Systemic Anti Cancer Treatment Protocol

Weekly Docetaxel Prostate Cancer Unlicensed Use

PROCTOCOL REF: MPHADOCWE
(Version No: 1.2)

Approved for use in:

For the treatment of patients with, hormone resistant metastatic prostate cancer that have a WHO performance status 0-2.

Available as a treatment option for patients unable to tolerate the 3 weekly regimen.

Please NOTE: Regimen not recommended by NICE. This is unlicensed use. Please refer to the 'CCC Unlicensed Medicines Policy' for full details on consenting, prescribing, documentation and supply of unlicensed medicines. As per trust policy please provide the 'Unlicensed Medicines Information' to patients and carers as appropriate

Dosage:

Drug	Dose	Route	Frequency
Dexamethasone 30 minutes before chemotherapy	8mg	PO	30 minutes BEFORE chemotherapy
Docetaxel	**30mg/m^2**	IV	Weekly for 5 weeks followed by a week break
Prednisolone	10mg once daily	Oral	Once daily in the morning (continuous throughout treatment)

Repeat at 7 day intervals for 5 weeks followed by a week break up to 5 cycles (one cycle = six weeks)

Supportive Treatments:

Domperidone 10mg three times a day

Steroid Aftercare

Abrupt withdrawal after a prolonged period can lead to acute adrenal insufficiency, hypotension or death. Withdrawal can also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss.

The magnitude and speed of dose reduction in corticosteroid withdrawal should be determined on a case-by–case basis, taking into consideration the underlying condition that is being treated, and individual patient factors such as the likelihood of relapse and the duration of corticosteroid treatment. *Gradual* withdrawal of systemic corticosteroids should be considered in those whose disease is unlikely to relapse.

Once the patient has completed their chemotherapy regime the steroid dose should be tapered as follows:

1. Stop pre-docetaxel dexamethasone tablets.
2. Taper prednisolone to 10mg daily for seven days then reduce to 5mg daily for seven days then stop.*

*This can be customised to suit each patient on an individual basis.

Extravasation risk:

Docetaxel: Vesicant

Refer to the CCC policy for the ‘Prevention and Management of Extravasation Injuries’.

Administration:

Day	Drug	Dose	Route	Diluent and rate
1, 8, 15, 22 and 29	**Dexamethasone**	**8mg**	**PO**	30 minutes BEFORE chemotherapy
	Docetaxel	**30mg/m^2**	**IV**	Sodium Chloride 0.9% 250mL over 1 hour
	Prednisolone	**10mg once daily in the morning**	**PO**	Continuous throughout treatment

Interactions with other medicinal products
Concomitant use of medicines which induce, inhibit or are metabolised by cytochrome P450-3A such as ciclosporin, ketoconazole, erythromycin, may affect levels of docetaxel refer to summary of product of characteristics for more detailed information. In case of a combination with CYP3A4 inhibitors, the occurrence of docetaxel adverse reactions may increase, as a result of reduced metabolism. Therefore, close clinical surveillance is warranted and a dose-adjustment of docetaxel may be suitable during the treatment with the strong CYP3A4 inhibitor

Main Toxicities:

Docetaxel	
Haematological	Myelosuppression - Neutropenia is the most frequent adverse reaction of docetaxel. Neutrophil nadirs usually occur at a median of 7 days but this interval may be shorter in heavily pre-treated patients.

Gastrointestinal	Stomatitis, abdominal pain, diarrhoea - may be early manifestations of serious gastrointestinal toxicity and should be evaluated and treated promptly.
Cardiovascular	Congestive heart failure (CHF) Fluid retention - Patients with severe fluid retention such as pleural effusion, pericardial effusion and ascites should be monitored closely
Neuropathies	Peripheral neurotoxicity
Hypersensitivity	Patients should be observed closely for hypersensitivity reactions especially during the first and second infusions. Hypersensitivity reactions may occur within a few minutes. Facilities for the treatment of hypotension and bronchospasm should be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localised rash with or without pruritus do not require interruption of therapy. However, severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate treatment **(please refer to the trusts Hypersensitivity- Management Prevention Policy for full details).** Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel.
Ocular	Cystoid macular oedema (CMO). Patients with impaired vision should undergo a prompt and complete ophthalmologic examination.
Respiratory disorders	Epistaxis, dyspnoea, cough Acute respiratory distress syndrome, interstitial pneumonia/pneumonitis, interstitial lung disease, pulmonary fibrosis and respiratory failure have been reported and may be associated

	with fatal outcome. If new or worsening pulmonary symptoms develop, patients should be closely monitored, promptly investigated, and appropriately treated.
Additional side effects	Cutaneous reactions - Localised skin erythema of the extremities (palms of the hands and soles of the feet) with oedema followed by desquamation has been observed. Nail changes, fluid retention, alopecia, steroid side effects Infertility - contraceptive measures must be taken by both men and women during treatment and for men at least 6 months after cessation of therapy

Investigations:

CYCLE	Pre	1	1	1	1	1	1	2	Ongoing
Week		1	2	3	4	5	6	7	→
Informed Consent	X								
Clinical Assessment	X	X					TREATMENT BREAK	X	Every 6 weeks
SACT assessment (to include PS and toxicities)		X	X	X	X	X		X	Every treatment
FBC	X	X	X	X	X	X		X	Every treatment
U&E & LFTs	X			X				X	Every 3 weeks
PSA	X	X						X	Every 6 weeks
CT scan	X								Every 12 weeks
Height recorded	X								
Weight recorded	X	X	X	X	X	X		X	Every treatment

Dose Modifications and Toxicity Management:

A dose reduction to 70-80% of the full dose is required for patients with a WHO performance status of 2.

Consider dose reduction to 25mg/m^2 for any grade 2 reaction that has required a treatment delay

Docetaxel	**Recommended dose reduction for toxicity management**
First dose reduction of 80%	**25mg/m^2**

Haematological Toxicity:

Proceed on each treatment day if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Omit treatment for 1 week and refer to advice below-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

- In the event of febrile neutropenia or neutrophils < 0.5 x 10^9/L for more than 1 week, give docetaxel 25mg/m^2 for all further cycles.
- If platelets < 50 x 10^9/L, consider dose reduction to 25mg/m^2 after recovery - discuss with Consultant first.
- If the patient continues to experience these side effects at the lower dose, review treatment plan.

Hepatic impairment
AST and/or ALT > 1.5- 5 x ULN concomitant with ALP > 2.5 – 5.0 x ULN and normal Bilirubin- **consider 75% of the original dose**.
AST or ALT >1.5-5 x ULN concomitant with ALP ≤ 2.5-6 x ULN and/or bilirubin ≤ 1-1.5 x ULN- **consider 50% of the original dose**
Bilirubin > 1.5 x ULN or AST/ALT > 10 x ULN or ALP > 6 x ULN: not recommended

Renal impairment
Excretion is predominately via hepatic metabolism. Renal impairment is unlikely to affect elimination. No dose reduction required.

References:

BNF. *Prednisolone.* Available from: https://bnf.nice.org.uk/drug/prednisolone.html [Accessed on 3/12/18]

Clatterbridge cancer centre. *Steroid tapering guidance.* Available from: https://extranet.clatterbridgecc.nhs.uk/application/files/7115/3138/6265/Steroid_Tapering_Guidance_V2.0.pdf [Accessed on 22/11/18]

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Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.

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