

FOLFIRINOX modified adjuvant – local funding required

INDICATION (ICD10) C25

1. Adjuvant pancreatic cancer. PS 0, 1 (unlicensed) - local funding required

REGIMEN

Day 1 Premedication: Atropine 250mcg subcutaneously 30 minutes prior to treatment
 IRINOTECAN 150mg/m² 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/m² in #ml glucose 5% IV infusion over 2 hours
 FLUOROURACIL 2400mg/m² 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 6-12 cycles (review after 4 cycles)

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	Consider adding GCSF

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 10⁹/L ≥1.5 (1.0-1.5 discuss with consultant)

Platelets x 10⁹/L ≥100 (75-100 discuss with consultant)

Serum creatinine

DPYD (dihydropyrimidine dehydrogenase) test

Baseline weight and every cycle

MAIN TOXICITIES 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 $<1.5 \times 10^9/L$ or platelets $<100 \times 10^9/L$ delay 1 week, only treat when neutrophils and platelets are above these limits.

If >1 delay or 1 delay ≥ 2 weeks reduce 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. ACCORD trial