DOCETAXEL FLUOROURACIL OXALPLATIN (FLOT)

INDICATION (ICD10) C15, C16

1. Peri-operative use in resectable gastric or gastro-oesophageal junction adenocarcinoma. Suitable for fit patients only, with PS 0, 1 (unlicensed)

REGIMEN

Day 1 Premedication: Dexamethasone 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days
DOCETAXEL 50mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes
CALCIUM FOLINATE 350mg in glucose 5% infusion over 2 hours concurrently with oxaliplatin
OXALIPLATIN 85mg/m^2 in #ml glucose 5% IV infusion over 2 hours
FLUOROURACIL 2600mg/m^2 continuous IV infusion over 24 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 generally half that of calcium folinate.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 14 days for 4 cycles before surgery, plus a further 4 cycles after surgery.

ANTI-EMETICS

Moderately emetogenic day 1
Low emetogenic risk day 2

CONCURRENT MEDICATION REQUIRED

Docetaxel	Ensure premedication given before docetaxel. This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. Loperamide prn every docetaxel cycle
Fluorouracil	Mouth and bowel support eg Loperamide, benzydamine mouthwash
Oxaliplatin	Flush with glucose 5% after infusion
GCSF	GCSF starting at least 24 hours after chemotherapy

EXTRAVASATION AND TYPE OF LINE / FILTERS

Docetaxel – exfoliant
Fluorouracil – inflammitant
Oxaliplatin – exfoliant

Central line

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
DPYD (dihydropyrimidine dehydrogenase) test
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Docetaxel	Cutaneous reactions, peripheral neuropathy or fluid retention, hypersensitivity 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

Haematological

If neutrophils <1.5x10^9/L or platelets <100x10^9/L delay treatment, if neutrophils and platelets recover within 2 weeks then 100% dose.
If after 2 weeks delay counts have not recovered give ≤75% oxaliplatin dose and ≤75% docetaxel dose but maintain fluorouracil dose unless platelets <10x10^9/L and neutrophils <0.5x10^9/L. Discuss with Consultant.
If neutrophils 1.0-1.5x0^9/L and platelets 75-100x10^9/L Consultant decision

Non-haematological

General persistent toxicity Consultant decision

Docetaxel
Discuss dose reductions if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Oxaliplatin
If patients develop acute laryngopharyngeal dysaesthesia infuse the next cycle over 6 hours.
If symptoms persist give 80% dose.
If persistent sensory symptoms occur, withdraw treatment

Hepatic impairment

Docetaxel

ALT and/or AST >1.5xULN and ALP >2.5xULN	recommended SPC dose for 100mg/m^2 is give 75mg/m^2
Bilirubin >ULN and ALT and AST >3.5xULN with ALP >6xULN	should not be used unless strictly indicated.

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, but no need for dose adjustment is expected in mild and moderate (without renal impairment).	
Bilirubin >85micromol/L	not recommended

Oxaliplatin
No dose adjustment is needed.

Renal impairment
Fluorouracil

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.

Docetaxel
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. Al-Batran et al; Proceedings ASCO 2017; JCO 35 (supplement); abstract 4004
2. Al-Batran et al; Lancet Oncology 2016; 17: 1697–1708
3. Al-Batran et al; Annals of Oncology 2008; 19 (11): 1882–1887