CISPLATIN DOCETAXEL FLUOROURACIL (TPF)

INDICATION (ICD10) C49

1. Locally advanced head and neck cancers in induction or unresectable disease. PS 0, 1, 2

REGIMEN

Day 1 Prehydration

CISPLATIN 80mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours

Posthydration

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 75mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes

FLUOROURACIL 3200mg/m^2 over 96 hours via an infusor

diluent volume for dose prescribed as per national standardised product specification

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days up to 4 cycles

ANTI-EMETICS

Highly emetogenic day 1

Low emetogenic risk days 2, 3 and 4

CONCURRENT MEDICATION REQUIRED

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.
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

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin – exfoliant

Docetaxel – exfoliant

Fluorouracil - inflammitant

Filter not required

Central line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E, Mg^{++} and LFTs every cycle

Neutrophils x 10^9/L ≥1.5

Platelets x 10^9/L ≥100

Ideally EDTA GFR should be used

Creatinine clearance (GFR) calculated, at the Consultants discretion

Serum creatinine

Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

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

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

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.
Fluorouracil	Cimetidine slightly increases exposure to fluorouracil Metronidazole increased toxicity Phenytoin concentration increased Warfarin

DOSE MODIFICATIONS

Haematological

If neutrophils <1.5x10^9/L and/or the platelet count <100x10^9/L delay the second course by one week, recheck blood count.
If satisfactory (>1.5x10^9/L and >100x10^9/L) give 75% dose cisplatin and fluorouracil
If not satisfactory delay by a further week and recheck blood count, if satisfactory (>1.5x10^9/L and >100x10^9/L) then give 75% dose cisplatin and fluorouracil with GCSF or at Clinician's give 50% dose cisplatin and fluorouracil.
If still unsatisfactory after 2 week delay chemotherapy should usually be discontinued.

In patients who experienced severe or cumulative cutaneous reactions or severe peripheral neuropathy during docetaxel therapy, the dose of docetaxel should be reduced from 75 to 60mg/m². If the patient continues to experience these reactions at 60mg/m², the docetaxel should be discontinued, cisplatin and fluorouracil may continue with dose reductions.

Non-haematological

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

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

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 or AST >3.5xULN with ALP >6xULN	should not be used unless strictly indicated.

Fluorouracil

Bilirubin <85micromol/L or ALT/AST <180	give 100% dose
Bilirubin >85micromol/L or ALT/AST >180	not recommended

Renal impairment

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, switch to an appropriate carboplatin containing regimen

REFERENCES

1.
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