

Chemotherapy Protocol

PROSTATE

DOCETAXEL(75)-PREDNISOLONE (6 cycles)

Regimen

- Prostate-Docetaxel (75)-Prednisolone (6 cycles)

Indication

- First line treatment of prostate cancer in combination with androgen deprivation therapy for the treatment of hormone naive metastatic prostate cancer (this is an unlicensed indication).
- Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Docetaxel	Hypersensitivity, fluid retention, neuropathy, joint pains, nail changes, fatigue
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

Drugs

- FBC, LFTs, PSA and U&Es prior to each cycle

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. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

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

Prior to cycle one the following criteria should be met;

Criteria	Eligible Level
Neutrophils	1x10 ⁹ /L or greater
Platelets	50x10 ⁹ /L or greater

Dose modifications based on haematological parameters apply to docetaxel only.

Neutrophils (x10 ⁹ /L)	Dose Modifications (docetaxel)
1 or greater	100%
less than 1 on the day of treatment or less than 1 with fever/infection at any time or less than 0.5 for more than 7 days	1 st Occurrence Delay until recovery to 1x10 ⁹ /L or greater and then give 60mg/m ² 2 nd Occurrence Delay until recovery to 1x10 ⁹ /L or greater then give 45mg/m ²
Platelets (x10 ⁹ /L)	Dose Modifications (docetaxel)
50 or greater	100%
less than 50	1 st Occurrence Delay until recovery to 50x10 ⁹ /L or greater then give 60mg/m ² 2 nd Occurrence Delay until recovery to 50x10 ⁹ /L or greater then give 45mg/m ²

Hepatic Impairment

Consider weekly scheduling if there is a mild or moderate hepatic impairment

Drug	Bilirubin (µmol/L)		AST/ALT (units/L)		Alk Phos (units/L)	Dose (% of original dose)
Docetaxel	N/A		greater than 1.5xULN	and	greater than 2.5xULN	Give 75%
	greater than ULN	and/or	greater than 3.5xULN	and	greater than 6xULN	Not Recommended

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Docetaxel	N/A	No dose adjustment needed

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 60mg/m² or discontinued as appropriate.

The following recommendations apply to docetaxel only. The prednisolone should be continued if the docetaxel is delayed. It should be stopped if the docetaxel is stopped but may require a reducing schedule.

Peripheral Neuropathy

Peripheral neuropathy at NCI-CTC grade 3 should result in a dose reduction from 75mg/m² to 60mg/m² once the neuropathy has resolved to NCI-CTC grade 2 or below. If the NCI-CTC grade 3 neuropathy occurred at doses lower than 75mg/m² or a NCI-CTC grade 4 toxicity develops consider stopping treatment.

Lacrimation

Excessive lacrimation is related to cumulative docetaxel doses and occurs after a median of 400mg/m². Symptomatic treatment with hypromellose 0.3% eye drops four times a day may help. However, if the ocular irritation continues reduce the docetaxel dose to 60mg/m².

Skin

Delay the docetaxel where a NCI-CTC grade 3 cutaneous toxicity is present on day one of the cycle until it resolves to NCI-CTC grade 1 or below. The subsequent doses of docetaxel should be reduced from 75mg/m² to 60mg/m². If it occurs with a dose of 60mg/m² or if there is no recovery after two weeks, docetaxel treatment should be stopped. Where a NCI-CTC grade 3 cutaneous toxicity occurs between cycles with recovery by day one then reduce the docetaxel dose as described. Docetaxel should be stopped in response to a NCI-CTC grade 4 cutaneous toxicity.

Stomatitis

A NCI-CTC grade 2 stomatitis should result in a delay in treatment until it has become NCI-CTC grade 1 or below. Treatment may then be re-started at the previous dose. For a NCI-CTC grade 3 stomatitis delay treatment until it has recovered to NCI-CTC grade 1 or below then reduce the dose to 60mg/m². Treatment should be stopped in relation to a NCI-CTC grade 4 stomatitis.

[Regimen](#)

Docetaxel is highly myelosuppressive and in those with poor bone marrow reserves (for example due to extensive prior treatment, bone metastasis or extensive skeletal radiation) consider a starting dose of 60mg/m² with a view to increase to 75mg/m² if well tolerated.

Not all patients will require prednisolone. Please check with the relevant consultant before prescribing if prednisolone is to be included.

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Docetaxel	75mg/m ²	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Prednisolone	5mg twice a day	1-21 incl.	Oral

[Dose Information](#)

- Docetaxel will be banded as per the agreed bands.
- Docetaxel induced fluid retention can lead to weight gain. This is not a reason to alter the doses
- Docetaxel doses of more than 200mg should be diluted in 500ml sodium chloride 0.9% (maximum concentration 0.74mg/ml)
- Prednisolone is available as 5mg, 25mg (uncoated) and 2.5mg and 5mg (enteric coated) tablets. A soluble formulation is available.

[Administration Information](#)

- Docetaxel hypersensitivity reactions tend to occur with the first or second infusion. 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.
- Prednisolone should be taken with or after food.

[Extravasation](#)

- Docetaxel - exfoliant

Additional Therapy

- Premedication
 - dexamethasone 8mg oral at 12 hours, 3 hours and 1 hour prior to docetaxel
- Antiemetics
 - 15-30 minutes prior to chemotherapy
 - metoclopramide 10mg oral or intravenous

As take home medication

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

Additional Information

- Docetaxel is not licensed to treat this indication and is therefore 'off label'. In order to use medicines that are unlicensed, or used for an unlicensed indication, each provider organisation must assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics committee (or similar) and NHS England may ask for assurance of this process.

Coding (OPCS)

- Procurement – X71.1
- Delivery – X72.3

References

1.NHS England. Clinical Commissioning Policy Statement: Docetaxel in combination with androgen deprivation therapy for the treatment of hormone naive metastatic prostate cancer. B15/PS/a.

REGIMEN SUMMARY

Docetaxel (75)-Prednisolone (6 cycles)

Cycles 1, 2, 3, 4, 5

Day minus 1

1. Dexamethasone 8mg oral at 12 hours, 3 hours and 1 hour prior to docetaxel (from TTO)*

Day 1

2. Warning – Check if Prednisolone required
3. Dexamethasone from TTO (see above)*
4. Metoclopramide 10mg oral or intravenous
5. Docetaxel 75mg/m² in 250ml sodium chloride 0.9% intravenous infusion over 60 minutes
Administration Instructions
Ensure the patient has taken the dexamethasone pre-medication prior to treatment. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone premedication administer dexamethasone 20mg intravenous 15-30 minutes prior to chemotherapy

Take Home Medicines

6. Prednisolone 5mg twice a day oral for 21 days
Administration Instructions
Take with or after food. The dose of this medicine may need to be reduced gradually before stopping treatment.
7. Dexamethasone 8mg oral at 12 hours, 3 hours and 1 hour prior to docetaxel
8. Metoclopramide 10mg oral three times a day for 3 days then 10mg three times a day when required for nausea.

Cycle 6

Day minus 1

9. Dexamethasone 8mg oral at 12 hours, 3 hours and 1 hour prior to docetaxel (from TTO)*

Day 1

10. Warning – Check if Prednisolone required
11. Dexamethasone from TTO (see above)*
12. Metoclopramide 10mg oral or intravenous
13. Docetaxel 75mg/m² in 250ml sodium chloride 0.9% intravenous infusion over 60 minutes
Administration Instructions
Ensure the patient has taken the dexamethasone pre-medication prior to treatment. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone premedication administer dexamethasone 20mg intravenous stat 15-30 minutes prior to chemotherapy

Take Home Medicines

14. Prednisolone 5mg twice a day oral for 21 days

Administration Instructions

Take with or after food. The dose of this medicine may need to be reduced gradually before stopping treatment.

15. Metoclopramide 10mg oral three times a day for 3 days then 10mg three times a day when required for nausea.

* In Aria Planner the dexamethasone TTO will appear on day 1 of treatment. This is the supply for the next cycle.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	June 2016	None	Dr Debbie Wright Pharmacist	Dr Simon Crabb 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 Hospitals 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.