FOLFOXIRI

Indication

Metastatic colorectal cancer

Regimen details

Drug	Fluid	Time
Irinotecan 165mg/m^2	250ml sodium chloride 0.9%	30 minutes
Oxaliplatin 85mg/m^2	500ml glucose 5%	2 hours
Folinic Acid 350mg	250ml glucose 5%	2 hours
5 Fluorouracil 3200mg/m^2		48 hours in infusor pump

Nb Atropine 250mcg *must* be prescribed before treatment commences. This is only to be administered in the event of a cholinergic reaction unless the patient has experienced such a reaction in a previous cycle.

Cycle frequency

Repeat every 2 weeks until disease progression or unacceptable toxicity

Administration

Patient needs central line insertion. Assess for PICC prior to commencement of treatment
Administer atropine 0.25mg s/c if patient experiences cholinergic reaction with first cycle

Administer oxaliplatin concurrently with folinic acid

Warning: administering irinotecan and folinic acid concurrently in the same line may result in precipitation

Emetogenicity

Moderate

Additional supportive medication

All patients must have access to loperamide with the advice to take 4mg at the onset of diarrhoea and to continue taking 2mg every 2 hours for at least 12 hours to a maximum of 48 hours (up to a maximum of 24mg/24 hours).

Pegfilgrastim 6mg given 24 hours after pump removal

Investigations – pre first cycle

FBC
U&E
LFT
Bone
CEA
CT Scan
Coagulation profile
DPYD Screen

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism- avoid use in patients with known DPD deficiency

Investigations –pre subsequent cycles

FBC, U&E, LFTs every cycle
Calcium and CEA every 2nd cycle
The liver function tests may be retrospectively looked at (i.e. after the chemotherapy treatment) **unless** they are known to be abnormal then they need to be repeated the day before so that the results are available pre-chemotherapy.
Consultation every 2nd cycle

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophil count	≥ 1.5 x 10^9/L (1.2-1.5 x 10^9/L contact **consultant**)
Platelet count	≥ 100 x 10^9/L
Hb	≥ 95 g/L
Bilirubin	≤ 1.5 x ULN
Alk Phos	< 5 x ULN
Creatinine clearance	> 50mL/min

If only Hb is low (below 95g/dl) please contact doctor to arrange for blood transfusion but continue with chemotherapy

Dose modifications

Renal impairment

Creatinine Clearance (ml/min)	**Irinotecan dose**	**Oxaliplatin dose**	**5FU dose**
>50	100%	100%	100%
30-50	Unclear guidance discuss	100%	100%
<30	Omit	Omit	80%

Hepatic impairment

Irinotecan and metabolites are cleared by biliary excretion
Delayed clearance in cholestasis

Bilirubin	**ALP**	**Irinotecan dose**	**Oxaliplatin**	**5FU dose**
<1.5 x ULN **and**	≤ 5 x ULN	100%	100%	100%
1.5-3 x ULN **or**	>5 x ULN	50%	100%	100%
>3 x ULN	any	Omit	50%	50%

Haematological toxicity

Grade I/II ANC No dose reduction
Grade III/IV Delay until recovered then proceed with 20% Irinotecan, oxaliplatin and 5FU reduction
If delay >1 week reduce oxaliplatin, 5FU and irinotecan dose by 20%.

Continue at reduced dose for subsequent cycles unless other toxicity occurs
If further delays for bone marrow suppression occur despite a 20% dose reduction consider further 20% dose reduction

Diarrhoea

Immediate (within 24 hours)	Incidence low due to use of atropine pre-med	Further dose of atropine 250 mcg stat
Delayed (>24 hours after irinotecan up to any time before next cycle)	Initial treatment	Treat early with high dose loperamide (up to a max of 24mg/24 hr)
	Lasts >24 hours	Add ciprofloxacin 500mg bd
	Lasts >48 hours	If >48 hours or symptoms of dehydration admit for rehydration and supportive management
	Grade 3-4	Manage as above, then delay further treatment until recovery then resume at Irinotecan 80% dose 5FU 80% dose
	Unresolved before next cycle	Delay 1 week

Patients presenting with diarrhoea must be carefully monitored until the symptoms have disappeared as a rapid deterioration can occur

Other dose modifications should be made as per the following table

Toxicity grade	**1st occurrence**	**2nd occurrence**	**3rd occurrence**	**4th occurrence**
0-1	100%	100%	100%	100%
2	Delay then 100%	Delay then 75%	Delay then 50%	Discontinue
3	Delay then 75%	Delay then 50%	Discontinue	
4	Delay then 50%	Discontinue		

Any delays should be until toxicity has resolved to grade 0-1

Hand foot syndrome ≥ grade 2: 20% dose reduction of 5FU

Side effects

Tiredness, diarrhoea and abdominal pain, acute cholinergic syndrome, nausea and vomiting, sore mouth/stomatitis, poor appetite, myelosuppression and thrombocytopenia, hand foot syndrome, cardiotoxicity (including coronary artery spasm, angina and tachycardia), ocular toxicity (excessive lacrimation, visual change, photophobia), infusion reactions, veno-occlusive disease, hair loss, neurotoxicity, ovarian failure/infertility transient cerebellar syndrome, confusion, thrombophlebitis

THIS PROTOCOL HAS BEEN DIRECTED BY DR LAU, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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