IRINOTECAN & CAPECITABINE (Xeliri)

An option for advanced or metastatic colorectal cancer in patients who are eligible for irinotecan-based chemotherapy
This regimen should not be used in combination with cetuximab

Drugs/Dosage:	Irinotecan	200mg/m^2	IV	Day 1
	Capecitabine	800mg/m^2	PO	BD on Days 1 – 14, then 7 days rest

Administration: Irinotecan in 250ml 0.9% sodium chloride over 60-90 minutes.
Capecitabine tablets should be swallowed with water within 30 mins after a meal.

Frequency: 3 weekly cycle, up to 8 cycles if still responding

Main Toxicities: myelosuppression; diarrhoea (see Comments); alopecia; mucositis; cholinergic syndrome – during administration; hand-foot syndrome (PPE); cardiotoxicity (uncommon); ovarian failure/infertility

Anti-emetics: Day 1 - highly emetogenic; Day 2 – Day 14 - mildly emetogenic

Extravasation: irinotecan is a non-vesicant

Regular Investigations:	FBC	Day 1
	LFTs & U&Es	Day 1
	CEA	every 6 weeks
	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 loperamide 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.

Dose Modifications:

Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 109/l or Diarrhoea ≥ Grade 1	Delay for 1 week. Repeat FBC. If recovered, proceed with treatment. If > 1 delay, or delay of ≥ 2 weeks, reduce irinotecan and capecitabine doses by 20% for subsequent cycles.

Reason for Update: indication wording updated	Approved by Consultant: Dr S Cummins
Version: 2	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 1	Date: 8.2.17
Prepared by: S Taylor	Checked by: C Tucker

Non-Haematological Toxicities:

Note that severe diarrhoea and/or severe mucositis early in capecitabine treatment can be the first presenting toxicity due to DPD enzyme deficiency, in which case potentially fatal neutropenia can quickly follow.

Toxicity due to capecitabine administration may be managed symptomatically and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced, it should not be increased at a later time.

Doses of capecitabine omitted for toxicity are not replaced or restored. Instead the patient should resume the planned treatment cycle.

Capecitabine Dose Adjustment Guidelines according to CTC

These dosing guidelines are for side effects including diarrhoea, vomiting, mucositis and PPE.

Common Toxicity Criteria	During Course of Therapy	Dose adjustment for next cycle (% of start dose)
Grade 1	Maintain dose level	Maintain dose level
Grade 2: 1st appearance	Interrupt until resolved to Grade 0–1*	Give 100% dose
Grade 2: 2nd appearance	Interrupt until resolved to Grade 0–1*	Give 75% dose
Grade 2: 3rd appearance	Interrupt until resolved to Grade 0–1*	Give 50% dose
Grade 2: 4th appearance	Discontinue treatment permanently	
Grade 3: 1st appearance	Interrupt until resolved to Grade 0–1*	Give 75% dose
Grade 3: 2nd appearance	Interrupt until resolved to Grade 0–1*	Give 50% dose
Grade 3: 3rd appearance	Discontinue treatment permanently	
Grade 4: 1st appearance	Discontinue permanently **or,** only with Consultant approval, interrupt until resolved to Grade 0-1	Give 50% dose (Consultant approval only)

***** For Grade ≥ 2 **diarrhoea**, capecitabine should not be restarted until resolved to Grade 0-1 **and** no loperamide has been given for 24 hours.

Cardiotoxicity: Exercise caution in patients with prior history of coronary heart disease, arrhythmias or angina.

Renal Impairment: Before every cycle, creatinine clearance should be calculated using Cockcroft and Gault. If borderline, an EDTA may be requested.

CrCl (ml/min)	Capecitabine Dose	Irinotecan Dose
> 50	Give 100% dose	Give 100% dose
30 – 50	Give 75% dose	Give 100% dose
< 30	Omit	Use with caution – no info

Hepatic Impairment:

Liver Function	Irinotecan Dose	Capecitabine Dose
Bilirubin 1. 5 –3 x ULN **or** ALP > 5 x ULN	Give 50% dose	-
*Bilirubin > 3x ULN	Omit irinotecan	-
*Bilirubin > 3x ULN **or** ALT / AST > 2.5 x ULN	-	Omit capecitabine

*Bilirubin > 3 x ULN: Note that significantly impaired hepatic function may be a sign of disease progression and require cessation of, or change in, treatment. **Always discuss deteriorating organ function with consultant**.

References: Reinacher-Schick et al; JCO 2008; 26 (15S): 4030