BC Cancer Protocol Summary for First-Line Treatment of Castration Sensitive, Metastatic Prostate Cancer Using DOCEtaxel and Androgen Deprivation Therapy

***Protocol Code**:* *GUPDOCADT*

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

***Contact Physician**:* *Dr. Kim Chi (VCC)*

ELIGIBILITY:

- Newly diagnosed, castration sensitive (i.e., hormone naïve) metastatic prostate cancer
- DOCEtaxel to be started within 4 months of initiation of androgen deprivation therapy or surgical castration
- High volume disease defined as visceral metastases or $\geq$ 4 bone metastases with at least 1 beyond the pelvis and vertebral column.
- ECOG performance status 0-2
- Life expectancy greater than 3 months
- Bilirubin less than ULN, AST/ALT less than 5 x ULN, Alkaline Phosphatase less than 6 x ULN

- **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 deprivation therapy:

Surgical castration or commence standard androgen deprivation therapy by ONE of the options:

Options	Refer to Protocols
LHRH agonist (goserelin or leuprolide or buserelin acetate)	GUPLHRH
LHRH agonist and anti-androgen*	GUPLHRH and GUPNSAA
LHRH antagonist (degarelix)	GUPLHRHA
LHRH antagonist and anti-androgen*	GUPLHRHA and GUPNSAA

* anti-androgen: bicalutamide, flutamide or niLUTAmide

DOCEtaxel:

DOCEtaxel to be started within 4 months of initiation of androgen deprivation therapy

Drug	Dose	BC Cancer Administration Guideline
DOCEtaxel	75 mg/m²	IV in 250 to 500 mL NS over 1 hour (see precaution #2) (use non-DEHP equipment)

Repeat every 21 days x 6 cycles
Discontinue treatment, if no response after 2 cycles.

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*		AST +/or ALT	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 AST) 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 (e.g., 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 (i.e., 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. Sweeney C, et al. Impact on overall survival (OS) with chemo-hormonal therapy versus hormonal therapy for hormone sensitive newly diagnosed metastatic prostate cancer (mPrCa): An ECOG-led phase III randomized trial. J Clin Oncol 2014;32:5s (suppl; abstr LBA2).