FOLFIRINOX metastatic

INDICATION (ICD10) C25
1. Advanced pancreatic cancer (unlicensed). PS 0, 1

REGIMEN
Day 1 Premedication: Atropine 250mcg subcutaneously 30 minutes prior to treatment
IRINOTECAN 180mg/m^2 in #ml diluent IV infusion over 30 minutes
CALCIUM FOLINATE 350mg in glucose 5% infusion over 2 hours concurrently with oxaliplatin via a Y site placed immediately before the injection site
OXALIPLATIN 85mg/m^2 in #ml glucose 5% IV infusion over 2 hours
FLUOROURACIL 400mg/m^2 IV bolus
FLUOROURACIL 2400mg/m^2 continuous IV infusion over 46 hours

diluent and diluent volume for dose prescribed as per national standardised product specification or licensed dose

NB Calcium folinate (calcium leucovorin) is not the same as calcium levofolinate.
Calcium levofolinate is a single isomer of folinic acid and the dose is generally half that of calcium folinate.

CYCLE FREQUENCY AND NUMBER OF CYCLES
Every 14 days for 12 cycles (may continue at clinician discretion)

ANTI-EMETICS
Highly emetogenic day 1
Low emetogenic risk day 2

CONCURRENT MEDICATION REQUIRED

Fluorouracil	Mouth and bowel support eg Loperamide, benzydamine mouthwash
Irinotecan	Ensure premedication atropine given 30 minutes prior to treatment
Oxaliplatin	Flush with glucose 5% before and after infusion
GCSF	GCSF to be added if delays / neutropenic sepsis.

EXTRAVASATION AND TYPE OF LINE / FILTERS
Fluorouracil – inflammitant
Irinotecan - irritant
Oxaliplatin – exfoliant

Central line (single lumen)

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Serum creatinine
DPYD (dihydropyrimidine dehydrogenase) test
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Fluorouracil	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function (consider ECG at baseline). Special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil. Stomatitis
Irinotecan	Acute cholinergic syndrome (including diarrhea and delayed diarrhoea, abdominal pain, hypotension, dizziness, malaise, increased salivation). Drink large volumes of fluid containing electrolytes and an appropriate antidiarrhoeal therapy - loperamide 4mg initially then 2mg every 2 hours, continuing for 12 hours after the last liquid stool (maximum of 48 hours in total).
Oxaliplatin	Peripheral sensory neuropathy and laryngeal spasm – avoid cold drinks and touching cold items

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Fluorouracil	Cimetidine slightly increases exposure to fluorouracil Metronidazole increased toxicity Phenytoin concentration increased Warfarin
Irinotecan	Aprepitant and fosaprepitant increases exposure to irinotecan. Carbamazepine decreases exposure to irinotecan, avoid. Enzalutamide, mitotane, phenobarbitone, phenytoin, primidone and rifampicin decreases exposure to irinotecan, avoid.

DOSE MODIFICATIONS

Haematological

If neutrophils <1.5x10^9/L or platelets <100x10^9/L delay 1 week, only treat when neutrophils and platelets are above these limits.
If >1 delay or 1 delay ≥2 weeks reduce all the irinotecan, oxaliplatin and fluorouracil doses to give 80% for future cycles. A further dose reduction may be made at the Clinician's discretion.

Non-haematological

Irinotecan
If patients suffer from severe diarrhoea, which required IV rehydration or neutropenic fever, consider reduction in subsequent cycles, discuss with SpR or Consultant.

Oxaliplatin
If patients develop acute laryngopharyngeal dysaesthesia infuse the next cycle over 4 hours.
If symptoms persist give 80% dose.
If persistent sensory symptoms occur, withdraw treatment

Hepatic impairment

Fluorouracil

Significantly impaired hepatic function eg bilirubin >50micromol/L may be a sign of disease progression and require cessation of, or change in, treatment. Always discuss deteriorating liver function with consultant.	
If hepatic function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected in mild and moderate (without renal impairment).	
Bilirubin >85micromol/L	not recommended

Irinotecan

Bilirubin 1.5-3xULN or ALP >5xULN	give 50% dose
Bilirubin >3xULN	not recommended

Oxaliplatin

No dose adjustment is needed.

Renal impairment

Fluorouracil

If renal function is impaired, the recommended dose can be reduced to give 50% to 70% dose, but no need for dose adjustment is expected.

Irinotecan

Not recommended in renal impairment, use with caution.

Oxaliplatin

CrCl >30ml/min	give 100% dose
CrCl <30ml/min	Dose reduce (consider 50% of original dose)

REFERENCES

1. Conroy T et al; NEJM 2011; 364: 1817–1825 (advanced)
2. Marsh, RDW et al; Cancer Med 2015; 4 (6): 853-863