Lancashire & South Cumbria Cancer Network
Systemic Anticancer Treatment Protocol

Drug regimen
mFOLFIRINOX

Indications for use
Adjuvant pancreatic cancer (3-12 weeks post op. Performance status 0-1)

Regimen

DRUG	FLUID	TIME	
Oxaliplatin 85mg/m²	500mls 5% Glucose	2 hours	Administered concurrently
Folinic Acid 350mg	250mls 5% Glucose	2 hours	
Irinotecan 150mg/m^2	250ml NaCl 0.9%	90 minutes	
5-Fluorouracil 2400mg/m^2		46 hours in infusor pump	

Regimen to be repeated every 2 weeks for 12 cycles

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.

Investigation prior to initiating treatment
FBC
U&Es
Mg
LFT
CT Scan
Ca19-9 <180

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle). Patients require DPD testing prior to administration. Dose adjustments should be made in accordance with local DPD policy.

Caution
Oxaliplatin should always be administered before fluoropyrimidines
Avoid cold drinks for 2-3 days after Chemotherapy

Investigations and consultations prior to each cycle
FBC
U&Es
Mg
LFT (every 4 weeks)
CT Scan (after 6 cycles)

Acceptable levels for treatment to proceed (if outside these delay one week or contact consultant)
Acceptable blood range: Neutrophils ≥1.5, platelets ≥100, Hb ≥ 10g/dl, Bilirubin <1.5xULN
If Neutrophils 1.2 – 1.5 contact **consultant**

If U&E abnormal check with consultant

Side Effects
Myelosuppression; mucositis; diarrhoea; neurotoxicity; allergic reactions; coronary artery spasm; palmar/plantar erythema; ovarian failure/infertility

Dose Modification Criteria

Haematological

	Irinotecan	**Oxaliplatiin**	**5-Fluorouracil**
1st occurrence of low neutrophils, febrile neutropenia*, or neuts < 0.5 for > 7 days	Reduce to 80% dose	Maintain full dose of Oxaliplatin	No change
2nd occurrence	Maintain reduced dose	Reduce to 75%	No change
3rd occurrence	Stop treatment		

*For any febrile neutropenia or a 2nd episode of low neutrophils, G-CSF prophylaxis should also be initiated with subsequent cycles, starting on Day 5 of each cycle.

Thrombocytopenia

	Irinotecan	**Oxaliplatin**	**5-Fluorouracil**
1st occurrence of low platelets	Maintain full dose	Reduce to 75%	Reduce 5FU to 75% of original dose
2nd occurrence	Reduce to 80% dose	Maintain reduced dose	Maintain reduced dose
3rd occurrence	Stop treatment		

Renal Impairment:

GFR (ml/min)	**Irinotecan**	**Oxaliplatin**	**5-FU**
>50	Full	Full	Full
30-49	50% Dose	Full	80% dose
<30	Regimen may not be appropriate		

Hepatic Impairment:

Bilirubin	**Irinotecan**	**Oxaliplatin**	**Fluorouracil**
<1.5 –3 x ULN	Clinical decision	Full dose	50-75% dose reduction
> 3x ULN	Omit	50% dose	Omit

Diarrhoea:
If diarrhoea from the previous cycle, even if not severe, has not resolved (without loperamide for at least 24 hours) by the time the next cycle is due, delay 1 week.

1st occurrence of grade 3-4 diarrhoea, or diarrhoea + fever: Reduce irinotecan to 80%, maintain full dose oxaliplatin and 5FU,

2nd occurrence of above**:** Maintain irinotecan reduced dose, reduce to oxaliplatin to 75%, 5FU reduce to 75% of previous dose

3rd occurrence: Stop treatment

Neurological Toxicity:

Toxicity	Duration of toxicity 1-7 days	Duration of toxicity >7 days	Persistent between cycles
Cold-related dysaesthesia	No reduction	No reduction	Withhold oxaliplatin until recovery then restart at 60mg/m^2 Omit oxaliplatin if recurs
Paraesthesia without pain	No reduction	No reduction	Withhold oxaliplatin until recovery then restart at 60mg/m^2 Omit oxaliplatin if recurs
Paraesthesia with pain or functional impairment	No reduction	Reduce to 60mg/m^2 on subsequent cycles Omit oxaliplatin if recurs	Omit oxaliplatin Discuss with consultant
Acute laryngopharyngeal dysaesthesia	Increase infusion duration to 6 hrs.		

Stomatitis:
If mouth ulcers ≥ Grade 2 develop, reduce the 5FU doses (bolus and infusion) by 25% for subsequent cycles unless further toxicity occurs

Specific Information on Administration
Patient needs central line insertion. Assess for PICC prior to commencing treatment
Oxaliplatin should not mix with sodium chloride.
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. Nb this exceeds the maximum recommended dose of loperamide

References
Conroy T et al. (2018) FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer N Engl J Med; 379:2395-2406

THIS PROTOCOL HAS BEEN DIRECTED BY DR MITCHELL LEAD CLINICIAN FOR UPPER GI CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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