Carboplatin and Cabazitaxel

Indication

Selected patients with rapidly progressive metastatic prostate cancer, after failure of first line chemotherapy and ARTA, and with specified DNA repair abnormalities such as BRCA1 and 2, and ATM, as per Corn et al (see References)
Histological evidence of prostate adenocarcinoma, small cell carcinoma of the prostate, or both
ECOG Performance status 0-2, occasional PS 3 patients may be considered if it is thought that their deterioration is due to rapid disease progression and there is appropriate consent

Exclusion
Prior radiotherapy to >40% bone marrow.
Any radiotherapy within 7 days
Prior radionucleotide therapy with samarium-153 or P-32 within 8 weeks or strontium-89 or radium-223 within 12 weeks
Prior surgery or chemotherapy within 4 weeks
Active grade ≥2 neuropathy
Active grade ≥2 stomatitis
Severe hypersensitivity to docetaxel or Polysorbate 80
Severe illness
Active infection

Regimen details

Cabazitaxel 20mg/m^2 IV in 250ml 0.9% sodium chloride over 1 hour
Carboplatin AUC 5 (Calvert formula) IV in 500mls 5% glucose over 1 hour

Prednisolone – 10mg orally once daily continuous

Cycle frequency

3 weekly

Number of cycles

Up to 10

Administration

Infuse cabazitaxel via a 0.2µm in-line filter

Monitor patient closely for hypersensitivity reactions, especially during first and second cycles

Pre-medication

Premedication 30 minutes prior to each administration:
Antihistamine: Chlorphenamine 10mg IV
Steroid: Dexamethasone 8mg IV
H2 Antagonist: Ranitidine – 50mg IV (or available alternative)

Emetogenicity Moderately

Moderate

Additional supportive medication

Filgrastim, to start 48 hours after chemotherapy for 7 days
Prednisolone 10 mg od or 5mg bd
Proton pump inhibitor

Loperamide PRN (supply with cycle 1)

Extravasation

Irritant

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)

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	≥ 1.0 x 10^9/L Or > 0.5 if there was marrow involvement at baseline in which case discuss with consultant
Platelet count	≥ 100 x 10^9/L Or > 50 if there was marrow involvement at baseline in which case discuss with consultant
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 1.5 x ULN unless liver metastases at baseline in which case </= 4 x ULN
AST	< 1.5 x ULN unless liver metastases at baseline in which case </= 4 x ULN

Dose modifications

Please note that dose reductions /delays in context of either marrow infiltration or liver metastases at baseline should be reviewed in the context of baseline investigations

Neutropenia ≥ 7 days or febrile neutropenia:

- 1st episode - withhold treatment until resolved then reduce cabazitaxel 15mg/m^2 and carboplatin to AUC4
- 2nd episode – reduce carboplatin to AUC 3
- 3rd episode – withdraw treatment

Thrombocytopenia:

- Grade 3 – delay until resolved
- Grade 4 – delay until resolved and reduce cabazitaxel dose to 15mg/m2 and carboplatin to AUC4; withdraw in case of recurrence

Nausea/vomiting – Escalate antiemetic prophylaxis. If, despite this grade ≥3 nausea/vomiting occurs then reduce dose of cabazitaxel to 15mg/m^2. Withdraw treatment if this recurs

Diarrhoea: Grade ≥3 – delay treatment until resolved then restart cabazitaxel at 15mg/m^2; if diarrhoea recurs at grade ≥3 at reduced dose then withdraw treatment

Stomatitis:

- Grade 3 – withhold treatment until grade 1 then restart cabazitaxel at 15mg/m^2
- Grade 4 – withdraw treatment

Peripheral neuropathy:

- Grade 1 – no change
- Grade 2 – Reduce cabazitaxel dose to 15mg/m^2
- Grade 3 – withdraw treatment

Liver toxicity – if AST/ALT >1.5x ULN or bilirubin >ULN then delay until resolved and reduce cabazitaxel dose to 15mg/m^2 (unless due to prior liver mets as described above)

If treatment delayed > 2 weeks for any toxicity then withdraw therapy

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Thromboembolic events, febrile neutropenia, neutropenia, thrombocytopenia, lymphopenia, hypokalaemia, UTI, anaemia

- **Frequently occurring side effects**

Fatigue, nausea, diarrhoea, constipation, dyspnoea, vomiting, alopecia, paraesthesia, dysgeusia, neuropathy, pain, dizziness, anorexia, hypomagnesaemia

- **Other side effects**

Weight loss, fever, oedema, hypersensitivity reactions

Significant drug interactions

– for full details consult product literature/ reference texts

Avoid medicinal products that are strong inducers or inhibitors of CYP3A

Additional comments

Prescribe TTO loperamide with cycle 1. Instruct patient to take at onset of diarrhoea and to contact chemotherapy helpline

Cabazitaxel contains 573.3 mg ethanol 96% (15% v/v), equivalent to 14 ml of beer or 6 ml of wine, which may be harmful for those suffering from alcoholism and should be taken into account in high-risk groups such as patients with liver disease, or epilepsy

References

Corn et al. Cabazitaxel plus carboplatin for the treatment of men with metastatic castration resistant prostate cancers; a randomised, open label phase 1-2 trial. Lancet Oncol 2019; 20: 1432–43

THIS PROTOCOL HAS BEEN DIRECTED BY DR BIRTLE, CONSULTANT FOR UROLOGICAL CANCER

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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