Systemic Anti Cancer Treatment Protocol

PALBOCICLIB

PROTOCOL REF: MPHAPALBR
(Version No: 1.0)

Approved for use in:

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

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

Dosage:

Drug	Dosage	Route	Frequency
Palbociclib	125mg	Oral	Once daily for 21 days of each 28 day cycle

Extravasation risk:

Not applicable

Administration:

Palbociclib capsules should be taken at approximately the same time each day.
It should be taken with food, and swallowed whole.

Note: the capsules contain lactose.

Drug Interactions

Palbociclib is metabolized by the cytochrome CYP3A4 pathway and therefore drugs that induce or inhibit this enzyme should be avoided where possible.

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

Main Toxicities:

Neutropenia, leukopenia, anaemia, thrombocytopenia, infection, fatigue, nausea, stomatitis, alopecia and diarrhoea.

Febrile neutropenia was reported in 1.8% (Finn et al,.2016).

Thromboembolic events occurred in < 2% of patients (Paloma-3; Turner et al., 2015)

Investigations and Treatment Plan:

	Pre	C1	C1D14	C2	C2D14	C3	Ongoing
Medical Assessment	X	X				X	Every 3 months
Nursing Assessment		X	X	X	X	X	Every cycle
FBC	X		X	X	X	X	Every cycle
U&E & LFT	X			X		X	Every cycle
CT scan	X					X	As clinically indicated
Informed Consent	X						
PS recorded	X	X	X	X	X	X	
Toxicities documented	X	X	X	X	X	X	
Weight recorded	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

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

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

Haematological toxicity

Proceed on day 1 of each cycle if:-

ANC ≥ 1. x 10^9/L	Platelets ≥ 50 x 10^9/L

Please note the criteria above are based on SPC however entry criteria prior to cycle 1 for PALOMA-2 were ANC ≥ 1.5 x 10^9/L & Platelets > 100 x 10^9/L. For patients that present with immunosuppression prior to commencing any therapy these should be taken into account.

FBC should be monitored on day 14 of cycle 1 and cycle 2 – see table below

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 ≥ 38.5^{o}C	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

Non-haematological toxicities

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.

Hepatic impairment

No dose adjustments are required in mild impairment

Insufficient data available for patients with moderate/severe (i.e. bilirubin > 1.5 times ULN)

Renal impairment

No dose adjustments are required for mild to moderate impairment (CrCl > 30mL/min)

Insufficient data for patients with severe impairment or receiving dialysis.

From APRIL 2017 until 30 SEPTEMBER 2017 palbociclib is available through a free of charge access scheme for registered patients – documentation must be completed and forwarded to pharmacy

References:

SmPC for IBRANCE

Finn et al. Palbociclib and letrozole in advanced breast cancer NEJM 2016 375:1925-1936

Turner et al., 2015 Palbociclib in Hormone-Receptor–Positive Advanced Breast Cancer. NEJM 2016 373: 209-19.