SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

PALBOCICLIB

Locally advanced or metastatic breast cancer

PROTOCOL REF: MPHAPALBR
(Version No. 1.2)

Approved for use in:

Locally advanced or metastatic breast cancer, ER positive (HER2 negative) in combination with an aromatase inhibitor in women previously untreated ((i.e. no previous chemotherapy or hormone treatment for advanced disease)

In pre or peri menopausal women, goserelin administration will also be required.

Blueteq required - see criteria for full details on eligibility

Dosage:

Drug	Dose	Route	Frequency	
Palbociclib	125mg	Oral	Once daily for 21 days, repeated every 28 days	Until disease progression or unacceptable toxicity

Administration + Counselling Points:

Capsules should be taken at approximately the same time each day.
It can be taken with or without food (but not be taken with grapefruit or grapefruit juice), and swallowed whole. No capsule should be ingested if broken, cracked or not intact.

If relevant, ensure appropriate contraceptive measures are discussed.

Note: the capsules contain lactose.

Emetogenic risk:

Low emetogenicity.

Supportive treatments:

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

Extravasation risk:

Not applicable

Dosing in renal and hepatic impairment:

Renal	Palbociclib	No dose adjustments needed if CrCl ≥ 15ml/min. There is insufficient data for patients receiving dialysis

Hepatic	Palbociclib	No dose adjustments necessary for mild – moderate impairment. Reduction to 75mg daily is recommended for patients with severe hepatic impairment (Child-Pugh class C).
		*Assessing a Child-Pugh score (for an adult patient)

Parameters	1 point	2 points	3 points
Total bilirubin (µmol/L)	< 34	34–50	> 50
Serum albumin (g/L)	> 35	28–35	< 28
Prothrombin time, prolongation (s) *Or* INR	< 4 < 1.7	4–6 1.7-2.3	> 6 >2.3

Ascites	None	Mild to Moderate (diuretic responsive)	Severe (diuretic refractory)
Hepatic encephalopathy	None	Grade I–II (or suppressed with medication)	Grade III–IV (or refractory to medication)

Child-Pugh Class
A (5-6 points)
B (7-9 points)
C (10 or more points)

INR: International Normalised Ratio.

Please note: assessment of Child-Pugh Class is to help guide clinical teams when prescribing and pharmacists when screening.

Interactions:

Please refer to the SPC for a detailed list of interactions:
https://www.medicines.org.uk/emc/product/11962

Palbociclib is metabolized by the cytochrome CYP3A4 pathway

INDUCERS (lowers palbociclib levels): Carbamazepine, phenobarbital, phenytoin, dexamethasone, rifabutin, rifampicin, St John's Wort, troglitazone, pioglitazone

INHIBITORS (increases palbociclib levels): Indinavir, nelfinavir, ritonavir, clarithromycin, erythromycin, itraconazole, ketoconazole, nefazodone, grapefruit juice, verapamil, diltiazem, cimetidine, amiodarone, fluvoxamine, mibefradil

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Palbociclib**	**125mg**	**PO**	Once daily for 21 days of 28 day cycle

Main toxicities:

Please refer to the SPC for a detailed list: https://www.medicines.org.uk/emc/product/11962

and fulvestrant: https://www.medicines.org.uk/emc/product/12022/smpc

Palbociclib	
Blood and lymphatic system	Neutropenia, leukopenia, anaemia, thrombocytopenia, febrile neutropenia
Metabolism and nutrition disorders	Decreased appetite
Eye disorders	Blurred vision, lacrimation increased, dry eye
Respiratory	Epistaxis, ILD/pneumonitis
Gastrointestinal disorders	Stomatitis, nausea, vomiting, diarrhea
Skin disorders	Rash, alopecia, dry skin
General disorders	Fatigue, pyrexia, taste disorders

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Informed Consent	X					
Clinical Assessment	X			X		As 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 & Magnesium	X		X	X	X	Every Cycle
CrCl (Cockcroft and Gault)	X	X	X	X		Every cycle
CT scan	X			X		Every 3 months for the first year and then as clinically indicated, cycle 4 can go ahead irrespective of CT date
Weight Recorded	X	X	X	X	X	Every cycle
Height Recorded	X					

Dose Modifications and Toxicity Management:

Dose Level	Dose
Recommended dose	125mg once daily
First dose reduction	100mg once daily
Second dose reduction	75mg once daily

If 75mg once daily is not tolerated then treatment should be discontinued.

Haematological toxicity:

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 50 x 10^9/L

FBC should be monitored on day 14 of cycle 1 and cycle 2

CTC grade	Dose modifications
Grade 1 or 2 (ANC ≥ 1.0 x 10^9/L)	No dose adjustment is required
Uncomplicated Grade 3 (ANC 0.5 to 0.9 x 10^9/L) All other grade 3 haematological toxicities except lymphopenia (unless associated with clinical events, e.g., opportunistic infections).	**Day 1 of cycle:** Withhold, repeat complete blood count monitoring within 1 week. When recovered to Grade ≤2, start the next cycle at the same dose. **Day 14 of first 2 cycles:** Continue at current dose to complete cycle. Repeat complete blood count on Day 21. Consider dose reduction in cases of prolonged (>1 week) recovery from Grade 3 neutropenia or recurrent Grade 3 neutropenia in subsequent cycles
Grade 3 neutropenia associated with a documented infection and/or fever ≥ 38.5ºC	Withhold palbociclib until recovery to grade ≤2 Reduce by one dose level
All grade 4 haematological toxicities except lymphopenia (unless associated with clinical events, e.g., opportunistic infections).	Withhold palbociclib until recovery to grade ≤2 Reduce by one dose level

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:

CTC grade	Dose modifications
Grade 1 or 2	No dose adjustment is required
Grade ≥ 3	Withhold until symptoms resolved to grade 1 or grade 2 (if not considered a safety risk for the patient) Resume at the next lower dose.
ILD/Pneumonitis suspected e.g shortness of breath or dry cough	Hold treatment and contact consultant for advice

References:

1. SmPC for Palbociclib, last updated April 2023 https://www.medicines.org.uk/emc/product/11962
2. Fulvestrant**:** https://www.medicines.org.uk/emc/product/12022/smpc
3. 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.
4. BNF available via: https://bnf.nice.org.uk/
5. Overall survival with palbociclib and fulvestrant in advanced breast cancer. NEJM 2018 379:1926-1936.Turner et al

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
	1.2	**Gabriella Langton**	Updated to new protocol format, updated renal and hepatic information from SPC