Chemotherapy Protocol

PANCREATIC CANCER

CAPECITABINE (RADIOTHERAPY)

Regimen

- Pancreatic Cancer – Capecitabine (Radiotherapy)

Indication

- Locally advanced, non-metastatic pancreatic cancer
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Capecitabine	Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain

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 starting treatment and every seven days therafter
- 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 the following criteria must be met;

Criteria	Eligible Level
Neutrophils	$1x10^9$/L or greater
Platelets	$75x10^9$/L or greater

Thereafter

Neutrophil ($x10^9$/L)	Platelet ($x10^9$/L)	Capecitabine Dose	Radiotherapy
1 or greater	Greater than 100	100%	Continue
1 or greater	75-100	75%	Continue
less than 1	less than 75	Omit for one week. Subsequent dose at 75%	Stop radiotherapy if the neutrophil count is less than $0.5x10^9$/L or the platelets are less than $50x10^9$/L. Re-check counts in 3 days. Restart the radiotherapy alone in the neutrophil count is greater than $0.5x10^9$/L and the platelets are greater than $50x10^9$/L. Restart capecitabine when the neutrophil count is greater than 1x109/L and the platelets are greater than $75x10^9$/L.

Kidney Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original)
Capecitabine	51 or greater	100
	30-50	75
	0-29	Contra-indicated

Liver Impairment

Drug	Recommendation
Capecitabine	Consider dose adjustments. Delays may be necessary if there are treatment related increases in bilirubin of more than 3xULN or ALT/AST of more than 2.5xULN. In patients with mild to moderate hepatic dysfunction due to liver metastasis 100% of the dose is probably acceptable

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.

NCI-CTC Grade 2

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

Regimen

42 day cycle for 1 cycle

Drug	Dose	Days	Administration
Capecitabine	830mg/m^2 twice a day	1, 2, 3, 4, 5, 8, 9, 10, 11, 12, 15, 16, 17, 18, 19, 22, 23, 24, 25, 26, 29, 30, 31, 32, 33, 36, 37, 38	Oral

The capecitabine will be administered on Monday, Tuesday, Wednesday, Thursday and Friday only (not weekends unless the patient is scheduled for radiotherapy on these days). This should include a morning dose of capecitabine prior to the start of radiotherapy. On the last day of radiotherapy a dose should be taken during both the morning and evening to complete the course. There are 28 fractions of radiotherapy hence 28 days of chemotherapy. Capecitabine is only given on the days of radiotherapy.

Dose Information

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

Administration Information

- Capecitabine should start on the morning of the first day of radiotherapy.
- Capecitabine is only taken Monday – Friday inclusive. No treatment is to be taken on a Saturday or Sunday unless the patient has had radiotherapy scheduled for those days. The capecitabine should be taken on the days of radiotherapy only
- Capecitabine should be taken with or after food

Additional Therapy

- Antiemetics

  As take home medication

  - metoclopramide 10mg three times a day when required

- Oral loperamide 4mg stat 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 policy for the treatment and prevention of mucositis.
- Gastric protection with a proton pump inhibitor or H_2 antagonist should be prescribed for 12 weeks starting on day one of radiotherapy.

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 on the morning of day one of the radiotherapy. 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. NCRI Upper GI Clinical Studies Group. SCALOP. Selective Chemoradiation in Advanced Localised Pancreatic Cancer. A multi-centre randomised phase II study of induction chemotherapyfollowed by gemcitabine or capecitabine based chemoradiotherapy for locally advanced non-metastatic pancreatic cancer. Clinical trial protocol version 4 issued 6th September 2010.

REGIMEN SUMMARY

Capecitabine RT

Day 1

1. Capecitabine 830mg/m^2 twice a day on Monday, Tuesday, Wednesday, Thursday and Friday for the duration of radiotherapy (days 1, 2, 3, 4, 5, 8, 9, 10, 11, 12, 15, 16, 17, 18, 19, 22, 23, 24, 25, 26, 29, 30, 31, 32, 33, 36, 37, 38)
Administration Instructions
Capecitabine should be taken on the morning and evening of radiotherapy treatment.

2. 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	Dr Deborah Wright Pharmacist
1.1	July 2014	OPCS codes updated Name added to regimen summary Disclaimer changed	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	Sept 2013	None	Dr Deborah Wright Pharmacist	Dr Andrew Bateman Consultant Clinical 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.