

Chemotherapy Protocol

COLORECTAL CANCER

CETUXIMAB (7 day)

This regimen may require funding

Regimen

- Colorectal Cancer – Cetuximab (7 day)

Indication

- Metastatic colorectal cancer positive for the wild type KRAS genotype and that has progressed after failure of oxaliplatin and irinotecan based therapy or who are intolerant to these agents.
- WHO performance status 0, 1, 2

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

- Prior to starting therapy confirm a positive wild type KRAS status
- 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 $1.5 \times 10^9/L$ |
| Platelets | equal to or more than $100 \times 10^9/L$ |

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

For haematological toxicity, if the neutrophil count is less than $1.5 \times 10^9/L$ or the platelet count less than $100 \times 10^9/L$, delay treatment until these levels are achieved. The decision to continue treatment should be made at the consultant's discretion.

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 acniform 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/m² and 150mg/m² 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 (12 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/m)

[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 10mg/min. The first infusion is given over 120 minutes. If this infusion rate is well tolerated subsequent infusions may be given over 60 minutes

[Additional Therapy](#)

- 30 minutes prior to cetuximab infusion;
 - chlorphenamine 10mg intravenous

- dexamethasone 8mg oral or intravenous
- H₂ 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 H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed

References

1. Cunningham D, Humblet Y, Siena S et al. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan refractory metastatic colorectal cancer. N Engl J Med 2004; 351: 337-335.

REGIMEN SUMMARY

Cetuximab (7 day)

Day One Cycle One

1. Chlorpheniramine 10mg intravenous
2. Dexamethasone 8mg oral or 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. H₂ 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;

- Ranitidine 50mg intravenous once only
- Famotidine 20mg oral once only
- Nizatidine 150mg oral once only
- Ranitidine 150mg oral once only

If there is no stock of these products due to national shortages treatment may proceed without the H₂ antagonist provided there is no instruction in the ARIA journal indication the patient **must have** H₂ antagonist treatment.

All infusion related reactions must be recorded in the ARIA journal and reported to the appropriate consultant. Many Trusts do not administer an H₂ 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/m² over 120 minutes intravenous infusion
6. Metoclopramide 10mg three times a day when required for the relief of nausea oral*

Cycle Two Onwards

1. Chlorpheniramine 10mg intravenous
2. Dexamethasone 8mg oral or 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. H₂ 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;

- Ranitidine 50mg intravenous once only
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5. Cetuximab 250mg/m² 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 |
|---------|--------------|--|--------------------------------|---|
| 1.2 | 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 Coding removed Dose banding updated | Arum Shortland Pharmacist | Dr Debbie Wright Pharmacist |
| 1.1 | May 2014 | Header changed Toxicity removed Bolus removed from supportive therapies Metoclopramide dose changed Disclaimer added | Dr Debbie Wright Pharmacist | Donna Kimber Pharmacy Technician |
| 1 | Feb 2012 | None | Dr Debbie Wright Pharmacist | Dr Tim Iveson 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 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.