Chemotherapy Protocol

BLADDER

CISPLATIN (35)-GEMCITABINE

Regimen

- Bladder-Cisplatin (35)-Gemcitabine

Indication

- For use in patients unable to tolerate standard cisplatin (70)-gemcitabine due to;
    - poor performance status
    - poor tolerance of cisplatin (70)-gemcitabine
    - impaired renal function

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity, highly emetogenic
Gemcitabine	Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza like symptoms, radiosensitising

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

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day 1 and 8 of treatment
- Calculated or measured creatinine clearance prior to each cycle. EDTA may be considered prior to cycle one or if, during treatment, there are significant changes in renal function.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities 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.

Haematological

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

Day 1

Neutrophils ($x10^9$/L)	**Dose Modifications (cisplatin and gemcitabine)**
more than or equal to 1	100%
less than 1	1st Occurrence Delay until recovery. 2nd Occurrence Delay until recovery then give 75% of the original dose.
Febrile Neutropenia	1st Occurrence Delay until recovery and then re-start treatment using 75% of the original dose.
Platelets ($x10^9$/L)	**Dose Modifications (cisplatin and gemcitabine)**
more than or equal to 100	100%
Less than 100	1st Occurrence. Delay until recovery then give 75% of the original dose. 2nd Occurrence Delay until recovery then give 50% of the original dose.

Day 8

Neutrophils ($x10^9$/L)	**Dose Modifications (cisplatin and gemcitabine)**
more than or equal to 1	100%
0.5 - 1	75%
less than 0.5	Omit
Platelets ($x10^9$/L)	**Dose Modifications (cisplatin and gemcitabine)**
more than or equal to 100	100%
50 - 100	75%
less than 50	Omit

Hepatic Impairment

Drug	Bilirubin µmol/L	AST/ALT units/L	Dose (% of original dose)
Cisplatin	N/A	N/A	No dose adjustment needed
Gemcitabine	greater than 30*	N/A	Initiate treatment with a dose of 800mg/m^2

*Limit reflects local practice and may vary from published sources

Renal Impairment

This regimen has been tolerated in patients with creatinine clearances as low as 40ml/min

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	40 or greater	100%
	less than 40	Consider alternative
Gemcitabine	30 or greater	100%
	less than 30	Consider dose reduction

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.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 75% of the original dose or discontinued as appropriate.

Regimen

21 day cycle for 3 - 6 cycles (3 cycles will be set in Aria)

First line treatment – 6 cycles

Adjuvant – 4 cycles

Neoadjuvant – 3 cycles

Drug	Dose	Days	Administration
Cisplatin	35mg/m^2	1 and 8	Intravenous infusion in 1000ml sodium chloride 0.9% plus 20mmol potassium chloride at a rate of cisplatin of 1mg/min (minimum 60 minutes)
Gemcitabine	1000mg/m^2	1 and 8	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Dose Information

- Cisplatin will be dose banded according to the CSCCN agreed bands
- Gemcitabine will be dose banded according to the CSCCN agreed bands

Administration Information

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

- Cisplatin pre and post hydration as follows

  Pre

  Furosemide 40mg when required oral or intravenous

  500ml sodium chloride 0.9% with 8mmol magnesium sulphate over 30 minutes

  Post

  500ml sodium chloride 0.9% over 30 minutes

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

- Mouthwashes according to local or national policy on 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.

Coding (OPCS)

- Procurement – X70.5
- Delivery – X72.1 & X72.4

References
1. Hussain SA, Stocken DD, Riley P et al. A phase I/II study of gemcitabine and fractionated cisplatin in an outpatient setting using a 21 day schedule in patients with advanced and metastatic bladder cancer. Br J Cancer 2004; 91 (5): 844-849.
2. von der Maase, Hansen SW, Roberts JT et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin and cisplatin in advanced or metastatic bladder cancer: results of a large randomised multinational multicentre phase III study. J Clin Oncol 2000; 18 (17): 3068-3077.
3. Dash A, Pettus JA, Herr HW, et al. A Role for Neoadjuvant Gemcitabine Plus Cisplatin in MuscleInvasive Urothelial Carcinoma of the Bladder: A Retrospective Experience. Cancer 2008;113:2471–7.

REGIMEN SUMMARY

Cisplatin (35)-Gemcitabine

Cycles One and Two

Day 1 and 8

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Furosemide 40mg when required oral or intravenous
4. Sodium chloride 0.9% 500ml with magnesium sulphate 8mmol over 30 minutes
5. Gemcitabine 1000mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
6. Cisplatin 35mg/m^2 in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of cisplatin 1mg/minute (minimum 60 minutes).
7. Sodium chloride 0.9% 500ml over 30 minutes

Take Home Medicines – Day 1

8. Dexamethasone 4mg oral twice a day for 3 days starting the day after chemotherapy
   Administration Instructions
   Dispense a supply for both day 1 and 8 of the cycle.
9. Metoclopramide 10mg oral three times a day when required for nausea
   Administration Instructions
   Dispense 10 days or an original pack if appropriate to cover day 1 and 8 of the cycle.
10. Ondansetron 8mg oral twice a day for 3 days starting on the evening of chemotherapy treatment
    Administration Instructions
    Dispense a supply for both day 1 and 8 of the cycle.

Cycle Three

Day 1 and 8

11. Warning – check number of cycles*
12. Dexamethasone 8mg oral or intravenous
13. Ondansetron 8mg oral or intravenous
14. Furosemide 40mg when required oral or intravenous
15. Sodium chloride 0.9% 500ml with magnesium sulphate 8mmol over 30 minutes
16. Gemcitabine 1000mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

17. Cisplatin 35mg/m^2 in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of cisplatin 1mg/minute (minimum 60 minutes)

18. Sodium chloride 0.9% 500ml over 30 minutes

Take Home Medicines – Day 1

19. Dexamethasone 4mg oral twice a day for 3 days starting the day after chemotherapy
    Administration Instructions
    Dispense a supply for both day 1 and 8 of the cycle.

20. Metoclopramide 10mg oral three times a day when required for nausea
    Administration Instructions
    Dispense 10 days or an original pack if appropriate to cover day 1 and 8 of the cycle.

21. Ondansetron 8mg oral twice a day for 3 days starting on the evening of chemotherapy treatment
    Administration Instructions
    Dispense a supply for both day 1 and 8 of the cycle.

*Warning to appear on Cycle 3 Day 1 only.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	May 2015	Header changed Comment re local bilirubin limit added Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text Mucositis recommendation changed Dexamethasone TTO clarified Metoclopramide TTO clarified Ondansetron TTO clarified Warning on C3 D1 only clarified Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Dec 2012	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Joanna Gale Consultant Medical Oncologist Dr Mathew Wheater 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 Hospitals 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.