BC Cancer Protocol Summary for Palliative Therapy for Metastatic Hormone Refractory Prostate Cancer Using DOCEtaxel and predniSONE

***Protocol Code**:* *GUPDOC*

***Tumour Group**:* *Genitourinary*

***Contact Physician**:* *Dr. Kim Chi*

ELIGIBILITY:

- ECOG performance status 1-2
- Life expectancy greater than 3 months
- Bilirubin less than ULN, AST/ALT less than 5 x ULN, Alkaline Phosphatase less than 6 x ULN
- Disease that is not amenable to radiation therapy and where an objective disease response is deemed crucial to improve symptoms (e.g. bulky lymph node disease)
- For other indications, or for more than 10 cycles, a BC Cancer "Compassionate Access Program" request must be approved.

- **EXCLUSIONS**:
- Patients not fitting the above criteria

TESTS:

- Baseline: CBC and differential, platelets, bilirubin, ALT, alk phos, PSA (see below)
- Before each treatment: CBC & diff, platelets
- Before Cycle 4 and anytime if clinically indicated*: bilirubin, ALT, alk phos, LDH (see Precaution #5 for guidelines)
- PSA every 3 weeks (PSA required, but results do not have to be available to proceed with treatment).

PREMEDICATIONS:

- dexamethasone 8 mg PO bid for 3 days, starting one day prior to each DOCEtaxel administration Patient must receive minimum of 3 doses pre-treatment.
- Additional antiemetics not usually required.
- DOCEtaxel-induced onycholysis and cutaneous toxicity of the hands may be prevented by wearing frozen gloves starting 15 minutes before DOCEtaxel infusion until 15 minutes after end of DOCEtaxel infusion; gloves should be changed after 45 minutes of wearing to ensure they remain cold during the entire DOCEtaxel infusion.

TREATMENT:

Androgen ablative therapy (eg, LHRH agonist, LHRH antagonist) should be maintained.

Drug	Dose	BC Cancer Administration Guideline
DOCEtaxel	75 mg/m²	IV in 250 mL* IV 250 mL NS over 1 hour (see precaution #2) (use non-DEHP equipment)
predniSONE**	10 mg daily (or 5 mg bid)	PO

*If 84 to 220 mg, use 250 mL bag. If greater than 220 mg, use 500 mL bag.
Repeat every 21 days x 6 cycles; if responding, continue to a total of 10 cycles.
Discontinue treatment, if no response after 2 cycles.

** may substitute with dexamethasone PO 1.5 mg daily based upon toxicity and patient tolerance

DOSE MODIFICATIONS:

1. **Hematological**:

ANC (x 10^9/L)	Platelets (x 10^9/L)	Dose	Dose after Neutropenic Sepsis on DOCEtaxel
greater than or equal to 1.5	greater than 90	100%	75%
1.0 to less than 1.5	70 to 90	75%	75%
less than 1.0	less than 70	delay	delay

2. **Hepatic dysfunction**:

Bilirubin		Alkaline Phosphatase*		ALT +/or AST	Dose
less than or equal to ULN	and	less than 2.5 x ULN	and	less than or equal to 1.5 x ULN	100%
less than or equal to ULN	and	2.5 to 5 x ULN	and	1.6 – 5 x ULN	75%
greater than ULN	or	greater than 5 x ULN	or	greater than 5 x ULN	discuss with contact physician

***except in the case of bony metastases and no known hepatic dysfunction**
ULN = upper limit of normal

PRECAUTIONS:

1. **Fluid retention**: Dexamethasone premedication must be given to reduce incidence and severity of fluid retention.
2. **Hypersensitivity** reactions to DOCEtaxel are common but it is not necessary to routinely initiate the infusion slowly. If slow initiation of infusion is needed, start infusion at 30 mL/h x 5 minutes, then 60 mL/h x 5 minutes, then 120 mL/h x 5 minutes, then complete infusion at 250 mL/h (for 500 mL bag, continue 250 mL/h for 5 minutes and then complete infusion at 500 mL/h). Refer to BC Cancer Hypersensitivity Guidelines.
3. **Extravasation**: DOCEtaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
4. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.

5. **Hepatic Dysfunction**: DOCEtaxel undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated ALT) may lead to increased toxicity and usually requires a dose reduction. Baseline bilirubin and liver enzymes are recommended before cycle 1 and then if clinically indicated (eg, repeat bilirubin and liver enzymes prior to each treatment if liver enzymes are elevated, liver metastases are present or there is severe toxicity such as neutropenia). If bilirubin and liver enzymes are normal and there is no evidence of liver metastases or severe toxicity, check bilirubin and liver enzymes after 3 cycles (ie, at cycle 4). Note: this information is intended to provide guidance but physicians must use their clinical judgement when making decisions regarding monitoring and dose adjustments.

Call Dr. Kim Chi or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Picus J, Schultz M, Cochrane J. A phase II trial of docetaxel in patients with hormone refractory prostate cancer. Long term results. Proc Am Soc Clin Oncol, 1999;18a (abstract1206).
2. Petrylak DP, Macarthur RB, O'Connor J, et al. Phase I trial of docetaxel with estramustine in androgen-independent prostate cancer. J Clin Oncol 1999;17:958-67.
3. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med 2004;351(15):1502-12.