Chemotherapy Protocol

GASTROINTESTINAL (UPPER) CANCER

CAPECITABINE-CISPLATIN

(RADIOTHERAPY)

Please note there is a capecitabine-cisplatin regimen that does not involve the administration of radiotherapy in use for gastrointestinal (upper) cancers. Please ensure you have the correct regimen.

Regimen

- Gastrointestinal Cancer (upper) – Capecitabine-Cisplatin RT

Indication

- First line (radical) therapy of oesophageal cancer as an alternative to surgery or in patients unsuitable for surgery
- WHO performance status 0, 1

Toxicity

Drug	Adverse Effect
Capecitabine	Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity

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

Monitoring

Regimen

- FBC, LFT's and U&E's prior to each cycle (consider formally measuring GFR prior to treatment with cisplatin on day 1 of cycle 1)
- Consider a formal audiology test if relevant
- 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 criteria must be met.

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $75x10^9$/L

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin less than 12g/dL during radiotherapy

For subsequent cycles if the neutrophils are less than $1x10^9$/L and/or the platelets are less than $75x10^9$/L then delay treatment for 7 days and re-start treatment at the original dose provided counts recover to acceptable levels. If a 14 day delay is required to allow counts to recover or there are two separate delays of 7 days during treatment the dose of the cisplatin should be reduced to 80% of the original dose.

There is generally no need to reduce the dose of capecitabine for haematological toxicity.

Liver Impairment

Drug	Dose (% of original dose)
Capecitabine	There is little published information available. No dose reductions are necessary for those with mild to moderate hepatic dysfunction due to liver metastasis
Cisplatin	No dose reduction necessary

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Capecitabine	more than 51	100
	30-50	75
	less than 30	Do not use
Cisplatin	more than 60	100
	45-59	75
	less than 45	Consider carboplatin

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 palmer-plantar erythrodysesthesia among others.

Capecitabine

NCI-CTC Grade 2

Interrupt treatment until the toxicity resolves to NCI-CTC grade 0-1 then continue at the same dose. If the toxicity recurs for a second time, again interrupt treatment until it resolves to NCI-CTC grade 0-1 then resume therapy using 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 0-1 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 0-1 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 0-1 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 0-1.

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

Cisplatin

Neurotoxicity occurring at a NCI-CTC grade 2 or above or a new functional deterioration in hearing and / or tinnitus that does not resolve between cycles should be approached by substituting the cisplatin for carboplatin.

Regimen

21 day cycle for 4 cycles

Drug	Dose	Days	Route
Capecitabine	625mg/m^2 twice a day	1-21 incl	Oral
Cisplatin	60mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin per minute (minimum 120 minutes)

Day one of treatment should, where possible, be scheduled on a Monday or Tuesday. Radiotherapy is given during cycles three and four. Radiotherapy should normally commence on day one of cycle three (a Monday). Cycle three and four cisplatin should be administered on either day one or two (Monday or Tuesday) of

weeks one and four of the radiotherapy). The chemotherapy should be administered before the radiotherapy is given. The radiotherapy may be given during the cisplatin post hydration which may need to be interrupted for a short period of time.

Dose Information

- Capecitabine will be dose banded in accordance with the national dose bands
- Cisplatin will be dose banded in accordance with the national dose bands (1mg/ml)

Administration Information

Extravasation

- Cisplatin - exfoliant

Other

- Capecitabine should start on the evening of day 1
- Capecitabine should be taken with or after food

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy;

  - dexamethasone 8mg oral or intravenous
  - ondansetron 8mg oral or intravenous

  As take home medication;

  - dexamethasone 4mg twice a day oral for 3 days
  - metoclopramide 10mg three times a day when required oral
  - ondansetron 8mg twice a day oral for 3 days

- Cisplatin pre and post hydration as follows;

  Pre

  Furosemide 40mg oral or intravenous

  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

  Post

  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

  Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- Oral loperamide 4mg 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 guidelines for the treatment and prevention of mucositis

- Gastric protection with a proton pump inhibitor or a 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 short course of oral chemotherapy that must not be continued.

References

1. National Institute for Health and Clinical Excellence. Technology Appraisal 191. Capecitabine for the Treatment of Advanced Gastric Cancer. DOH: London.
2. Kang YK, Kang WK, Shin DB et al. Capecitabine / cisplatin versus fluorouracil / cisplatin as first line therapy in patients with advanced gastric cancer: a randomised phase III non-inferiority trial. Ann Oncol 2009; 20 (4): 666-673.
3. Lee SS, Kim SB, Park SI et al. Capecitabine and cisplatin chemotherapy (XP) alone or sequentially combined chemoradiotherapy containing XP regimen in patients with 3 different settings of stage IV esophageal cancer. Jpn J Clin Oncol 2007; 37 (11): 829-835.

REGIMEN SUMMARY

Capecitabine–Cisplatin RT

Day One

1. Dexamethasone 8mg oral or intravenous

2. Ondansetron 8mg oral or intravenous

3. Furosemide 40mg oral or intravenous

4. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

5. Cisplatin 60mg/m^2 in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a maximum rate of 1mg cisplatin/minute (minimum time 120 minutes)

6. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

Take Home Medicines

7. Capecitabine 625mg/m^2 twice a day oral for 21 days starting on the evening of day one of the cycle

8. Dexamethasone 4mg twice a day oral for 3 days starting on day two of the cycle

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

10. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day one of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
2.2	Nov 2020	Updated monitoring with DPD testing Dose banding statement updated Coding removed	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
2.1	May 2014	Header changed Toxicities removed Tabulated throughout Renal and hepatic function updated Mouthwash guidance updated Metoclopramide dose changed to 10mg Bolus removed from supportive treatments TTOs clarified Disclaimer added	Dr Debbie Wright Pharmacist	Donna Kimber Pharmacy Technician
2	Sept 2011	Indication changed to relect that it is radical therapy as an alternative to surgery or where surgery is unsuitable Performance status changed from 0.1,2 to 0,1	Dr Debbie Wright Pharmacist	Dr Andrew Jackson Consultant Clinical Oncologist
1	Apr 2011	None	Dr Debbie Wright Pharmacist	Dr Andrew Jackson Consultant 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.