Chemotherapy Protocol

HEAD AND NECK CANCER

CARBOPLATIN (AUC1.5)-RADIOTHERAPY

Regimen

- Head and Neck Cancer – Carboplatin(AUC1.5)-Radiotherapy

Indication

- SCC of the head and neck in those who have received cisplatin-docetaxel-fluorouracil (TPF) as induction treatment
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Carboplatin	Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances

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 (including magnesium) prior to each day 1 of treatment (day 1 is the day of chemo-radiotherapy)
- EDTA or calculated creatinine clearance before the first cycle

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 SACT 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

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

The haemoglobin needs to be maintained above 12g/dL throughout treatment. If it falls below this level consider a blood transfusion. Treatment can continue while this is organised.

Neutrophils ($x10^9$/L)	**Dose Modifications (carboplatin)**
Greater than or equal to 1.5	100%
Less than 1.5	Delay carboplatin until neutrophils are greater than or equal to $1.5x10^9$/L. Continue radiotherapy during this time.
Platelets ($x10^9$/L)	**Dose Modifications**
Greater than or equal to 100	100%
Less than 100	Delay chemotherapy for until platelets are greater than or equal to $100x10^9$/L . Continue radiotherapy during this time.

Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

Drug	**Bilirubin µmol/L**		**AST/ALT units**	**Dose (% of original dose)**
Carboplatin	N/A		N/A	No dose adjustment needed

Renal Impairment

Drug	**Creatinine Clearance (ml/min)**	**Dose (% of original dose)**
Carboplatin*	less than 20	Omit

* Significant changes in GFR of more than 10% may require dose adjustment. If there is more than a 30% change in serum creatinine during treatment perform an EDTA.

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 toxicities grade 2 and above, interrupt chemotherapy treatment until the toxicity has resolved to NCI-CTC grade 1 or below and then refer to the table below for dose modifications to be applied to all subsequent doses.

Continue radiotherapy regardless of any delays to carboplatin treatment.

Incidence	Grade 2	Grade 3	Grade 4
1st occurrence	Resume at original dose	Resume at 75% of original dose	Discontinue treatment
2nd occurrence of same toxicity	Resume at 75% of original dose	Resume at 50% of original dose	N/A
3rd occurrence of same toxicity	Resume at 50% of original dose	Discontinue treatment	N/A
4th occurrence of same toxicity	Discontinue treatment	N/A	N/A

Regimen

7 day cycle for 6 to 7 cycles starting on the first day of radiotherapy (7 cycles will be set in ARIA)

Drug	Dose	Days	Administration
Carboplatin	AUC 1.5 (maximum dose 225mg)	1	Intravenous infusion in 250ml glucose 5% over 30 minutes

Dose Information

- The recommended maximum dose when using a calculated creatinine clearance at AUC1.5 is 225mg. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.
- Carboplatin will be dose banded in accordance with the national dose bands (10mg/ml)

Administration Information

Extravasation

- Carboplatin – irritant
- Radiotherapy should commence within one hour of the end of the carboplatin infusion.

Other

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of carboplatin. Facilities for the treatment of hypotension and bronchospasm must be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of carboplatin and appropriate therapy

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy

  - Dexamethasone 8mg oral or intravenous equivalent
  - ondansetron 8mg oral or intravenous

  As take home medication

  - dexamethasone 4mg once a day for 2 days oral
  - metoclopramide 10mg three times a day oral as necessary

- 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.

References
1. Lorch JH, Goloubeva O, Haddad RI et al. Long term results of TAX324, a randomised phase III trial of sequential therapy with TPF versus PF in locally advanced squamous cell cancer of the head and neck. Lancet Oncol 2011; 12 (2): 153-159.

REGIMEN SUMMARY

Carboplatin (AUC1.5)-RT

Cycle 1 Day 1

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Carboplatin AUC 1.5 (maximum dose 225mg) intravenous infusion in 250ml glucose 5% over 30 minutes

Take home medicines

4. Dexamethasone 4mg once a day oral for 2 days starting the day after chemotherapy
5. Metoclopramide 10mg three times a day oral as necessary
   Administration instructions
   Please supply 60 tablets or 2 original packs if appropriate. If further supplies are required on subsequent days please add from the support folder.

Cycle 2 Day 1 Onwards

6. Dexamethasone 8mg oral or intravenous
7. Ondansetron 8mg oral or intravenous
8. Carboplatin AUC 1.5 (maximum dose 225mg) intravenous infusion in 250ml glucose 5% over 30 minutes

Take home medicines

9. Dexamethasone 4mg once a day oral for 2 days starting the day after chemotherapy

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Aug 2020	None	Dr Deborah Wright Pharmacist	Dr Sathish Harinarayanan 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, no responsibility can be taken for errors that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.