Systemic Anti Cancer Treatment Protocol

ABEMACICLIB and FULVESTRANT

PROTOCOL REF: MPHAABFUBR
(Version No: 1.0)

Approved for use in:

Locally advanced or metastatic breast cancer, ER positive (HER2 negative):

- Following disease progression on adjuvant/neoadjuvant endocrine therapy for early breast cancer or within 12 months of completing adjuvant endocrine therapy
- Following disease progression on 1st line endocrine therapy for metastatic/locally advanced breast cancer with no subsequent endocrine therapy (i.e. second line treatment), with no previous CDK4/6 inhibitor treatment

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

See blueteq criteria for full details on eligibility

Dosage:

Drug	Dosage	Route	Frequency
Abemaciclib tablets	150mg	Oral	Twice daily continuously
Fulvestrant injection	500mg	IM	Cycle 1 on day 1, 15 and 28 Then every 28 days

Treatment continues until disease progression or unacceptable toxicity

Supportive medicines:

Loperamide 2mg when required after each loose stool

Extravasation risk:

Not applicable

Administration:

Abemaciclib tablets should be taken at approximately the same time each day, ideally 12 hours apart.
It can be taken with or without food, and swallowed whole.

Note: the tablets contain lactose.

Fulvestrant is administered as two consecutive 5mL injections by slow intramuscular injection (1 to 2 minutes per injection), one into each buttock.

Drug Interactions

Abemaciclib is metabolized by the cytochrome CYP3A4 pathway

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

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

Abemaciclib may also interact with medicines via the P-glycoprotein mechanism, in particular those medicines with narrow therapeutic index such as digoxin or dabigatran.

Main Toxicities:

Abemaciclib: Neutropenia, anaemia, thrombocytopenia, diarrhea, infection, fatigue, nausea, stomatitis, alopecia, thrombosis and raised transaminases.
Fulvestrant: injection site reactions, hot flushes, nausea, rash, joint pains

Investigations and Treatment Plan:

If relevant, ensure appropriate contraceptive measures are discussed.

	Pre	C1	C1D14	C2	C2D14	C3	Ongoing
Medical Assessment	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 (AST and ALT)	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	150mg twice daily
First dose reduction	100mg twice daily
Second dose reduction	50mg twice daily

If 50mg twice 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 ≥ 100 x 10^9/L

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

CTC grade	Dose modifications - abemaciclib
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. Or recurrent grade 3 neutropenia.	Withhold abemaciclib 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 abemaciclib until recovery to grade ≤2 Reduce by one dose level

Non-haematological toxicities

DIARRHOEA

CTC grade	Dose modifications - abemaciclib
Grade 1	No dose adjustment is required
Grade 2	If does not resolve within 24 horus to grade 1, suspend treatment until improved, then can resume on current dose.
Grade 2 persistent or recurring Grade ≥ 3	Withhold until symptoms resolved to grade 1 Resume at the next lower dose.

Other non-haematological toxicities

CTC grade	Dose modifications - abemaciclib
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 – ALT and AST

CTC grade	Dose modifications - abemaciclib
Grade 1 (less than 3 X ULN) Grade 2 (between 3 and 5 x ULN)	No dose adjustment is required
Grade 2 persistent or recurring Grade 3 (between 5 and 20 x ULN)	Stop abemaciclib until returned to grade 1 Resume at next lower dose For grade 3 also withhold fulvestrant until returned to grade 1
Grade 4 (above 20 x ULN)	Discontinue

Renal impairment

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

Insufficient data for patients with severe impairment or receiving dialysis.

References:

SmPC for Verzenios

MONARCH2