IRINOTECAN Modified de Gramont

INDICATION (ICD10) C18, C20

1. Advanced colorectal cancer.
2. High grade neuroendocrine second line treatment (local funding)
   PS 0, 1, 2

REGIMEN

Day 1 Premedication: Atropine 250mcg subcutaneously 30 minutes prior to treatment
IRINOTECAN 180mg/m^2 in 250ml sodium chloride 0.9% (or licensed dose volume) IV infusion over 30 minutes
CALCIUM LEVOFOLINATE 175mg in glucose 5% IV infusion over 30 minutes
FLUOROURACIL 400mg/m^2 IV bolus
FLUOROURACIL 2400mg/m^2 continuous IV infusion over 46 hours

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

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 14 days for 6 to 12 cycles

ANTI-EMETICS

Moderately 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

EXTRAVASATION AND TYPE OF LINE / FILTERS

Fluorouracil – inflammitant
Irinotecan - irritant

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
Ideally EDTA GFR should be used
Creatinine clearance (GFR) calculated, at the Consultants discretion
Serum creatinine
DPD 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. 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).

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 and/or the platelet count <100x10^9/L delay one week, only treat when neutrophils and platelets are above these limits.
If grade 4 neutropenia consider giving 50% irinotecan and fluorouracil in palliative disease.If >1 delay or 1 delay ≥2 weeks give 80% irinotecan and fluorouracil 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.

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.

Bilirubin >85micromol/L	not recommended

Irinotecan

Bilirubin 24-50micromol/L	give 50% dose
Bilirubin >51micromol/L	Clinical decision

Renal impairment

Fluourouracil

CrCl >30ml/min	give 100% dose
CrCl <30ml/min	consider dose reduction

REFERENCES