OXALIPLATIN CAPECITABINE (OX)

INDICATION (ICD10) C15, C16, C17, D37

1. Advanced gastric, oesophageal cancer.
2. Unknown primary adenocarcinoma if appropriate (unlicensed)

PS 0, 1, 2

REGIMEN

Day 1	OXALIPLATIN	130mg/m^2 in 500ml* glucose 5% IV infusion over 2 hours
Days 1 to 21	CAPECITABINE	625mg/m^2 twice daily (1250mg/m^2/day) oral continuously

*oxaliplatin doses 55mg to 200mg in 250ml glucose 5%

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days 6-8 cycles

ADMINISTRATION

Tablets should be taken 12 hours apart.
Swallowed with water within 30 minutes after a meal, or dissolve in 200ml luke warm water, stir thoroughly (squash may be added if unpalatable).

ANTI-EMETICS

Moderately emetogenic day 1
Low emetogenic risk days 2 to 21

CONCURRENT MEDICATION REQUIRED

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

EXTRAVASATION AND TYPE OF LINE / FILTERS

Oxaliplatin - exfoliant

Peripheral or central line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs and creatinine 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

Capecitabine	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function. To minimise risk of anthracycline induced cardiac failure signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. All patients should be told to report any cardiac symptoms immediately and should be told to stop the medication immediately if any suspicion of cardiac problems. 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)

Capecitabine	Brivudine and analogues should be avoided Warfarin Phenytoin Allopurinol

DOSE MODIFICATIONS
Haematological

Platelets $\geq 100 \times 10^9$/L neutrophils $\geq 1.5 \times 10^9$/L	Give 100% dose
Platelets $50\text{-}100 \times 10^9$/L neutrophils $0.5\text{-}1.5 \times 10^9$/L	Stop capecitabine, delay oxaliplatin until recovery. Restart capecitabine at 100% dose give 75% oxaliplatin doses on subsequent cycles
Platelets $25\text{-}49 \times 10^9$/L neutrophils $< 0.5 \times 10^9$/L	Stop capecitabine, delay oxaliplatin and epirubicin until recovery. Restart capecitabine at 100% dose, give 50% 75% oxaliplatin doses on subsequent cycles
Platelets $< 25 \times 10^9$/L	Stop capecitabine, delay oxaliplatin until recovery. Restart capecitabine at 100% dose and oxaliplatin 75%

Non-haematological

Capecitabine

Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction).

Once the dose has been reduced it should not be increased at a later time.

When capecitabine is stopped for toxicity, the doses are omitted and not delayed.

Toxicity Grades	Dose changes within a treatment cycle	Dose adjustment for next cycle/dose (% of starting dose)
Grade 2 - 1st appearance	Interrupt until resolved to grade 0-1	100%
Grade 2 - 2nd appearance	Interrupt until resolved to grade 0-1	75%
Grade 2 - 3rd appearance	Interrupt until resolved to grade 0-1	50%
Grade 2 - 4th appearance	Discontinue treatment permanently	Not applicable
Grade 3 - 1st appearance	Interrupt until resolved to grade 0-1	75%
Grade 3 - 2nd appearance	Interrupt until resolved to grade 0-1	50%
Grade 3 - 3rd appearance	Discontinue treatment permanently	Not applicable
Grade 4 - 1st appearance	Discontinue permanently OR if physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	50%
Grade 4 - 2nd appearance	Discontinue treatment permanently	Not applicable

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

Capecitabine

Bilirubin of >3xULN or ALT/AST >2.5xULN	Interrupt Capecitabine Treatment may be resumed when bilirubin decreases to <3xULN or hepatic aminotransferases decrease to <2.5xULN.

Renal impairment

Capecitabine

CrCl (ml/min) >50	give 100% dose
CrCl (ml/min) 30-50	give 75% dose
CrCl (ml/min) <30	contraindicated

REFERENCES

1. REAL 2 trial
2. REAL 3 standard arm