**Chemotherapy Protocol**

# PANCREATIC CANCER

## CAPECITABINE and GEMCITABINE

### Regimen

- Pancreatic Cancer– Capecitabine-Gemcitabine

### Indication

- Adjuvant treatment of pancreatic cancer
- First line treatment of advanced pancreatic cancer
- WHO Performance status 0, 1, 2

### Toxicity

| Drug | Adverse Effect |
|---|---|
| Capecitabine | Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain |
| Gemcitabine | Diarrhoea, constipation, rash, respiratory problems (pneumonitis), influenza like symptoms, radiosensitising, transient elevation of LFTs |

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 treatment (days 1, 8, 15)
- 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 |
|---|---|
| Neutrophil | equal to or more than $1.5x10^9$/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 the day of gemcitabine administration, if the neutrophils are 0.5–$1x10^9$/L and/or the platelets 50-100 $x10^9$/L then administer 75% of the original dose. If the neutrophils are less than $0.5x10^9$/L and the platelets less than $50x10^9$/L omit the gemcitabine for 7 days.

Patients who have had a dose reduction due to decreased neutrophil or platelet count should have their next dose according to neutrophil and/or platelet count on the day of gemcitabine administration, i.e. they can have their dose escalated back to 100% dose if their blood count is adequate. However, if after dose reduction to 75%, their blood count on the day of the next gemcitabine administration is still inadequate i.e. neutrophil count between 0.5-$1x10^9$/L or platelet count between 50-$100x10^9$/L the same dose (dose reduction to 75% of original dose) should be given.

Where dose omissions occur the dose should not be replaced and patients should maintain the same cycle schedule.

Capecitabine doses do not, in general, require dose modification for haematological toxicity.

### *Hepatic Impairment*

| Drug | Bilirubin (µmol/L) | | AST/ALT | Dose (% of original dose) |
|---|---|---|---|---|
| Capecitabine | greater than 3xULN | or | greater than 2.5xULN | If treatment related consider delaying treatment.<br>For mild/moderate hepatic dysfunction due to liver metastasis dose modification may not be necessary. |
| | | | | |
| Gemcitabine | Consider dose reductions especially where the bilirubin is raised | | | |

*Renal Impairment*

| Drug | Creatinine Clearance (ml/min) | Dose (% of original dose) |
|---|---|---|
| Capecitabine | 51 or greater | 100% |
| | 30-50 | 75% |
| | less than 30 | Contra-indicated |
| | | |
| Gemcitabine | Consider dose adjustments when the CrCl is less than 30ml/min | |

*Other Toxicities*

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*

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 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 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 NCI-CTC grade 0-1.

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

*Gemcitabine*

If an episode of neutropenic sepsis occurs, all subsequent courses should be subject to the following dose adjustments. The gemcitabine should be withheld until the patient has fully recovered and then re-instated at 75% of the original dose with

no further re-escalation. If this occurs in a patient already receiving 75% of the full dose, then a further dose reduction to 50% of the full dose should be made.

Modifications are not usually required for other non-haematological toxicities. In exceptional cases, treatment delay may be necessary until the toxicity has resolved. If this happens, a 25% dose reduction should be made for all subsequent courses.

## Regimen

**28 day cycle for 6 cycles**

| Drug | Dose | Days | Administration |
|---|---|---|---|
| Capecitabine | 830mg/m$^2$ twice a day | 1-21 incl | Oral |
| Gemcitabine | 1000mg/m$^2$ | 1, 8, 15 | Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes |

## Dose Information

- Capecitabine will be dose banded in accordance with the national dose bands
- Gemcitabine will be dose banded in accordance with the national dose bands (100mg/ml)

## Administration Information

### *Extravasation*

- Gemcitabine – neutral

### *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 on **days 1, 8, 15** only

  - metoclopramide 10mg oral or intravenous

As take home medication on **day 1** only;

- 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 national or local guidelines for the treatment 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. Cunningham D, Chau I, Stocken DD et al. Phase III randomised comparison of gemcitabine versus gemcitabine plus capecitabine in patients with advanced pancreatic cancer. J Clin Oncol 2009: 27 (33); 5513-5518.

## REGIMEN SUMMARY

## Capecitabine-Gemcitabine

### Day One

1. Metoclopramide 10mg oral or intravenous

2. Gemcitabine 1000mg/$m^2$ intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

### Day Eight

3. Metoclopramide 10mg oral or intravenous

4. Gemcitabine 1000mg/$m^2$ intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

### Day Fifteen

5. Metoclopramide 10mg oral or intravenous bolus

6. Gemcitabine 1000mg/$m^2$ stat intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

### Take Home Medicines (day one only)

7. Capecitabine 830mg/$m^2$ twice daily for 21 days oral

8. 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<br>Dose banding statement updated<br>Coding removed | Donna Kimber<br>Pharmacy Technician | Rebecca Wills<br>Pharmacist |
| 1.1 | July 2014 | Header changed<br>Tabulation throughout<br>< or > symbols written out in full.<br>NCI-CTC added to toxicity grades<br>Bolus removed from intravenous bolus<br>Stat removed<br>Treatment of mucositis changed<br>Pyridoxine removed<br>Metoclopramide dose changed to 10mg throughout<br>Name added to regimen summary<br>OPCS codes updated<br>Disclaimer added | Dr Deborah Wright<br>Pharmacist | Donna Kimber<br>Pharmacy Technician |
| 1 | Aug 2010 | None | Dr Deborah Wright<br>Pharmacist | Dr Tim Iveson<br>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.