Chemotherapy Protocol

PANCREATIC CANCER

CISPLATIN-GEMCITABINE

(RADIOTHERAPY)

Regimen

- Pancreatic Cancer – Cisplatin-Gemcitabine RT

Indication

- Locally unresectable non-metastatic pancreatic cancer
- WHO Performance status 0, 1
- Palliative intent

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
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, LFTs and U&Es on days 1, 8, 22 and 29 of the cycle (consider formally measuring GFR prior to treatment with cisplatin on day 1 cycle 1)
- Consider a formal audiology test if relevant

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.

Haematology

Prior to prescribing cycle one 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 is symptomatic of anaemia or haemoglobin less than 12g/dL during radiotherapy

On any subsequent day of chemotherapy treatment if the neutrophil count is between $0.5x10^9$/L and $1x10^9$/L and / or the platelet count is between $50x10^9$/L and $75x10^9$/L administer 75% of the original dose for both cisplatin and gemcitabine. Reduce the dose of cisplatin and gemcitabine to 50% of the original dose if the neutrophil count is less than $0.5x10^9$/L and / or the platelet count less than $50x10^9$/L.

Consider stopping treatment after a second dose reduction or interruption due to haematological toxicity.

Hepatic Impairment

Drug	Bilirubin (µmol/L)		AST/ALT	Dose (% of original dose)
Cisplatin	No dose reductions necessary			
Gemcitabine	Consider dose reductions especially where the bilirubin is raised			

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	more than 60	100
	45 - 59	75
	less than 45	consider alternative
Gemcitabine	Consider dose adjustments when the CrCl is less than 30ml/min	

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, stomatitis and palmer-plantar erythrodysesthesia among others.

For patients with NCI-CTC grades 3–4 non-haematological toxicity (excluding nephrotoxicity), reduce the dose to 75% of the original dose and 50% of the original dose for those with a NCI-CTC grade 4 non-haematological toxicity.

Radiation therapy should be stopped when a grade 3–4 gastrointestinal toxicity or grade 4 haematological toxicity occurs.

Regimen

42 day cycle for 1 cycle

Drug	Dose	Days	Administration
Cisplatin	30mg/m^2	1, 8, 22, 29	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 60 minutes)
Gemcitabine	300mg/m^2	1, 8, 22, 29	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Day 1 is defined as the first day of radiotherapy treatment. The cisplatin and gemcitabine should be administered before the radiotherapy. Radiotherapy may be given during the cisplatin post hydration which may be interrupted for a short period of time.

Dosage Information

- Cisplatin will be dose banded as per the CSCCN agreed bands
- Gemcitabine will be dose banded as per the CSCCN agreed bands

Administration

Extravasation

- Cisplatin – exfoliant
- Gemcitabine - neutral

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 only when required oral or intravenous bolus

  Post

  1000ml sodium chloride 0.9% with 8mmol 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.

- 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

Coding

- Procurement – X70.8
- Delivery – X72.9, X72.4

References
1. Brunner TB, Grabenbauer GG, Meyer T et al. Primary resection versus neoadjuvant chemoradiation followed by resection for locally resectable or potentially resectable pancreatic carcinoma without distant metastasis. A multi-centre prospectively randomised phase II study of the Interdisciplinary Working Group Gastrointestinal Tumours (AIO, ARO and CAO). BMC Cancer; 2007; 7:

REGIMEN SUMMARY

Cisplatin-Gemcitabine RT

Day 1, 8, 22, 29

1. Dexamethasone 8mg oral or intravenous

2. Ondansetron 8mg oral or intravenous

3. Furosemide 40mg only when required oral or intravenous

4. Gemcitabine 300mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

5. Cisplatin 30mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 60 minutes)

6. 1000ml sodium chloride 0.9% with 8mmol magnesium sulphate intravenous infusion over 60 minutes

Take Home Medicines

7. Dexamethasone 4mg twice a day oral for 3 days starting on the day after chemotherapy

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

9. Ondansetron 8mg twice a day oral for 3 days starting on the evening of chemotherapy

The gemcitabine forms the pre-hydration for cisplatin. Please ensure in Planner that the administration instructions for cisplatin reflect this.

Should the gemcitabine therapy be omitted for any reason please remember to prescribe sodium chloride 0.9% 250ml over 30 minutes as pre-hydration.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
2.1	July 2014	Header changed Toxicity removed Bolus removed Tabulation throughout Metoclopramide dose changed Disclaimer added	Dr Debbie Wright Pharmacist	Donna Kimber Pharmacy Technician
2	Oct 2011	Post hydration fluid changed in the main text to reflect that in the regimen summary. Magnesium in the post hydration reduced to 8mmol to reflect the agreement for cisplatin hydration regimens	Dr Debbie Wright Pharmacist	Rebecca Wills Pharmacist
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.