SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

ABEMACICLIB and AROMATASE INHIBITOR
Locally Advanced and Metastatic Breast Cancer

PROTOCOL REF: MPHAAAIBR
(Version No. 1.1)

Approved for use in:

Locally advanced or metastatic breast cancer, ER positive (HER2 negative) as **FIRST LINE** endocrine treatment.

*****************BLUETEQ REGISTRATION REQUIRED**************

Dosage:

Drug	Dose	Route	Frequency
Abemaciclib	**150mg**	Oral	28 day cycle until disease progression or unacceptable toxicity
Letrozole or alternative Aromatase Inhibitor	**See BNF for dosing of each**	Oral	Once Daily until disease progression or unacceptable toxicity

Aromatase inhibitor to be initiated at CCC, 1 month's supply given then further supply to be obtained from the GP.

Administration and Counselling Points:

- Abemaciclib is available as 50mg, 100mg and 150mg tablets.
- Abemaciclib tablets should be taken at approximately the same time each day, ideally 12 hours apart.
- The tablets can be taken with or without food and swallowed whole.
- Please note the tablets **contain lactose.**

- Abemaciclib should not be taken with grapefruit or grapefruit juice.
- If relevant, ensure appropriate contraceptive measures are discussed.

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

Loperamide 2mg: TWO capsules to be taken initially followed by ONE capsule after each loose stool (maximum daily dose 16mg), to be taken when required

Extravasation risk:

Not applicable

Dosing in renal and hepatic impairment:

Renal	Abemaciclib	No dose adjustments are required for mild to moderate impairment (CrCl ≥ 30mL/min) Insufficient data for patients with severe impairment or receiving dialysis

Hepatic	Abemaciclib	No dose adjustments are necessary in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment. In patients with severe (Child Pugh C) hepatic impairment, a decrease in dosing frequency to ONCE daily is recommended.

Child-Pugh Scoring			
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)

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.

For further information see individual SPCs located at: Home - electronic medicines compendium (emc)

Main toxicities:

Abemaciclib
Neutropenia, anaemia, thrombocytopenia, diarrhea, infection, fatigue, nausea, stomatitis, alopecia, thrombosis and raised transaminases.

For further information see individual SPCs located at: Home - electronic medicines compendium (emc)

Investigations and treatment plan:

Mid cycle blood test no longer required routinely with cycle 1 and cycle 2 as audit results have demonstrated these do not change the dosing plan
However for patients with history of neutropenia due to other conditions or medications can have day 14 checks if indicated

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	X				
Clinical Assessment	X			X	3 monthly and 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
CT scan	X				As clinically indicated, usually every 3 months for first year then extended interval
Weight recorded	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Abemaciclib:

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:

Administer Abemaciclib on day 1 of each cycle if:-

ANC ≥ 1.0 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 above

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. 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. Or recurrent grade 3 neutropenia.	Withhold abemaciclib until recovery to grade ≤2 Reduce by one dose level
All grade 4 haematological toxicities (ANC < 0.5 x 10^9/L) 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 toxicity:

DIARRHOEA

CTC grade	Dose modifications - abemaciclib
Grade 1	No dose adjustment is required
Grade 2	If does not resolve within 24 hours 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.

Hepatic impairment – ALT and AST

CTC grade	Dose modifications – abemaciclib and fulvestrant
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
Elevation in AST and/or ALT > 3 x ULN WITH total bilirubin > 2 x ULN, in the absence of cholestasis	Discontinue
Grade 4 (above 20 x ULN)	Discontinue

Interstitial lung disease (ILD)/pneumonitis

CTC grade	Management recommendations
Grade 1 or 2	No dose adjustment required.
Persistent or recurrent Grade 2 toxicity that does not resolve with maximal supportive measures within 7 days to baseline or Grade 1	Suspend dose until toxicity resolves to baseline or Grade 1. Resume at next lower dose.
Grade 3 or 4	Discontinue abemaciclib.

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.

References:

1. National Institute for Health and Care Excellence (Feb 2019). Abemaciclib with an aromatase inhibitor for treating hormone receptor-positve, HER2 – negative, locally advanced or metastatic breast cancer [TA 563].
2. Summary of Product Characteristics, Verzenios®, Abemaciclib, Eli Lilly, last updated May 2022, http://www.medicines.org.uk [accessed 23/02/23]
3. Goetz, Matthew P, Toi, Masakazu et al. MONARCH 3. Abemaciclib as initial therapy for advanced breast cancer. *J. Clin Oncol* 35: 3638-3646
4. 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.
5. BNF available via: https://bnf.nice.org.uk/

Circulation/Dissemination

Date added into Q-Pulse	28th April 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
March 2023	1.1	**Gabriella Langton**	Updated to new format