Systemic Anti Cancer Treatment Protocol

Docetaxel
Prostate Cancer

PROCTOCOL REF: MPHADOCPC
(Version No: 1.2)

Approved for use in:

Prostate cancer:

- Metastatic hormone naïve
- Metastatic hormone resistant/sensitive
- PS 0-1

Dosage:

Drug	Dose	Route	Frequency
Dexamethasone	8mg twice daily	Oral	For three days, commencing 24 hours before docetaxel
Docetaxel	**75mg/m^2**	IV	Day one of a 21 day cycle
Prednisolone	10mg once daily	Oral	Once daily in the morning (continuous throughout treatment)

Repeat at 21 day intervals

- **Hormone naïve patients- 6 cycles**
- **Hormone (castrate) resistant patients-10 cycles**

Supportive Treatments:

Domperidone 10mg three times a day.

GCSF secondary prophylaxis, dose as per trust guidance. To be used for 7 days starting on day three of cycle.

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 and those who are on steroids for longer than 6 months should have a longer tapering off period.

Extravasation risk:

Docetaxel: vesicant

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	**Dexamethasone tablets*** commencing 24 hours before docetaxel	**8mg twice daily for three days**	**PO**	
	Docetaxel	**75mg/m^2**	**IV**	Sodium Chloride 0.9% 250mL over 1 hour
	Prednisolone	**10mg once daily in the morning**	**PO**	Continuous throughout treatment

*Pre-medication (to prevent hypersensitivity reactions and fluid retention):

- Dexamethasone 8mg oral tablets twice daily for 3 days, commencing in the morning, 24 hours prior to the docetaxel dose.
- If dexamethasone has not been taken, then this can be replaced with an 8mg intravenous dose on the day of chemotherapy.

Interactions with other medicinal products

Concomitant use 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 and tenderness, diarrhoea - may be early manifestations of serious gastrointestinal toxicity and should be evaluated and treated promptly.
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 following the initiation of the infusion of docetaxel, thus facilities for the treatment of hypotension and bronchospasm should be available. Minor symptoms such as flushing or localised cutaneous reactions do not require interruption of therapy. Severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate therapy. Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel.

Ocular	Cystoid macular oedema (CMO) has been reported in patients treated with docetaxel. Patients with impaired vision should undergo a prompt and complete ophthalmologic examination.
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 and Treatment Plan:

Cycle	Pre	C1	C2	C3	C4	C5	Ongoing
Informed consent	X						
Clinical assessment	X			X			Every 6 weeks
SACT assessment (to include PS and toxicities)	X	X	X	X	X	X	Every cycle
FBC	X		X	X	X	X	Every cycle
U&E & LFTs	X		X	X	X	X	Every Cycle
PSA	X	X		X		X	Every 6 weeks
CT scan	X						If clinically indicated *
Height recorded	X						
Weight recorded	X	X	X	X	X	X	Every cycle

Recommended after 4-6 cycles if clinically indicated. For hormone naïve patients no imaging is required until after treatment is complete.

Dose Modifications and Toxicity Management:

Consider dose reduction for any grade 2 reaction that has required a treatment delay

Docetaxel	**Recommended dose reduction for toxicity management**
First dose reduction of **80%**	**60mg/m^2**

Haematological Toxicity:

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Delay 1 week and refer to advice below-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

These Haematological guidelines assume that patients are well with a good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

In the event of febrile neutropenia or neutrophils < 0.5 x 10^9/L for more than 1 week, give docetaxel 60mg/m^2 for all further cycles. If platelets < 50 x 10^9/L, consider dose reduction to 60mg/m^2 after recovery - discuss with Consultant first. If the patient continues to experience these side effects at the lower dose, review treatment plan.

Those patients who are hormone sensitive, secondary prophylactic treatment with GCSF can be considered for subsequent cycles if admission for neutropenic sepsis or deferral due to neutropenia at day 1 of cycle.

Hepatic impairment:

Docetaxel
For those patients with serum bilirubin > ULN and/or ALT and AST > 3.5 times the ULN associated with alkaline phosphatase > 6 times the ULN, no dose-reduction can be recommended and docetaxel should not be used unless strictly indicated.

Renal impairment:

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

References:

Docetaxel Accord 160 mg/8 ml concentrate for solution for infusion, summary of Product Characteristics, Accord Healthcare limited, Middlesex. 22/05/2012. Available from www.medicines.org.uk Last updated 29/5/2019.

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