Chemotherapy Protocol

HEAD AND NECK CANCER

CISPLATIN (80)-DOCETAXEL(40)-FLUOROURACIL(2800)

In-Patient Regimen

Regimen

- Head and Neck Cancer – InP-Cisplatin(80)-Docetaxel(40)-Fluorouracil (2800)

Indication

- Neoadjuvant or advanced squamous cell carcinoma of the head and neck

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Docetaxel	Hypersensitivity, fluid retention, neuropathy, joint pains, nail changes, fatigue
Fluorouracil	Diarrhoea, stomatitis

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 each cycle
- Patients with complete or partial dihydropyrimidine dehydrogenase (DPD) deficiency are at increased risk of severe and fatal toxicity during treatment with fluorouracil. 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 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.

Criteria	Eligible Level
Neutrophils	$1.5x10^9$/L or greater
Platelets	$100x10^9$/L or greater

Defer treatment for 7 days if the neutrophil count is less than $1.5x10^9$/L and / or the platelet count is less than $100x10^9$/L. If the counts have recovered to these levels at 7 days resume treatment. Consider using a 75% dose reduction. If the counts do not recover delay a further seven days. If they are satisfactory at 14 days treatment can be re-started using a 50% dose reduction.

Hepatic Impairment

Drug	Bilirubin (µmol/L)	Alk Phos	AST/ALT units	Dose
Cisplatin	N/A	NA	N/A	No dose reduction necessary
Docetaxel	NA	2.5xULN or greater	1.5xULN	Give 75%
	Greater than ULN	6xULN or greater	3.5xULN or greater	Not recommended
Fluorouracil	less than 85	NA	less than 180	100%
	more than 85	NA	more than 180	Contra-indicated

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	more than 60	100
	45-59	75
	less than 45	consider carboplatin
Docetaxel		No dose adjustment required
Fluorouracil		Consider dose reduction in severe renal impairment only

Other

A cycle of chemotherapy should be delayed for up to two weeks to allow for a reduction in the severity of toxic events of NCI-CTC grade 3 or more to a severity of NCI-CTC grade 1 or less (with the exception of alopecia, fatigue, malaise, and nail changes). Delays beyond two weeks required discontinuation of chemotherapy

Cisplatin

Modifications in the dose of cisplatin are necessary for peripheral sensory and motor neurotoxicity, ototoxicity, or nephrotoxicity. Consider stopping treatment for patients with neurotoxicity or ototoxicity of NCI-CTC grade 3 or more.

Docetaxel

Lacrimation

Excessive lacrimation is related to cumulative docetaxel doses and occurs after a median of 400mg/m². Symptomatic treatment with hypromellose 0.3% eye drops four times a day may help. However, if the ocular irritation continues consider reducing the docetaxel dose.

Skin

Delay the docetaxel where a NCI-CTC grade 3 cutaneous toxicity is present on day one of the cycle until it resolves to NCI-CTC grade 1 or below. Consider a dose reduction. If it occurs with a reduced dose of or if there is no recovery after two weeks, docetaxel treatment should be stopped. Where a NCI-CTC grade 3 cutaneous toxicity occurs between cycles with recovery by day one then reduce the docetaxel dose as described. Docetaxel should be stopped in response to a NCI-CTC grade 4 cutaneous toxicity.

Fluorouracil

Modifications in the dose of fluorouracil are necessary for mucositis and diarrhoea.

Regimen

21 day cycle for 4 cycles

Drug	Dose	Days	Administration
Cisplatin	20mg/m^2	1, 2, 3, 4	Intravenous infusion in 1000ml sodium chloride 0.9% with potassium chloride 20mmol at a maximum rate of 1mg cisplatin/min (minimum time 60 minutes)
Docetaxel	40mg/m^2	2	Intravenous infusion in 250ml sodium chloride over 60 minutes
Fluorouracil	700mg/m^2	1, 2, 3, 4	Intravenous infusion in 1000ml sodium chloride 0.9% over 22 hours

Dose Information

- Cisplatin will be dose banded in accordance with the national dose bands (1mg/ml)
- Docetaxel will be dose banded in accordance with the national dose bands (20mg/ml)
- Docetaxel induced fluid retention can lead to weight gain. This is not a reason to alter the doses
- Docetaxel doses of more than 200mg should be diluted in 500ml sodium chloride 0.9% (maximum concentration 0.74mg/ml)
- Fluorouracil will be dose banded in accordance with the national dose bands (50mg/ml)

Administration Information

Extravasation

- Cisplatin – exfoliant
- Docetaxel - exfoliant
- Fluorouracil - inflammitant

Other

- Docetaxel hypersensitivity reactions tend to occur with the first or second infusion. For minor symptoms such as flushing or localised rashes the infusion should not be interrupted. For severe reactions including profound hypotension, bronchospasm and generalised erythema discontinue the infusion immediately.

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy
  - dexamethasone 8mg once a day for 4 days
  - ondansetron 8mg once a day oral for 4 days
  - metoclopramide 10mg three times a day when required oral

  As take home
  - dexamethasone 4mg each morning for 2 days then 2mg each morning for 2 days starting on day 5 of the cycle
  - metoclopramide 10mg three times a day when required

- Furosemide 40mg oral or intravenous bolus when required

- Pre-cisplatin hydration with 500ml sodium chloride 0.9% with 8mmol magnesium sulphate over 30 minutes

- Mouthwashes as per local or national guidelines

- 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

Other Information

- This regimen has been adapted locally from the references below

References
1. Vermorken JB et al. EORTC 24971/TAX 323 Study Group. Cisplatin, fluorouracil and docetaxel in unresectable head and neck cancer. N Engl J Med 2007; 25: 357 (17): 1695-1704.
2. Lorch JH, Goloubeva O, Haddad RI et al. Induction chemotherapy with cisplatin and fluorouracil alone or in combination with docetaxel in locally advanced squamous cell cancer of the head and neck: long term results of the TAX 324 randomised phase III trial. Lancet Oncol 2011; 12 (2): 153-159.

REGIMEN SUMMARY

InP-Cisplatin(80)-Docetaxel(40)-Fluorouracil(2800)

Day 1

1. Warning – Check supportive medication prescribed
   Administration instructions
   1. Dexamethasone 8mg once a day, days 1, 2, 3, 4 oral or equivalent intravenous dose
   2. Ondansetron 8mg once a day, days 1, 2, 3, 4 oral or intravenous
   3. Furosemide 40mg when required oral or intravenous
2. Sodium chloride 0.9% 500ml with magnesium sulphate 8mmol over 30 minutes
3. Cisplatin 20mg/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)
4. Fluorouracil 700mg/m^2 intravenous infusion 1000ml sodium chloride 0.9% over 22 hours

Day 2

5. Warning – Check supportive medication prescribed
   Administration instructions
   1. Dexamethasone 8mg once a day, days 1, 2, 3, 4 oral or equivalent intravenous dose
   2. Ondansetron 8mg once a day, days 1, 2, 3, 4 oral or intravenous
   3. Furosemide 40mg when required oral or intravenous
6. Sodium chloride 0.9% 500ml with magnesium sulphate 8mmol over 30 minutes
7. Cisplatin 20mg/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)
8. Docetaxel 40mg/m^2 intravenous infusion in 250ml sodium chloride over 60 minutes
9. Fluorouracil 700mg/m^2 intravenous infusion 1000ml sodium chloride 0.9% over 22 hours

Day 3, 4

10. Warning – Check supportive medication prescribed
    Administration instructions
    1. Dexamethasone 8mg once a day, days 1, 2, 3, 4 oral or equivalent intravenous dose
    2. Ondansetron 8mg once a day, days 1, 2, 3, 4 oral or intravenous
    3. Furosemide 40mg when required oral or intravenous
11. Sodium chloride 0.9% 500ml with magnesium sulphate 8mmol over 30 minutes
12. Cisplatin 20mg/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)
13. Fluorouracil 700mg/m^2 intravenous infusion 1000ml sodium chloride 0.9% over 22 hours

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Nov 2020	Updated monitoring with DPD testing Dose banding updated Coding removed	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	July 2015	None	Dr Deborah Wright Pharmacist	Dr K Bradley 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 Trust

All actions have been taken to ensure these protocols are correct. However, it remains the responsibility of the prescriber to ensure the correct drugs and doses are prescribed for patients.