Cisplatin and capecitabine (anal cancer)

Indication

Treatment of metastatic/recurrent squamous anal cancer

Regimen details

Day 1	Cisplatin	60mg/m^2	IV	1 hour
Day 1-21	Capecitabine	625mg/m^2	PO	Twice daily

Cycle frequency

21 days

Number of cycles

Up to 8 cycles

Administration

Cisplatin is administered in 500mL sodium chloride 0.9% over 60 minutes following the pre and post hydration protocol.

Patients should be advised to drink at least 2 litres of fluid over the following 24 hours.

Patient must be able to comply with oral chemotherapy regimen. Tablets should be taken 12 hours apart, after food and swallowed whole with a glass of water.

Pre-medication

Antiemetics and hydration as per local policy

Emetogenicity

This regimen has a moderate emetogenic potential

Additional supportive medication

Loperamide if required.
Metoclopramide 10mg tds prn.
Topical emollients to prevent PPE

Extravasation

Cisplatin Exfoliant (group 4)

Investigations – pre first cycle

Investigation	**Validity period**
FBC	14 days
U+E (including creatinine)	14 days
LFTs (including AST)	14 days
Bone profile	14 days
DPYD mutation testing	none
Hepatitis B serology (HBsAG, HBcAb)	none
HIV serology (for squamous anal cancers)	none

HbA1c	3 months
Random glucose	14 days
ECG	28 days
Calculated Creatinine Clearance	14 days

Investigations –pre subsequent cycles

FBC, U&Es and LFTs (including AST), calculated creatinine clearance, random glucose, magnesium, calcium

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophil count	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 50 mL/min (see dose modifications below)
Bilirubin	≤ 2.5 x ULN
AST/ALT	< 3 x ULN

Dose modifications

- **Haematological**

Defer treatment for 1 weeks if neutrophil count <1.5 x 10_9/L and/or platelets <100 x 10_9/L and delay next cycle until recovery. Recommence with consideration of dose modification.

- **Renal impairment**

CrClearance (mL/min)	**Cisplatin**	**Capecitabine**
>60	100% dose	100%
50-60	75%	100%
45-49	50% or carboplatin AUC5	75%
30-44	Carboplatin AUC5	75%
20-29	Carboplatin AUC5	Omit
<20	Discontinue	Discontinue

- **Hepatic impairment**

Note that significant impairment may be a sign of disease progression and require cessation or change of treatment.

Capecitabine: Lack of information available. In patients with mild to moderate hepatic dysfunction due to liver metastases (bilirubin <3x ULN and/or AST/ALT <2.5-5x ULN), probably no dose reduction necessary, consultant decision.

Cisplatin: Little information available. Probably no dose reduction necessary, consultant decision

- **DPYD variants**

All patients due to receive fluoro-pyrimidine based therapy should have a DPD test prior to starting treatment. Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle).

Any patient who has not had a DPD test should be discussed with the consultant prior to going ahead. Patients with variants should be considered for a dose modification following national advice for recommended dose adjustments.

https://www.uksactboard.org/_files/ugd/638ee8_4d24d37a598c485d9ef4d1ba90abccd5.pdf

Where a patient has had significant toxicities but the DPD test has shown none of the variants to be present, a further test can be conducted to test the presence of rarer variants.

- **Other toxicities**

Other toxicities should be managed by symptomatic treatment and/or dose modification (e. by treatment interruption or undertaking a dose reduction).
Once the dose has been reduced, it should not be increased at a later time.

Haematological and non- haematological dose adjustment guidelines according to Common Toxicity Criteria

Toxicity grade	1st dose event	2nd dose event	3rd dose event	4th dose event
0-1	100%	100%	100%	100%
2	Delay* then 100%	Delay * then 70%	Delay * then 50%	discontinue
3	Delay* then 80%	Delay * then 50%	discontinue	discontinue
4	Discontinue or delay * then 50%	discontinue	discontinue	discontinue

* Stop treatment immediately and delay until toxicity resolved to grade 0-1

Patients presenting with diarrhea must be carefully monitored until the symptoms have disappeared as a rapid deterioration can occur.
Any delays should be until toxicity has resolved to grade 0-1

Neurotoxicity or ototoxicity:
- ≥ Grade 2: permanently stop cisplatin and switch to carboplatin AUC 5.

Diarrhoea: reduce dose as follows:
- Grade 2: 75% dose
- Grade 3: 50% dose
- Grade 4: discontinue or 50% dose (consultant decision)

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Infertility
Cardiomyopathy
Nephrotoxicity
Secondary malignancy
Severe toxicity due to DPD deficiency
*Coronary artery spasm is a recognised complication of capecitabine treatment, although the evidence base regarding aetiology, management and prognosis is not particularly strong.
Should a patient receiving capecitabine present with chest pains, stop the treatment. Standard investigation and treatment of angina may be required. If re-challenge is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the capecitabine should be permanently discontinued.

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Diarrhoea
Stomatitis and mucositis
Palmar-plantar erythema
Fatigue

- **Other side effects**

Skin reactions
Nail changes
Taste disturbances

Significant drug interactions

– for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

Folinates: Avoid concomitant use of folinic and folic acid – enhanced toxicity of capecitabine.
Co-trimoxazole/trimethoprim: Avoid if possible – enhances antifolate effect. If essential, monitor FBC regularly.
Phenytoin and fosphenytoin: Toxicity has occurred during concomitant therapy- monitor levels regularly
Sorivudine and its analogues: Co-administration can cause increased toxicity which may be fatal.
Allopurinol: A decrease in capecitabine activity has been shown when taken in combination with allopurinol. Avoid if possible
Antacids: the use of antacids with capecitabine can decrease absorption-avoid.

Additional comments

Cardiotoxicity has been associated with fluoropyrimidine therapy, with adverse events being more common in patients with a prior history of coronary artery disease. Caution must be taken in patients with a history of significant cardiac disease, arrhythmias or angina pectoris

Fertility/Contraception

Patients should agree to use an acceptable method of birth control to avoid pregnancy for the duration of treatment and for 6 months afterwards. Breastfeeding should be discontinued during treatment.

References

- Summary of Product Characteristics (Capecitabine) accessed 20th September 2024 via www.medicines.org.uk
- Summary of Product Characteristics (Cisplatin) accessed 20th September 2024 via www.medicines.org.uk
- Personalised Medicine Approach for Fluoro-pyrimidine-based Therapies. UK Chemotherapy Board V2 September 2024 accessed 7th March 2025 via https://www.uksactboard.org/_files/ugd/638ee8_4d24d37a598c485d9ef4d1ba90abccd5.pdf
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THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON, DESIGNATED LEAD CLINICIAN FOR ANAL CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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