Chemotherapy Protocol

BREAST CANCER

CAPECITABINE-LAPATINIB

This protocol may require funding

Regimen

- Breast Cancer – Capecitabine-Lapatinib

Indication

- Treatment of locally advanced or metastatic HER2 positive breast cancer where there has been an inadequate response to anthracycline, taxane and trastuzumab containing therapy

- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Capecitabine	Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain
Lapatinib	Cardiac failure, pneumonitis, diarrhoea, insomnia, headache, rash

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

Monitoring

Regimen

- FBC, U&E's and LFT's prior to each cycle

- Cardiac function must be assessed prior to starting lapatinib and twelve weekly thereafter unless there are signs of cardiac impairment where four to eight weekly may be more appropriate. If LVEF drops 10 ejection points from baseline and to below 50%, lapatinib should be suspended and a repeat LVEF assessment performed within 21 days

- Patients with complete or partial dihydropyrimidine dehydrogenase (DPD) deficiency are at increased risk of severe and fatal toxicity during treatment with capecitabine. All patients should be tested for DPD deficiency before initiation (cycle 1) to minimise the risk of these reactions.

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

Prior to prescribing cycle one the following treatment criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $100x10^9$/L

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL

On subsequent cycles if the counts on day one are below these criteria for neutrophil and/or platelets then delay treatment for at least seven days and up to fourteen days. Treatment should only be re-started when these levels are reached. The capecitabine may be resumed at the original dose or where the delay has been longer than fourteen days or has occurred for a second time with 75% of the original dose. If these levels are not reached despite a dose reduction consider stopping therapy. For lapatinib, on the first occurrence, if the counts return to eligible levels within fourteen days then re-start treatment at the original dose. For a second occurrence that resolves in the same time period consider reducing the dose to 1000mg per day.

Liver Impairment

Drug	Dose (% of original dose)
Capecitabine	There is a lack of information available. In patients with mild to moderate hepatic dysfunction due to liver metastases, 100% of the dose dose is probably acceptable.
Lapatinib	No information available

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Capecitabine	51-80 30-50 less than 30	100% 75% C/I
Lapatinib	No dose reductions are required for mild to moderate renal impairment	

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes. Dose limiting toxicities include diarrhoea, abdominal

pain, emesis, stomatitis and palmar-plantar erythrodysesthesia among others. If chest pain occurs consider stopping capecitabine.

Capecitabine

If chest pain occurs consider stopping capecitabine.

NCI-CTC Grade 2

Interrupt treatment until the toxicity resolves to NCI-CTC grade 1 or below then continue at the same dose. If the toxicity recurs for a second time again interrupt treatment until it resolves to NCI-CTC grade 1 or below then resume therapy at 75% of the original dose. If the same adverse effect develops on a third occasion once more interrupt treatment until it resolves to NCI-CTC grade 1 or below then continue at 50% of the original dose. Stop treatment if the toxicity re-appears on a fourth instance.

NCI-CTC Grade 3

Interrupt treatment until the toxicity resolves to NCI-CTC grade 1 or below then continue treatment using 75% of the original dose with prophylaxis if appropriate. If the toxicity recurs for a second time again interrupt treatment until it resolves to NCI-CTC grade 1 or below and then resume therapy at 50% of the original dose. If the same adverse effect develops on a third occasion discontinue capecitabine.

NCI-CTC Grade 4

Discontinue treatment unless the responsible consultant considers it to be in the best interest of the patient to continue at 50% of the original dose once the toxicity has resolved to grade 1 or below.

When capecitabine is stopped for toxicity, the doses are omitted and not delayed.

Lapatinib

In asymptomatic individuals who have more than a 20% decrease in left ventricular ejection fraction (LVEF) from baseline should continue on lapatinib and have a repeat LVEF assessment within fourteen days. If this repeat measurement confirms the first measurement temporarily discontinue the lapatinib. If the LVEF recovers in the following twenty-one days the lapatinib may be re-started at a dose of 1000mg daily. The LVEF should then be re-checked within fourteen days and every four weeks thereafter. If the LVEF still shows a decrease of more than 20% from baseline stop the lapatinib.

Lapatinib should be stopped if a NCI-CTC grade 3 and above left ventricular systolic dysfunction or interstitial pneumonitis occurs.

For a NCI-CTC grade 3 dermatological reaction or a NCI-CTC grade 2 reaction that has not improved with in fourteen days using supportive medications stop the lapatinib for up to fourteen days. If the symptoms resolve to NCI-CTC grade 1 re-start the lapatinib at the original dose. Treatment should be discontinued if a NCI-CTC grade 3 reaction recurs after one re-challenge.

If a NCI-CTC grade 4 dermatological reaction occurs stop lapatinib treatment.

For other NCI-CTC grade 1 adverse events the dose of lapatinib should be maintained.

For NCI-CTC grade 2 adverse effects maintain the dose for the first or second appearance once the symptoms have resolved to NCI-CTC grade 1 or below. For a third or fourth appearance interrupt treatment until the symptoms are NCI-CTC grade 1 and re-start the lapatinib at 1000mg per day.

For a NCI-CTC grade 3 toxicity interrupt treatment until it resolves to NCI-CTC grade 1 or below (up to fourteen days) and then consider dose reducing to 1000mg per day.

For a NCI-CTC grade 4 adverse event interrupt treatment until it resolves to NCI-CTC grade 1 or below. Consider stopping treatment thereafter.

Regimen

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Capecitabine	1000mg/m^2 twice a day	1-14 incl.	Oral
Lapatinib	1250mg once a day	1-21 incl.	Oral

Dose Information

- Capecitabine will be dose banded in accordance with the national dose bands

Administration Information

- Capecitabine should start on the evening of day 1
- Capecitabine should be taken with or after food
- Lapatinib should be taken on an empty stomach either one hour after or before food

Additional Therapy

- Antiemetics

  As take home medication;

  - metoclopramide 10mg three times a day when required oral

- Loperamide 4mg oral after the first loose stool then 2-4mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours).

- Mouthwashes according to local or national policy on the treatment of mucositis

- Gastric protection with a proton pump inhibitor or H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- The National Patient Safety Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.

- Ensure the total daily dose of capecitabine is divided into two doses given twelve hours apart (the first should be administered in the evening of day one of the cycle). Serious toxicity has occurred where the total daily dose has been given twice a day.

- It must be made clear to all staff, including those in the community, that this is a course of oral chemotherapy that must not be continued and should be prescribed under the supervision of an oncologist

- Patients should be assessed for suitability for oral chemotherapy prior to starting treatment.

References

1. Cameron D, Casey M, Oliva C et al. Lapatinib plus capecitabine in women with HER2 positive advanced breast cancer: the final survival analysis of a phase III randomised trial. Oncologist 2010; 15 (9): 924-934.

REGIMEN SUMMARY

Capecitabine-Lapatinib

Take Home Medicines

1. Capecitabine 1000mg/m² twice a day for 14 days oral

2. Lapatinib 1250mg once a day for 21 days oral

3. Metoclopramide 10mg three times a day when required oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Nov 2020	Updated monitoring with DPD testing Dose banding statement updated Coding removed	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.1	August 2014	Header changed Toxicities removed Information tabulated throughout ≥ removed and written in full Hepatic and renal impairment updated Metoclopramide dose changed to 10mg Mucositis recommendation changed Disclaimer added	Donna Kimber Pharmacy Technician	Dr Debbie Wright Pharmacist
1	June 2011	None	Dr Debbie Wright Pharmacist	Dr Ellen Copson Consultant Medical Oncologist Dr Caroline Archer 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 Hospital 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.