

Chemotherapy Protocol

Breast Cancer

Abemaciclib-Letrozole

Regimen

- Breast Cancer – Abemaciclib-Letrozole

Indication

- Abemaciclib in combination with an aromatase inhibitor is indicated for the treatment previously untreated, hormone receptor-positive, HER2- negative, locally advanced or metastatic breast cancer that is not amenable to curative treatment and where;
 - the patient has had no prior treatment with a CDK 4/6 inhibitor unless either palbociclib or ribociclib has had to be stopped within 6 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression or abemaciclib has been received as part of any compassionate use scheme and the patient meets all the other criteria set out here.
 - the patient is male or is female and either post-menopausal or if pre- or peri- menopausal has undergone ovarian ablation or suppression with LHRH agonist treatment
 - the patient has had no previous hormone therapy for locally advanced or metastatic disease i.e. is hormone therapy naïve for locally advanced/metastatic breast cancer. Previous hormone therapy with anastrozole or letrozole whether as adjuvant therapy or as neoadjuvant treatment is allowed as long as the patient has had a disease-free interval of 12 months or more since completing treatment with neoadjuvant or adjuvant anastrozole or letrozole.
 - that abemaciclib will only be given in combination with an aromatase inhibitor.
 - that treatment will continue until there is progressive disease or excessive toxicity or until the patient chooses to discontinue treatment, whichever is the sooner.
 - that treatment breaks of up to 6 weeks are allowed, but solely to allow toxicities to settle
 - an ECOG performance status of 0 or 1 or 2

Toxicity

Treatment breaks of up to 6 weeks are allowed but solely to allow toxicities to settle.

Drug	Adverse Effect
Abemaciclib	Infection, myelosuppression, peripheral neuropathy, fatigue, mucositis, anorexia, eye disorders, venous thromboembolism, diarrhoea, raised liver enzymes
Letrozole	Osteoporosis, headache, somnolence, hot flushes, alopecia, arthralgia, rash, vaginal dryness, asthenia, liver abnormalities, depression, insomnia

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFTs and U&Es at baseline and then every two weeks for the first eight weeks. (a four week supply may be dispensed on day 1 of each cycle even though monitoring may be every two weeks). The frequency of monitoring can then reduce to once every four weeks for a further eight weeks and then as indicated (patients should be assessed every 12 weeks as a minimum)

Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well. In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

Haematological

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L)

Prior to prescribing cycle 1 the following criteria must be met.

Criteria	Eligible Level
Neutrophils	Equal to or more than $1.5 \times 10^9/L$
Platelets	Equal to or more than $100 \times 10^9/L$

No dose reductions are required for letrozole due to myelosuppression. For abemaciclib, dose adjustments for haematological toxicity are described in the table below;

Abemaciclib Dose Adjustments	
Recommended dose	150 mg twice daily
First dose adjustment	100 mg twice daily
Second dose adjustment	50 mg twice daily

Doses of abemaciclib should be adjusted as follows for haematological toxicity.

Toxicity (NCI CTC)	Management Recommendations
Grade 1 or 2	No dose adjustment required.
Grade 3	Suspend dose until toxicity resolves to NCI grade 2 or less. Dose reduction is not required.
Grade 3, recurrent; or grade 4	Suspend dose until toxicity resolves to NCI grade 2 or less. Resume at next lower dose.
Patient requires administration of blood cell growth factors	Suspend abemaciclib dose for at least 48 hours after the last dose of blood cell growth factors was administered and until toxicity resolves to NCI grade 2 or less. Resume at next lower dose unless the dose was already reduced for the toxicity that led to the use of the growth factor.

Hepatic Impairment

No dose change for letrozole is recommended in patients with mild hepatic disease. Caution is advised in patients with moderate to severe hepatic impairment

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) should be monitored prior to the start of abemaciclib therapy, every two weeks for the first two months, monthly for the next two months, and as clinically indicated.

Toxicity (NCI CTC)	Management Recommendations (Abemaciclib)
Grade 1 or 2	No dose adjustment required.
Persistent or recurrent grade 2 or grade 3	Suspend dose until toxicity resolves to baseline or Grade 1. Resume at next lower dose.
Grade 4	Discontinue abemaciclib.

Renal Impairment

No dose change is recommended for letrozole in patients with mild or moderate renal impairment. In patients with severe renal impairment, administration of letrozole should be performed with caution

No dose adjustments for abemaciclib are necessary in patients with mild or moderate renal impairment. There are no data regarding abemaciclib administration in patients with severe renal impairment, end stage renal disease, or in patients on dialysis. Abemaciclib should be administered with caution in patients with severe renal impairment, with close monitoring for signs of toxicity.

Other

Abemaciclib

Diarrhoea

Treatment with antidiarrhoeal agents, such as loperamide, should be started at the first sign of loose stools.

Diarrhoea	Management Recommendations (Abemaciclib)
Grade 1	No dose adjustment required.
Grade 2	If toxicity does not resolve within 24 hours to Grade 1 or less, suspend dose until resolution. Dose reduction is not required.
Grade 2 that persists or recurs after resuming the same dose despite maximal supportive measures	Suspend dose until toxicity resolves to Grade 1 or less. Resume at next lower dose.
Grade 3 or 4 or requires hospitalisation	

Other toxicities should be managed as follows;

Toxicity (not haematology or diarrhoea or liver)	Management Recommendations (Abemaciclib)
Grade 1 or 2	No dose adjustment required.
Persistent or recurrent grade 2 toxicity that does not resolve with maximal supportive measures to baseline or Grade 1 within 7 days	Suspend dose until toxicity resolves to grade 1 or less. Resume at next lower dose.
Grade 3 or 4	

Regimen

28 day cycle until disease progression or intolerance (twelve cycles will be set in ARIA)

In pre – or perimenopausal women, the endocrine therapy should be combined with a LHRH agonist. This is not included in the regimen on ARIA.

Drug	Dose	Days	Route
Abemaciclib	150mg twice a day	Days 1-28 inclusive	Oral
Letrozole	2.5mg once a day	Days 1-28 inclusive	Oral

Dose Information

- Abemaciclib is available as 150mg, 100mg and 50mg film coated tablets
- Letrozole is available as 2.5mg tablets

Administration Information

- If the patient vomits or misses a dose of abemaciclib, an additional dose should not be taken that day. The next prescribed dose should be taken at the usual time

Supportive Treatments

- Loperamide 4mg after the first loose stool and 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to abemaciclib
- It must be made clear to all staff, including those in the community, that abemaciclib should only be prescribed under the supervision of a consultant oncologist
- Abemaciclib interacts with many other agents, especially those that affect CYP 3A4. Always check for drug interactions.
- In pre or perimenopausal women, the endocrine therapy should be combined with a LHRH agonist.
- Treatment breaks of up to 6 weeks are allowed but solely to allow toxicities to settle

References

1. National Institute of Health and Clinical Excellence. TA 563. Abemaciclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer. DOH:London

REGIMEN SUMMARY

Abemaciclib-Letrozole

Cycle One

Day One

1. Abemaciclib 150mg twice a day for 28 days oral
Administration Instructions
Oral SACT
2. Letrozole 2.5mg once a day for 28 days oral
3. Loperamide 4mg after the first loose stool and 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours
Administration Instructions
Take 4mg after the first loose stool and then 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours. Please supply one original pack size

Cycle Two Onwards

Day One

4. Abemaciclib 150mg twice a day for 28 days oral
Administration Instructions
Oral chemotherapy
5. Letrozole 2.5mg once a day for 28 days oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Dec 2023	Under Hepatic Impairment: Changed Anastrozole to Letrozole	Tom Hurst Pharmacy Technician	Donna Kimber Pharmacy Technician
1	Feb 2020	None	Donna Kimber Pharmacy Technician	Dr J Bradbury Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
 NHS Isle of Wight
 Portsmouth Hospitals NHS Trust
 Salisbury NHS Foundation Trust
 University Hospital Southampton NHS Foundation Trust
 Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.