose adjustment section However note that on day 1 neutrophil count is required to be 1.5 x 10^9/L or above before proceeding with treatment
Diarrhoea	Hold treatment until diarrhoea has resolved to grade 1 Loperamide should be initiated at the first episode of diarrhoea If persists beyond 24 hours then advise patient to contact triage line For patients with excessive cholinergic response (e.g. abdominal cramping, diarrhoea, salivation etc) then atropine can be added to future cycles. Important to remember to assess for infectious causes.
Hypersensitivity	Anaphylactic reactions have occurred in the clinical trials. Other events noted within 24 hours of the infusion include dyspnoea, rash, pruritis, hypotension, wheezing, facial/tongue oedema, urticaria and bronchospasm

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 1 D8	Cycle 2	Cycle 2 D8	Cycle 3	Cycle 3 D8	Ongoing
Informed Consent	X							
Clinical Assessment	X					X		As clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFTs & Magnesium	X	X	X	X	X	X	X	Every Cycle
CrCl (Cockcroft and Gault)	X	X		X		X		Every cycle
CT scan	X					X		Every 3 months or as clinically indicated
ECG								If clinically indicated
Full observations	X							Repeat if clinically indicated
Blood glucose								If clinically indicated
Weight recorded	X	X	X	X	X	X	X	Every cycle
Height	X							

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

ANC ≥ 1.5 x 10^9/L	Plt ≥ 100 x 10^9/L

Delay 1 week on day 1 if-

ANC ≤ 1.4 x 10^9/L	Plt ≤ 99 x 10^9/L

Proceed on day 8 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Omit on day 8 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

On day 8 of the cycle if blood results do not meet the above levels the patient will miss that dose and proceed to the next cycle.

Neutropenia	Occurrence	Dose Modification
Grade 4 lasting beyond 7 days **Or** Grade 3 febrile neutropenia **Or** grade 3 to 4 neutropenia that requires delay of next cycle by more than 2 weeks	First	25% dose reduction and give filgrastim until counts recover - review filgrastim days and duration
	Second	50% dose reduction
	Third	Discontinue treatment
Grade 3 or 4 neutropenia that delays next cycle beyond 3 weeks to allow recovery to grade 1	First	Discontinue treatment

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

Non-Haematological Toxicity	Occurrence	Dose Modification
Grade 4 which recovers to grade 1 within 3 weeks **Or** any grade 3 to 4 nausea, vomiting, diarrhea that is not controlled with medication **Or** other grade 3 to 4 toxicity persisting for more than 48 hours despite optimal medical management **Or** any grade 3 or 4 toxicity which delays next dose of treatment by more than 2 weeks with delayed recovery to grade 1	First	25% dose reduction
	Second	50% dose reduction
	Third	Discontinue treatment
Grade 3 to 4 anaemia/ thrombocytopenia **or** non-haematological toxicity, grade 3 nausea **or** grade 3 to 4 vomiting which does not recover to grade 1 within 3 weeks	First	Discontinue treatment

References:

1. Trodelvy 180 mg powder for concentrate for Solution for Infusion SmPC, Gilead Sciences Ltd Limited accessed via the electronic medicines compendium athttps://www.medicines.org.uk/emc (Last updated 7th July 2022).

2NEJM 2021; 384:1529-1541 Bardia et al, Sacituzumab govitecan in metastatic triple negative breast cancer

Circulation/Dissemination

Date added into Q-Pulse	13th October 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
February 2022	1.0	**Helen Flint** **Consultant Pharmacist**	New Regimen Protocol V1.0
May 2023	1.1	**Gabriella Langton** **Advanced Pharmacist**	**Updated spelling errors, added additional comment to help with indication and addition of filgrastim as prophylaxis**