

## Chemotherapy Protocol

### COLORECTAL CANCER

#### IRINOTECAN

##### Regimen

- Colorectal Cancer– Irinotecan

##### Indication

- Second line treatment of advanced colorectal cancer
- WHO performance status 0, 1
- Palliative intent

##### Toxicity

Drug	Adverse Effect
Irinotecan	Acute cholinergic syndrome, diarrhoea (may be delayed), myelosuppression

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

##### Monitoring

##### *Drugs*

- FBC, U&E's and LFT's prior to each cycle

##### 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*

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

If the neutrophils are less than  $1.5 \times 10^9/L$  and/or the platelets are less than  $100 \times 10^9/L$  then delay treatment for 7 days. If the counts recover at this time restart the irinotecan at 80% of the original dose. If a 14 day delay is required to allow counts to recover or

there are two separate delays of 7 days during treatment consider reducing the dose of irinotecan to 50% of the original dose or stopping treatment.

This is one of the few regimens where asymptomatic low nadir neutrophil counts are an indication for dose modification. Where this figure is less than  $0.5 \times 10^9/L$  or where there has been an episode of febrile neutropenia the subsequent irinotecan dose should be reduced to 80% of the original dose.

### *Hepatic Impairment*

Drug	Bilirubin $\mu\text{mol/L}$	Dose
Irinotecan	less than 26	350mg/m <sup>2</sup>
	26 - 51	200mg/m <sup>2</sup>
	more than 51	Clinical decision

### *Renal Impairment*

Drug	Dose (% of original dose)
Irinotecan	Dose reduction probably not required

### *Other Toxicities*

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. Dose limiting toxicities include diarrhoea, abdominal pain, emesis, stomatitis and palmer-plantar erythrodysesthesia among others.

Irinotecan is associated with a number of toxic reactions. The next cycle of treatment should not be administered until all toxicities have resolved to 0 or 1 of the National Cancer Institute Common Toxicity Criteria scale (NCI-CTC). Diarrhoea must have resolved completely. Where a NCI-CTC grade 3 or above event has occurred the irinotecan dose must be reduced to 80% of the original dose.

### Regimen

#### **21 day cycle for 8 cycles**

Drug	Dose	Days	Administration
Irinotecan	350mg/m <sup>2</sup>	1	Intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes

### Dose Information

- Irinotecan will be dose banded as per the CSCCN agreed bands
- The maximum daily dose of irinotecan is 700mg

- In those individuals who have had prior radical radiotherapy to the pelvis or who are 70 years of age and above or who have a performance status of 2 consider using irinotecan 300mg/m<sup>2</sup> (maximum dose 600mg).

### Administration Information

#### *Extravasation*

- Irinotecan - irritant

### Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy

- ondansetron 8mg oral or intravenous
- dexamethasone 8mg oral or intravenous

As take home medication

- dexamethasone 4mg twice a day for 3 days oral
- metoclopramide 10mg three times a day when required oral
- Subcutaneous atropine 250mcg immediately prior to irinotecan for the prevention of acute cholinergic syndrome. A further 250mcg subcutaneous dose may be given to relieve cholinergic symptoms if they develop.
- Oral loperamide 2mg every two hours once first liquid stool appears and continue until 12 hours after the last liquid stool. Do not use for longer than 48 hours.
- Consider oral ciprofloxacin 500mg twice a day where diarrhoea continues for more than 24 hours. Review the patient before starting this treatment.
- Gastric protection with a proton pump inhibitor or a H<sub>2</sub> antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

### Coding

- Procurement – X70.5
- Delivery – X72.3

### References

1. Kim GP, Sargent DJ, Mahoney MR et al. Phase III non-inferiority trial comparing irinotecan with oxaliplatin, fluorouracil and leucovorin in patients with advanced colorectal cancer previously treated with fluorouracil. J Clin Oncol (2008); 27 (17); 2848-2854.

## REGIMEN SUMMARY

### Day 1

1. Atropine 250microgram subcutaneous for the prevention of irinotecan associated cholinergic symptoms
2. Dexamethasone 8mg oral or intravenous
3. Ondansetron 8mg oral or intravenous
4. Irinotecan 350mg/m<sup>2</sup> intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes
5. Atropine 250microgram subcutaneous when required for the treatment of irinotecan associated cholinergic symptoms

### Take Home Medicines

6. Dexamethasone 4mg twice a day for 3 days oral starting the day after chemotherapy
7. Metoclopramide 10mg three times a day when required oral

## DOCUMENT CONTROL

Version	Date	Amendment	Written/Amended By	Approved By
1.2	May 2014	Header changed Intravenous added to supportive treatments Metoclopramide dose changed to 10mg Atropine added as a standard treatment prior to irinotecan Dexamethasone TTO clarified Disclaimer added	Dr Debbie Wright Pharmacist	Donna Kimber Pharmacy Technician
1.1	January 2013	Document control table added. Duration of infusion of irinotecan changed from 30 minutes to 90 minutes in the regimen and regimen summary. OPCS procurement code changed from X71.1 to X70.5. Adverse effects tabulated Liver / kidney impairment recommendation tabulated Dose table tabulated Atropine dose changed to 250mcg. Antiemetics changed to oral. Twice daily changed to twice a day. Mouthwashes changed	Rebecca Wills Pharmacist	Dr Debbie Wright Pharmacist
1	August 2010	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.