# IRINOTECAN OXALIPLATIN Modified de Gramont modified (FOLFOXIRI modified) (neoadjuvant) – local funding required

## INDICATION (ICD10) C18, C20

1. Neoadjuvant rectal cancer

## 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 2 hours concurrently with oxaliplatin |
| | **OXALIPLATIN** | 85mg/m$^2$ | IV infusion | #ml glucose 5% over 2 hours |
| | **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

## 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 GCSF |

## EXTRAVASATION AND TYPE OF LINE / FILTERS

Fluorouracil – inflammitant
Irinotecan - irritant
Oxaliplatin – exfoliant

Central line (single lumen)

## INVESTIGATIONS

Blood results required before SACT administration

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| FBC, U&E including $Mg^{++}$ and LFTs<br>Neutrophils ≥1.5x$10^9$/L (1.0-1.5 discuss with Dr)<br>Platelets ≥100x$10^9$/L | baseline and every cycle |
| EDTA GFR or<br>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 TOXICITES AND ADVERSE REACTIONS

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| Fluorouracil | Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds<br>Diarrhoea – treat with loperamide or codeine<br>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.<br>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<br>Metronidazole increased toxicity<br>Phenytoin concentration increased<br>Warfarin |
| Irinotecan | Aprepitant and fosaprepitant increases exposure to irinotecan.<br>Carbamazepine decreases exposure to irinotecan, avoid.<br>Enzalutamide, mitotane, phenobarbitone, phenytoin, primidone and rifampicin decreases exposure to irinotecan, avoid. |

## DOSE MODIFICATIONS

### Haematological

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

If >1 delay or 1 delay ≥2 weeks reduce 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**
This regimen would not normally be given to jaundiced patients.

Fluorouracil

| | |
|---|---|
| Significantly impaired hepatic function eg bilirubin >50micromol/L may be a sign of disease progression and require cessation of, or change in, treatment.<br>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 >51micromol/L | not recommended |

Oxaliplatin
No dose adjustment is needed.

**Renal impairment**
Fluorouracil

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|---|
| 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

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

**REFERENCES**

PRODIGY23

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 |