IRINOTECAN MONOTHERAPY

Second line use in advanced gastro-oesophageal cancer, for patients who are not eligible for a clinical trial.

Drug/Dosage:	Irinotecan	180mg/m^2	IV D1
Administration:	In 250ml 0.9% Sodium Chloride over 30 - 90 minutes		
Frequency:	2 weekly cycle Up to 8 cycles if still responding		
Main Toxicities:	myelosuppression; diarrhoea (see Comments); alopecia; cholinergic syndrome – during administration; ovarian failure/infertility		
Anti-emetics:	highly emetogenic		
Extravasation:	non-vesicant		
Regular Investigations:	FBC	D1	
	LFTs	D1	
	U&Es	D1	
	CT scan	after 4 cycles	

Comments:

Cholinergic syndrome can be controlled by giving Atropine 0.25mg subcutaneously at time of irinotecan administration. Should the syndrome develop, a further dose of atropine may be given.

Diarrhoea may occur within 30 – 90 minutes of infusion, or may be delayed. Once a liquid stool occurs, loperamide 4mg should be taken immediately, followed by one tablet 2 hourly for at least 12 hours, and for 12 hours following the last liquid stool. Patients should be instructed to drink large volumes of water / electrolytes. Concomitant fever or vomiting will require hospitalisation for IV hydration.

If diarrhoea persists for 24 hours despite the loperamide, a prophylactic course of ciprofloxacin 250mg po bd for 7 days should be started.
After 48 hours of persistent diarrhoea, the patient should be hospitalised for parenteral support, further management of diarrhoea and review of treatment.

N.B. Loperamide and ciprofloxacin must be dispensed to patients on discharge, and patient should be given information leaflet and counselled to ensure they know how and when to use them.

Ciprofloxacin prophylaxis (250mg po bd) should be commenced in patients with neutrophils < 0.5 x 10^9/l, even in the absence of diarrhoea. Patients who develop severe neutropenia are especially at risk of infection if they are also suffering from diarrhoea.

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Version: 1	Approved by Consultant: Dr G Middleton
Supersedes: None	Date: 17.1.12
Prepared by: S Taylor	Checked by: C Tucker

Dose Modifications:

Haematological Toxicity:	Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l	Delay for 1 week. Repeat FBC. If recovered, resume treatment.

If more than 1 delay, or 1 delay of ≥ 2 weeks occurs, reduce irinotecan dose by 20% for subsequent cycles.
If a further delay for myelotoxicity occurs despite a 20% dose reduction, a further 20% dose reduction may be made.

Renal Impairment: If CrCl < 30ml/min, irinotecan should be used with caution, as there is no information in this setting.

CrCl (ml/min)	Irinotecan Dose
< 30	Give 50% dose

Hepatic Impairment:

Liver Function	Irinotecan Dose
Bilirubin 1.5 – 3 x ULN **or** ALP > 5 x ULN	Give 50% dose
Bilirubin > 3 x ULN	Omit irinotecan

Diarrhoea: For management of diarrhoea, see "Comments" section.

If diarrhoea from the previous cycle, even if not severe, has not resolved by the time the next cycle is due, delay 1 week. If there is more than 1 delay for this reason, reduce the irinotecan dose by 20% for subsequent cycles.

After an episode of severe diarrhoea (Grade 3-4), delay chemotherapy until full recovery, then reduce the irinotecan dose by 20% and continue at the lower dose for subsequent cycles unless further toxicity occurs.

References: Park, SH et al; Proceedings ASCO 2011; abstract 4004