Systemic Anti Cancer Treatment Protocol

Irinotecan Single Agent 2-weekly or 3-weekly

PROTOCOL REF: MPHACOLIRI
(Version No: 1.0)

Approved for use in:

Advanced colorectal cancer second or third line

Contraindications to or progressed on fluoropyrimidine therapy

PS 0-1

Second line treatment of locally advanced and metastatic gastric / gastro-oesophageal junction adenocarcinoma

Dosage:

2-Weekly

Drug	Dosage	Route	Frequency
Irinotecan	180mg/m^2	IV	Every 14 days

OR

3-Weekly

Drug	Dosage	Route	Frequency
Irinotecan	350mg/m^2	IV	Every 21 days

Consider reducing the dose to 300mg/m^2 for patients over 70 years

Supportive treatments:

Domperidone 10mg oral tablets, up to 3 times a day or as required

Loperamide 4mg immediately after first liquid stool followed by 2mg every 2 hours for at least 12 hours

Extravasation risk:

Irritant – Follow trust/network extravasation policy.

Administration:

2-Weekly

Day	Drug	Dosage	Route	Diluent and Rate
1	**Dexamethasone** 30 mins prior to chemotherapy	8mg	PO	
1	**Ondansetron** 30 mins prior to chemotherapy	16mg	PO	
1	**Atropine**	600 micrograms	SC	Always prior to irinotecan
1	**Irinotecan**	180mg/m^2	IV	250mL Glucose 5% IV infusion over 60 to 90 minutes

OR

3-Weekly

Day	Drug	Dosage	Route	Diluent and Rate
1	**Dexamethasone** 30 mins prior to chemotherapy	8mg	PO	
1	**Ondansetron** 30 mins prior to chemotherapy	16mg	PO	
1	**Atropine**	600 micrograms	SC	Always prior to irinotecan
1	**Irinotecan**	350mg/m^2	IV	250mL Glucose 5% IV infusion over 60 to 90 minutes

Administer cycle 1 over 90 minutes, and then cycle 2 onward over 60 minutes if tolerated.

Give for 6 cycles and review, continue therapy subject to patient choice, tolerability, and response

Contra – indicated - chronic inflammatory bowel disease and/or bowel obstruction
Discontinue treatment if PS deteriorates to >2

Main Toxicities:

Myelosuppression, diarrhoea, alopecia, cholinergic syndrome during administration, ovarian failure/infertility

Cholinergic syndrome: Diarrhoea, sweating, blurred vision, dizziness within first 24 hours after irinotecan.

Diarrhoea: This may occur within 30-90 minutes of the infusion or may be delayed. Ensure patients are dispensed loperamide and that they know how and when to take them

Neutropenia with diarrhoea is a life threatening complication and requires immediate admission and management.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Medical Assessment	X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
CT scan	X					
Informed Consent	X					
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if all apply:-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Delay 1 week on day 1 if any apply:-

ANC ≤ 0.9 x 10^9/L	Platelets ≤ 99 x 10^9/L

If platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need assessment and chemotherapy dose reduction as detailed below.

Always allow full recovery before proceeding with treatment. Doses should be adjusted according to the worst degree of adverse effect over the preceding administration.

Toxicity	Irinotecan Dose
Grade 4 neutropenia or Grade 3 febrile neutropenia or Grade 3 / 4 diarrhoea or Grade 4 thrombocytopenia or leucopenia	Delay treatment until recovery and reduce next dose by 25%

Non-haematological toxicity

Renal	Calculate CrCl using Cockroft and Gault formula at baseline and before each cycle and adjust dose according to table. **Creatinine Clearance (mL/min)** / **Irinotecan Dose** <30 / Use with caution No information on using irinotecan in severe renal impairment – discuss with consultant

<table>
<tr><td>Hepatic</td><td>
<table>
<tr><th>Liver function</th><th>Irinotecan dose</th></tr>
<tr><td>Bilirubin 1.5 – 3 x ULN or ALP > 5 x ULN</td><td>50%</td></tr>
<tr><td>Bilirubin > 3 x ULN</td><td>50%</td></tr>
<tr><td>Bilirubin > 3 x ULN or
ALT/AST > 2.5 x xULN</td><td>–</td></tr>
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Note that significantly impaired hepatic function might be a sign of disease progression and require cessation or change of treatment. Always discuss deteriorating organ function with consultant</td></tr>
<tr><td>Diarrhoea within first 24 hours</td><td>This is likely to be caused by an acute cholinergic syndrome, do not take loperamide within the first 24 hours. Advise patient to contact chemotherapy team and consider repeat dose of atropine</td></tr>
<tr><td>Delayed diarrhoea (after 24 hours post irinotecan)</td><td>Once a liquid stool occurs loperamide 4mg should be taken immediately, followed by 2mg every 2 hours for at least 12 hours, and for 12 hours following the last liquid stool. Patients should be instructed to drink large volumes of water or electrolytes.
Do not continue high dose loperamide for longer than 48 hours
Any concomitant fever or vomiting will require hospitalisaton for rehydration
If diarrhoea persists for 24 hours despite loperamide, start ciprofloxacin 250mg orally bd for 7 days.
If diarrhoea persists after 48 hours then patients should be hospitalised for further management and treatment review.
Do not use loperamide prophylactically even if delayed diarrhoea occurred in previous cycles.
For first episode of diarrhoea grade 2 or higher, delay treatment for 1 to 2 weeks until completely resolved* and reduce dose of irinotecan by 20% in subsequent cycles. (see table below for capecitabine adjustment)</td></tr>
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References:

Cunningham, D et al, Lancet 1998; Vol 352: 1413 – 1418

Rougier et al, Lancet 1998; Vol 352; 1407 – 1412

Electronic Medicines Compendium, Irinotecan

https://www.medicines.org.uk/emc/medicine/27592