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	IV infusion	#ml glucose 5% IV infusion over 2 hours
	CALCIUM FOLINATE	350mg	IV infusion	250ml glucose 5% over 2 hours
	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

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 half that of calcium folinate).

CYCLE FREQUENCY AND NUMBER OF CYCLES

Adjuvant colorectal - every 14 days for 6-12 cycles
Metastatic colorectal - every 14 days usually for 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
Oxaliplatin	Flush with glucose 5% before and after infusion

ADMINISTRATION

Calcium folinate	concurrently with oxaliplatin via a Y site placed immediately before the injection site.

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 Neutrophils ≥1.5x10^9/L (colorectal 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 ≥100x10^9/L (colorectal ≥75)	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 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 (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
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

DPYD variant identified follow national or local DPD dose modification guidelines.

Haematological

Neutrophils <1.5x10^9/L and/or platelet count <100x10^9/L	delay one week, only treat when neutrophils and platelets are above these limits.
Grade 4 neutropenia	consider giving 50% oxaliplatin and fluorouracil in palliative disease.
If >1 delay or 1 delay ≥2 weeks give 80% oxaliplatin and fluorouracil for future cycles. A further dose reduction 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.	
If hepatic function is impaired, the recommended dose can be reduced to give 50% to 70% dose.	
Bilirubin >85micromol/L	not recommended

Oxaliplatin

No dose adjustment is needed.

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.

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)

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, magnesium & 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. DPD deficiency may lead to life threatening toxicity.
CT scan	X					By cycle 6, Inform consultant team if not book
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle