Chemotherapy Protocol

PROSTATE

CABAZITAXEL-PREDNISOLONE

Regimen

- Prostate-Cabazitaxel-Prednisolone

Indication

- Castrate resistant metastatic prostate cancer previously treated with docetaxel containing regimens
- Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cabazitaxel	Hypersensitivity reactions, diarrhoea, constipation, peripheral neuropathy, cough, dyspnoea, back pain, arthralgia, fatigue, anorexia, dysgeusia, myelosuppression, nausea
Prednisolone	Weight gain, GI disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, osteoporosis

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC, LFT's, PSA and U&E's prior to day one of treatment

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Dose modifications based on haematological parameters apply to cabazitaxel only.

Neutrophils (x10^9/L)	Dose Modifications (cabazitaxel)
1 or greater	100%
less than 1	Delay until recovery then give 100% dose
NCI-CTC grade 3 neutropenia despite growth factors or febrile neutropenia	1st Occurrence Delay until the neutrophils are 1x10^9/L or greater then give 20mg/m^2 2nd Occurrence Discontinue treatment
Platelets (x10^9/L)	**Dose Modifications (cabazitaxel)**
100 or greater	100%
Less than 100	1st Occurrence Delay until the platelets are 100x10^9/L or greater then give 20mg/m^2 2nd Occurrence Discontinue treatment

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units	Dose (% of original dose)
Cabazitaxel	1 – 1.5xULN	or	1.5xULN or greater	The maximum dose is 20mg/m^2
	1.6 – 3xULN	and/or	1.5xULN or greater	The maximum recommended dose is 15mg/m^2
	3xULN or greater			Not recommended

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cabazitaxel	50 - 80	100
	31-49	Limited data, treat with caution and monitor for toxicity
	30 or less or end stage renal disease	No data, treat with caution and monitor for toxicity

Renal disorders, have been reported in association with sepsis, severe dehydration due to diarrhoea, vomiting and obstructive uropathy. Renal failure including cases with fatal outcome has been observed. Appropriate measures should be taken to identify the cause and intensively treat the patients if this occurs.

Adequate hydration should be ensured throughout treatment with cabazitaxel. The patient should be advised to report any significant change in daily urinary volume immediately. Serum creatinine should be measured at baseline, with each blood count and whenever the patient reports a change in urinary output. Cabazitaxel treatment should be discontinued in case of renal failure occurring at NCI-CTC Grade 3 or above.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose should then be reduced to 20mg/m^2 or discontinued as appropriate.

Diarrhoea occurring at NCI-CTC grade 3 or above or diarrhoea persisting despite appropriate treatment, including fluid and electrolyte replacement, then delay treatment until improvement or resolution of the symptoms. Seek advice from the relevant consultant about whether to continue treatment or reduce the dose.

Peripheral neuropathy occurring at NCI-CTC grade 2 or above, delay treatment until improvement, and seek advice from the relevant consultant.

Treatment should be discontinued if a patient continues to experience any of these reactions after re-starting therapy.

Regimen

21 day cycle for up to 10 cycles

Drug	Dose	Days	Administration
Cabazitaxel	20mg/m^2	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Prednisolone	5mg twice a day	1-21 inclusive	Oral

The prednisolone should be continued even if the cabazitaxel is delayed.

Dose Information

- Carbazitaxel is myelosuppressive. The licensed dose is 25mg/m^2. The dose in ARIA has been set at 20mg/m^2 as, in general, these patients have poor bone marrow reserves (for example, due to extensive prior treatment, bone metastasis or extensive skeletal radiation). In those with a performance status of 0 or 1 and who tolerate the lower dose well, consider an increase to 25mg/m².

- Cabazitaxel will be dose banded in accordance with the national dose bands (10mg/ml).

- Prednisolone is available as 5mg and 25mg (uncoated) and 2.5mg and 5mg (enteric coated) tablets. It is available as 5mg soluble tablets.

Administration Information

- Hypersensitivity reactions tend to occur with the first or second infusion of cabazitaxel. For minor symptoms such as flushing or localised rashes the infusion should not be interrupted. For severe reactions including profound hypotension, bronchospasm and generalised erythema discontinue the infusion immediately.

- Cabazitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter.

- Prednisolone should be taken with or after food.

Extravasation

- Cabazitaxel – exfoliant

Other

Additional Therapy

- Premedication

  At least 30 minutes prior to chemotherapy

  - chlorphenamine 10mg intravenous bolus
  - dexamethasone 8mg oral or intravenous bolus
  - H_2 Antagonist – according to local formulary choice and availability

  Antiemetics

  15-30 minutes prior to chemotherapy

  - metoclopramide 10mg oral or intravenous bolus

  As take home medication

  - metoclopramide 10mg oral three times a day for 3 days then as required

  - Growth factor according to local formulary choice. For example;
    - filgrastim or bioequivalent 30 million units once a day subcutaneous for five days starting on day five of the cycle
    - lenograstim or bioequivalent 33.6 million units once a day subcutaneous for five days starting on day five of the cycle
    - pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two of the cycle

- Mouthcare for the prophylaxis or treatment of mucositis in accordance with local guidelines

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- Patients who stop cabazitaxel may require a gradual withdrawal of the prednisolone.

References
1. Jevtana Summary of Product Characteristics. Available at https://www.medicines.org.uk/emc/product/4541, last updated April 2017
2. de Bono JS, Oudard S, Ozguroglu M *et al.* Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet.* 2010; **376** (9747): 1147-1154

REGIMEN SUMMARY

Cabazitaxel-Prednisolone

Day 1

1. Chlorphenamine 10mg intravenous bolus

2. Dexamethasone 8mg intravenous bolus

3. H_2 Antagonist – Availability and Choice
   Administration Instructions
   Administer according to local formulary choice and availability one of the following 30 minutes prior to chemotherapy;
   - ranitidine 50mg intravenous once only
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only

   If there is no stock of these products due to national shortages treatment may proceed without the H2 antagonist provided there is no instruction in the ARIA journal indicating the patient must have H2 antagonist treatment.

   All infusion related reactions must be recorded in the ARIA journal and reported to the appropriate consultant. Many Trusts do not administer an H2 antagonist from cycle three onwards. They have been left in the ARIA protocols so that decisions can be made on an individual Trust and patient basis.

4. Metoclopramide 10mg oral or intravenous bolus

5. Cabazitaxel 20mg/m^2 in 250ml sodium chloride 0.9% intravenous infusion over 60 minutes

Take Home Medicines

6. Prednisolone 5mg twice a day for 21 days oral
   Administration Instructions
   Patients who stop cabazitaxel may require gradual withdrawal of the prednisolone. Take in the morning and lunchtime with or after food.

7. Metoclopramide 10mg oral three times a day for 3 days then when required for the relief of nausea
   Administration Instructions
   Please supply 28 tablets or nearest appropriate original pack size.

8. Growth factor according to local formulary choice.
   Administration Instructions
   Growth factors according to local formulary choice. For example;
   - filgrastim or bioequivalent 30 million units once a day subcutaneous for five days starting on day five of the cycle
   - lenograstim or bioequivalent 33.6 million units once a day subcutaneous for five days starting on day five of the cycle
   - pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.4	November 2020	H2 antagonist instructions updated	Rebecca Wills Pharmacist	Donna Kimber Pharmacy Technician
1.3	Sept 2020	Cabazitaxel dose changed to 20mg/m^2 Additional of growth factor support Removal of ranitidine and replacement with H_2 antagonist instructions Hepatic dose reductions updated	Eleanor Taylor Pharmacist	Dr Deborah Wright Pharmacist
1.2	Sept 2018	CSCCN removed from header Metoclopramide dose changed Prednisolone administration instructions clarified Dose banding changed to national dose bands	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.1	May 2013	Renal impairment recommendations updated to reflect the SPC Administration instructions added under the prednisolone in the regimen summary	Dr Deborah Wright Pharmacist	Dr Mathew Wheater Consultant Medical Oncologist
1	Jan 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Joanna Gale Consultant Medical Oncologist Dr Mathew Wheater Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.