

# BCCA Protocol Summary for Palliative Therapy for Hormone Refractory Prostate Cancer Using mitoXANTRONE and predniSONE

**Protocol Code**

*GUPMX*

**Tumour Group**

*Genitourinary*

**Contact Physicians**

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## ELIGIBILITY:

- advanced androgen independent prostate cancer (progressive disease despite castrate testosterone level)
- Performance status 1 – 2 (symptomatic and ambulatory at least 50% of the day)
- evaluable or measurable disease

## EXCLUSIONS:

- history or increased risk of cardiac disease

## TESTS:

- Baseline: CBC and differential, platelets, bilirubin, PSA, symptom status, analgesic use, objective disease measurements
- Before each treatment: CBC and differential, platelets
- Every 3 weeks: PSA
- Every 6 weeks: symptom status, analgesic use, objective disease measurements
- If clinically indicated: bilirubin

## PREMEDICATIONS:

- Antiemetic protocol for low-moderate emetogenic chemotherapy protocols (see SCNAUSEA)

## TREATMENT:

Drug	Dose	BCCA Administration Guideline
mitoXANTRONE*	12 mg/m <sup>2</sup> on Day 1	IV in 50 mL NS or D5W over 5 mins
predniSONE**	10 mg daily (or 5 mg bid)	PO

\*A starting dose of 10 mg/m<sup>2</sup> may be considered for patients with extensive previous radiotherapy or carefully selected patients with adequate neutrophil and platelet counts after previous strontium treatment.

\*Optional: increase dose by 2 mg/m<sup>2</sup> per cycle to hematologic or subjective tolerance.

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

Repeat every 21 days until progression or cumulative maximum of mitoXANTRONE 140 mg/m<sup>2</sup>.  
Discontinue if no response after 2 cycles.

## DOSE MODIFICATIONS:

### 1. Hematological

ANC ( $\times 10^9/L$ )		Platelets ( $\times 10^9/L$ )	mitoXANTRONE Dose
greater than 1.9	and	greater than or equal to 90	consider dose escalation by 2 mg/m <sup>2</sup> (see above)
1.5 - 1.9	and	greater than or equal to 90	same dose as previous
1.0 - 1.4	and	greater than or equal to 90	reduce dose 2 mg/m <sup>2</sup> from previous
less than 1.0	or	less than 90	delay 1 week and reassess, then proceed at reduced dose if ANC greater than 1.5

2. **Renal dysfunction:** No dose modification required.

3. **Hepatic dysfunction:** Decrease dose by 50% if bilirubin greater than 50 micromol/L.

## PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Cardiotoxicity:** Maximum lifetime dose of mitoXANTRONE is 140 mg/m<sup>2</sup> for patients with no prior anthracycline, no thoracic radiation and normal cardiac function. mitoXANTRONE should be avoided in patients with congestive heart failure. Monitor for clinical evidence of cardiomyopathy as cardiotoxicity may occasionally occur at lower cumulative doses.
3. **Extravasation:** Although there are two cases of extravasation necrosis, mitoXANTRONE is considered a nonvesicant and the majority of extravasations result in a blue discolouration of the skin which slowly fades.
4. **Dyspepsia:** Consider histamine H2 blocker for dyspeptic history or symptoms of prednisone intolerance.

**Contact Dr. Kim Chi, Dr. Bernie Eigl or tumour group delegate at (604) 877-2730 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

## BENEFITS

In a phase 3 multicentre Canadian trial, palliation of symptomatic prostate cancer occurred in 29% of patients treated with concurrent low dose prednisone and mitoXANTRONE, and this was superior to consecutive use of the same agents. A minority of patients also showed a greater than 4-fold drop in PSA but this endpoint does not correlate well with palliative response. Complete pain relief, abolition of need for narcotics or a greater than 4-fold PSA drop without symptomatic deterioration could be considered reasonable evidence of benefit provided the treatment is well tolerated. There is no evidence of impact on overall survival.<sup>1</sup>

## References:

1. Tannock IF, Osoba D, Stockler MR et al. Chemotherapy with mitoxantrone plus prednisone or prednisone alone for symptomatic hormone-resistant prostate cancer: a Canadian randomized trial with palliative end points. J Clin Oncol 1996;14:1756-64.