SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Paclitaxel Weekly Neoadjuvant Breast Cancer

PROTOCOL REF: MPHAPWNBC
(Version No.: 1.1)

Approved for use in:

Neoadjuvant breast cancer patients who cannot tolerate standard neoadjuvant treatment at consultant discretion.

Dosage:

Drug	Dose	Route	Frequency	Duration
Paclitaxel	**80mg/m^2**	IV infusion	Every 7 days	12 weeks

Administration:

- Paclitaxel must be administered using a non-PVC giving set with a 0.22 micron filter.
- Paclitaxel in solution may show haziness which is attributed to the formulation of paclitaxel.
- Excessive shaking, agitation, or vibration of paclitaxel may induce precipitation and should be avoided

Review IV access, PICC line insertion is recommended

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

Metoclopramide 10mg tablets, three times a day when required

Ondansetron 8mg orally pretreatment can be added in patients with nausea

Loperamide 4mg stat and then 2mg after each loose stool can be added if diarrhea is a side effect

Extravasation risk:

Paclitaxel – vesicant

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

Dosing in renal and hepatic impairment:

If adjuvant zoledronate treatment is given in combination and renal function has dropped below 60ml/min then do not administer the zoledronate until the patients clinical team have reviewed the results and confirmed it is appropriate to continue.

Renal	No dose adjustments necessary

	Bilirubin and Transaminases	**Percentage dose**
Hepatic	Transaminases <10 x ULN and bilirubin ≤1.25 x ULN	Dose at 100%
	Transaminases <10 x ULN and bilirubin >1.25 – 2 x ULN	80%
	Transaminases <10 x ULN and bilirubin 2-5 x ULN	50%
	Transaminase ≥10 x ULN or bilirubin >5 x ULN	Contraindicated

Patients with severe hepatic impairment must not be treated with paclitaxel.

Patients with hepatic impairment may be at increased risk of toxicity, particularly grade III-IV myelosuppression. There is no evidence that the toxicity of paclitaxel is increased when given as a 3-hour infusion to patients with mildly abnormal liver function. No data are available for patients with severe baseline cholestasis.
Patients should be monitored closely for the development of profound myelosuppression.

Interactions:

Antiepileptics (CYP 3A4 inducers)

Phenytoin, carbamezapine and phenobarbital increase the clearance of paclitaxel and increase its maximum tolerated dose.

Ciclosporin

Levels of paclitaxel increased after oral administration of ciclosporin.

Fluconazole/Ketoconazole (CYP3A4 inhibitors)
Paclitaxel levels may be increased

Quinine and Verpamil
Paclitaxel levels possibly increased.

For more detailed interactions please refer to the SPC
https://www.medicines.org.uk/emc/product/3891/smpc#gref

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
	Dexamethasone	**6.6**	**IV**	30 mins before chemotherapy *Reduced to 3.3mg after cycle 1
	Chlorphenamine	**10mg**	**IV**	30 mins before chemotherapy
	PACLITAXEL	**80mg/m^2**	**IV infusion**	Sodium Chloride 0.9% 250mL over 60 minutes

- Premedication treatment of chlorphenamine and dexamethasone are given prior to paclitaxel to reduce the risk of hypersensitivity. Paclitaxel reactions commonly occur within the first few minutes of starting the infusion most likely with the first two cycles. See hypersensitivity policy for more information

Main toxicities:

Paclitaxel

Haematological	Neutropenia, anaemia, thrombocytopenia,
Cardiac and Vascular disorders	Risk of bradycardia and hypotension is common
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis
Musculoskeletal	Arthralgia, myalgia
Nervous system	Paclitaxel: peripheral neuropathy is very common
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.
Skin and subcutaneous tissue disorders	Alopecia Allergic skin rash frequently associated with pruritus
General disorders and administration site conditions	Malaise, fever, chills, urticaria, flu-like syndrome, rash, pruritus. Injection site reactions (including localised oedema, pain, erythema, induration, on occasion extravasation can result in cellulitis, skin fibrosis and skin necrosis)

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	X				
Clinical Assessment All patients on SACT should have **at least one F2F review during treatment.**	X			X	At week 12 or earlier if clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X	X	Every cycle
FBC	X	X	X	X	Every cycle
U&E & LFTs	X	X	X	X	Every Cycle
CT scan (if indicated by clinical stage of breast cancer)					
USS breast +/- MRI breast to be used pre-and post-treatment as clinically indicated/ as per MDT practice	X				After 12 weeks if clinically indicated
ECG					If clinically indicated
Respiratory Rate					If clinically indicated
Weight recorded	X	X	X	X	Every cycle
Height recorded	X				

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L **

**** If platelets are between 80 -100 x 10^9/L discuss with named consultant if can proceed**

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

Peripheral Neuropathy

Paclitaxel
CTCAE grade 2 peripheral neuropathy: withhold paclitaxel until the neuropathy recovers to grade 1 then dose reduce to 75% of the original dose. Where the peripheral neuropathy is ≥grade 3 omit further paclitaxel.

Grading and Management of Toxicity

Toxicities should be graded according to the CTCAE v4.0 criteria. Following assessment treatment should be withheld for any toxicity until resolved to grade 0/1. For dose modification, follow the general guidance below and discuss with treating clinician.

	Grade 2	Grade 3	Grade 4
1st appearance	Interrupt treatment until resolved to ≤ grade 1, then continue at 100% of original dose with prophylaxis where possible	Interrupt treatment until resolved to grade ≤ 1, then continue at 80% of original dose	Discontinue treatment

2nd appearance	Interrupt treatment until resolved to grade ≤ 1, then continue at 80% of original dose	Interrupt treatment until resolved to grade ≤ 1, then continue at 50% of original dose	
3rd appearance	Interrupt treatment until resolved to grade ≤ 1, then continue at 50% of original dose	Discontinue treatment	
4th appearance	Discontinue treatment		

References:

1. https://www.medicines.org.uk/emc
2. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.
3. BNF available via: https://bnf.nice.org.uk/

Circulation/Dissemination

Date added into Q-Pulse	9th November 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
	1	**Gabriella Langton** **Breast SRG Pharmacist**	New format, added line regarding lower platelets
	1.1	**Gabriella Langton** **Breast SRG Pharmacist**	**Removal of famotidine as per DTC approval, addition of AZS renal information, updated scan information and F2F review reminder**