

IRINOTECAN Modified de Gramont

INDICATION (ICD10) C18, C20

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

REGIMEN

Day 1	Premedication 30 minutes prior to irinotecan: Atropine 250mcg subcutaneously			
	IRINOTECAN	180mg/m ²	IV infusion	#ml diluent over 30 minutes
	CALCIUM FOLINATE	350mg	IV infusion	250ml glucose 5% over 30 minutes
	FLUOROURACIL	400mg/m ²	IV bolus	
	FLUOROURACIL	2400mg/m ²	IV infusion	continuous 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 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 Neutrophils $\geq 1.5 \times 10^9/L$ (1.0-1.5x10 ⁹ /L retest and if on an upward trend then can go ahead, if no access to retest then contact Dr) Platelets $\geq 75 \times 10^9/L$	baseline and every cycle
EDTA GFR or calculated CrCl at consultant's discretion.	baseline and every cycle
Serum creatinine	baseline and every cycle
DPYD (dihydropyrimidine dehydrogenase) test	baseline
Weight	baseline 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).

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 and St John's wort decreases exposure to irinotecan, avoid. Enzalutamide, mitotane, phenobarbitone, phenytoin, primidone and rifampicin decreases exposure to irinotecan, avoid.

DOSE MODIFICATIONS

Haematological

Neutrophils $<1.5 \times 10^9/L$ and/or platelet count $<100 \times 10^9/L$	delay one week, only treat when neutrophils and platelets are above these limits.
Grade 4 neutropenia	consider giving 50% irinotecan and fluorouracil in palliative disease or GCSF support for non-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 >50 micromol/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 >85 micromol/L	not recommended

Irinotecan

Bilirubin 24-50micromol/L	give 50% dose
Bilirubin >51micromol/L	not recommended

Renal impairment

Fluourouracil

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.

REFERENCES

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Alternate cycles or team discretion
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E, calcium, & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
Dihydropyrimidine dehydrogenase (DPYD) deficiency test	X					This test is normally only required if a patient has not had capecitabine or fluorouracil in the past. However a consultant may still request this test if capecitabine or fluorouracil was not tolerated previously. The result MUST be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary.
CT scan (advanced CRC patients)	X					Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle