OXALIPLATIN Modified de Gramont

INDICATION (ICD10) C15, C16, C17, C18, C20, C24, D37

1. Metastatic and adjuvant colorectal cancer
2. Advanced gastric, oesophageal cancer
3. Metastatic duodenum
4. Adjuvant duodenum
5. Unknown primary if appropriate eg Unknown primary adenocarcinoma with poor renal function
6. Locally advanced and metastatic 2nd line biliary tract and ampullary cancers (unlicensed) (local funding required)

PS 0, 1, 2

REGIMEN

Day 1 OXALIPLATIN 85mg/m^2 in 250ml* glucose 5% IV infusion over 2 hours
CALCIUM LEVOFOLINATE 175mg in glucose 5% IV infusion over 2 hours concurrently with oxaliplatin via a Y site placed immediately before the injection site
FLUOROURACIL 400mg/m^2 IV bolus
FLUOROURACIL 2400mg/m^2 continuous IV infusion over 46 hours
*oxaliplatin doses 225mg to 395mg in 500ml glucose 5%

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 12 cycles (review after 6 cycles)

ANTI-EMETICS

Moderately emetogenic day 1
Low emetogenic risk day 2

CONCURRENT MEDICATION REQUIRED

Fluorouracil	Mouth and bowel support eg Loperamide, benzydamine mouthwash
Oxaliplatin	Flush with glucose 5% before and after infusion

EXTRAVASATION AND TYPE OF LINE / FILTERS

Fluorouracil – inflammitant
Oxaliplatin – exfoliant

Central 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
ECG (possible ECHO) required if patient has preexisting cardiac disease
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
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

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 grade 4 neutropenia consider giving 50% oxaliplatin and fluorouracil in palliative disease.
If >1 delay or 1 delay ≥2 weeks reduce all the oxaliplatin and fluorouracil doses to give 80% for future cycles. Dose reductions may be made at the Clinician's discretion.

Non-haematological

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.

Bilirubin >85micromol/L	not recommended

Renal impairment

Fluourouracil

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

Oxaliplatin

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

REFERENCES

1. FOCUS trial (CR08); MRC Colorectal Cancer Group, (Protocol Version 6)
2. Andre, T et al; NEJM 2004; 350 (23): 2343–2351 (adjuvant crc)
3. Tsavaris et al; Invest New Drugs 2005; 23 (4): 369-375 (pancreas
4. Leal, JL et al; JCO 2014; 32; suppl 3: abstract 322 (cholangio)