Chemotherapy Protocol

HEAD AND NECK CANCER

CETUXIMAB RT (7 day)

Regimen

- Head and Neck Cancer – Cetuximab RT (7 day)

Indication

- Cetuximab in combination with radiotherapy is recommended as a possible treatment for people with locally advanced squamous cell carcinoma of the head and neck where all forms of platinum based therapy are considered in appropriate.

- Karnofsky performance status of above 90%

Toxicity

Drug	Adverse Effect
Cetuximab	Infusion related reactions, interstitial lung disease, skin reactions, electrolyte abnormalities, fatigue, abdominal pain, constipation

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

Monitoring

Drugs

- FBC, LFT's and U&E's prior to day one of cycle one of treatment and every 6 – 8 weeks thereafter

- Monitor for hypersensitivity reactions for 60 minutes after the end of the cetuximab infusion

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 on day one of 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 symptomatic of anaemia or has a haemoglobin of less than 12g/dL

Hepatic / Renal Impairment

Drug	Hepatic	Renal
Cetuximab	Administer only when the transaminases are 5xULN or below and the bilirubin is 1.5xULN or below	Administer only where the serum creatinine is 1.5xULN or below

Other

Cetuximab

Allergic or hypersensitivity reactions have occurred during the administration of cetuximab. For a NCI-CTC grade 1 reaction reduce the infusion rate by 50% (the total should not exceed 240 minutes). For a NCI-CTC grade 2 reaction, stop the infusion and administer supportive therapies as indicated. Once the reaction has resolved to NCI-CTC grade 1 or below resume the infusion at 50% of the previous rate. For a NCI-CTC grade 3 or 4 toxicity stop the infusion immediately and disconnect the tubing from the patient. Administer appropriate supportive therapies. Once recovered, patients should not receive cetuximab again.

Once the rate has been reduced it should not be increased on subsequent infusions.

If a second reaction occurs on the slower infusion rate the infusion should be stopped and no further treatment given.

An acneiform skin rash occurs in over 70% of those receiving cetuximab. The onset is normally within three weeks of starting therapy and often resolves after week twelve. For a NCI-CTC grade 1-2 reaction use symptomatic treatments such as topical or oral antibiotics and continue with the cetuximab. For a NCI-CTC grade 3 toxicity delay treatment until the toxicity resolves to NCI-CTC grade 2 or below. If this occurs within fourteen days resume cetuximab at the same dose. If more than fourteen days is required stop treatment. If the NCI-CTC grade 3 toxicity occurs for a second and third time the cetuximab may again be delayed for up to and including fourteen days with concomitant dose reductions to 200mg/m^2 and 150mg/m^2 respectively. Cetuximab dose reductions are permanent. The cetuximab must be

discontinued if more than two consecutive infusions are withheld or a fourth episode of a NCI-CTC grade 3 skin toxicity develops or a NCI-CTC grade 4 toxicity at any time.

UV radiation may worsen skin reactions. Sun safety practices should be followed during and for up to two months after the end of treatment.

Stop treatment if there is a confirmed pneumonitis.

Regimen

7 day cycle until intolerance or disease progression develops. The number of cycles will also depend on the diagnosis and radiotherapy fractination (8 cycles will be set in Aria)

Cycle One

Drug	Dose	Days	Route
Cetuximab	400mg/m^2	1	Intravenous infusion over 120 minutes

Cycle Two Onwards

Drug	Dose	Days	Route
Cetuximab	250mg/m^2	1	Intravenous infusion over 60 minutes

Dose Information

- Cetuximab will be dose banded in accordance with the national dose bands (5mg/mL)

Administration Information

Extravasation

- Cetuximab - neutral

Other

- Individuals should be monitored for hypersensitivity for sixty minutes after finishing the cetuximab infusion. Do not administer other chemotherapy during this period.

- The rate of administration of cetuximab must not exceed 5mg/min for the first infusion (minimum 120 minutes). If well tolerated subsequent infusions may be given at a rate of 10mg/min (minimum 60 minutes).

- The cetuximab should be administered before radiotherapy is given, when used concurrently. The first dose of cetuximab (cycle 1) may be started one week prior to the radiotherapy starting.

Additional Therapy

- 30 minutes prior to cetuximab infusion;

  - chlorphenamine 10mg intravenous
  - dexamethasone 8mg oral or equivalent dose intravenous
  - H_2 antagonist according to local formulary choice and availability
  - paracetamol 1000mg oral

- Antiemetics

  As take home medication

  - metoclopramide 10mg three times a day when required oral (supply day one cycle one only and then as required)

- 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. National Institute for Health and Clinical Excellence (2008). TA145. Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck. DOH: London.
2. Bonner JA, Harari PM, Giralt J. Radiotherapy plus cetuximab for squamous cell carcinoma of the head and neck. N Engl J Med 2006; 354 (6): 567-78.

REGIMEN SUMMARY

Cetuximab RT (7 day)

Day One Cycle One

1. Chlorphenamine 10mg intravenous

2. Dexamethasone 8mg oral or equivalent dose intravenous

3. Paracetamol 1000mg oral
   Administration Instructions
   Please check if the patient has taken paracetamol. The maximum dose is 4000mg in every 24 hours

4. H_2 antagonist according to local formulary choice and availability
   Administration Instructions:
   Administer according to local formulary choice and availability one of the following 30 minutes prior to chemotherapy;
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only
   - ranitidine 50mg intravenous once only

   There are stock shortages of H_2 antagonists. The administration may proceed without these agents being given unless there is a specific instruction from the prescriber in the ARIA journal that a H_2 antagonist must be administered. Many Trusts do not administer an H_2 antagonist from cycle three onwards.
   They have been left in the ARIA protocols so that decisions can be made on an individual Trust and patient basis.

5. Cetuximab 400mg/m^2 over 120 minutes intravenous infusion

6. Metoclopramide 10mg three times a day when required for the relief of nausea oral*

Cycle Two Onwards

7. Chlorphenamine 10mg intravenous bolus

8. Dexamethasone 8mg oral or equivalent intravenous bolus

9. Paracetamol 1000mg oral
   Administration Instructions
   Please check if the patient has taken paracetamol. The maximum dose is 4000mg in every 24 hours

10. H_2 antagonist according to local formulary choice and availability
    Administration Instructions:
    Administer according to local formulary choice and availability one of the following 30 minutes prior to chemotherapy;
    - famotidine 20mg oral once only
    - nizatidine 150mg oral once only
    - ranitidine 150mg oral once only
    - ranitidine 50mg intravenous once only

    There are stock shortages of H_2 antagonists. The administration may proceed without these agents being given unless there is a specific instruction from the prescriber in the ARIA journal that a H_2 antagonist must be administered. Many Trusts do not administer an H_2 antagonist from cycle three onwards.
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11. Cetuximab 250mg/m^2 over 60 minutes intravenous infusion

*The metoclopramide will only appear on day one cycle one. If further supplies are required they should be added from the support directory of Aria as necessary.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	October 2020	Update of premedication due to shortage of IV ranitidine. IV ranitidine changed to H_2 antagonist according to local formulary choice and availability Dose banding updated Coding removed	Arum Shortland Pharmacist	Dr Deborah Wright Pharmacist
1	Dec 2014	None	Dr Deborah Wright Pharmacist	Dr S Ramkumar 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.