

CISPLATIN CAPECITABINE

INDICATION (ICD10) C15

1. Neoadjuvant gastro-oesophageal carcinoma. (unlicensed) PS 0, 1, 2

REGIMEN

Day 1 Prehydration
 CISPLATIN 80mg/m² in 1000ml sodium chloride 0.9% IV infusion over 2 hours
 Posthydration
 Days 1 to 14 CAPECITABINE 1000mg/m² twice daily (2000mg/m²/day) oral

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 2 cycles prior to surgery

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

Highly emetogenic day 1
 Low emetogenic risk days 2 to 14

CONCURRENT MEDICATION REQUIRED

Capecitabine	Mouth and bowel support eg Loperamide, benzydamine mouthwash
Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin – exfoliant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
 FBC, U&E and LFTs every cycle
 Neutrophils x 10⁹/L ≥1.0
 Platelets x 10⁹/L ≥75
 Ideally EDTA GFR should be used
 Creatinine clearance (GFR) calculated, at the Consultants discretion
 Serum creatinine
 Baseline weight and every cycle
 DPYD (dihydropyrimidine dehydrogenase) test

MAIN TOXICITIES 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
Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Capecitabine	Brivudine and analogues should be avoided Warfarin Phenytoin Allopurinol
Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

DOSE MODIFICATIONS

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

Haematological

ANC $\geq 1 \times 10^9/L$ and/or platelets $\geq 75 \times 10^9/L$ give 100% dose

ANC $0.5-0.99 \times 10^9/L$ and/or platelets $50-74 \times 10^9/L$ OR any episode of neutropenic sepsis during the previous cycle. Stop chemotherapy until recovery. Restart with 75% dose cisplatin and capecitabine.

ANC $< 0.5 \times 10^9/L$ and/or platelets $< 50 \times 10^9/L$. Stop chemotherapy until recovery. Restart with 50% dose cisplatin and capecitabine.

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

Cisplatin

If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

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.
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Cisplatin

No need for dose adjustment

Renal impairment

Capecitabine

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

Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 50-59ml/min	give 75% dose
CrCl 40-49ml/min	give 50% dose (curative intent) not recommended (palliative intent)
CrCl <40ml/min	not recommended

REFERENCES