BC Cancer Protocol Summary for Palliative Therapy for Metastatic Castration Resistant Prostate Cancer Using Cabazitaxel and predniSONE

Protocol Code	*GUPCABA*
Tumour Group	*Genitourinary*
Contact Physician	*Dr. Christian Kollmannsberger*

ELIGIBILITY:

- ECOG performance status 0-2
- Life expectancy greater than 3 months
- Patients with metastatic castration resistant prostate cancer who have progressed on prior chemotherapy containing DOCEtaxel
- Patients with metastatic castration resistant prostate cancer who have progressed during 12 months of abiraterone (UGUPABI) or enzalutamide (UGUPENZ) before or after docetaxel.
- Patients with metastatic castration resistant prostate cancer who have progressed on apalutamide (UGUPAPA) or enzalutamide (UGUNMPENZ) after docetaxel

EXCLUSIONS:

- ECOG performance status greater than 2
- Clinically significant heart disease (LVEF less than 50% at baseline)
- Avoid if bilirubin, ALT or AST greater than 1.5 x ULN

TESTS:

- Baseline: CBC and differential, platelets, bilirubin, ALT, creatinine, sodium, potassium
- Before each treatment (every 3 weeks = 1 cycle): CBC and differential, platelets
- If clinically indicated: creatinine, bilirubin
- PSA every 3 weeks (PSA required, but results do not have to be available to proceed with treatment)

PREMEDICATIONS:

- Antiemetic protocol for low emetogenic chemotherapy protocols (see SCNAUSEA)
- 45 minutes prior to cabazitaxel
  - dexamethasone 8 mg IV in NS 50 mL over 15 minutes
- 30 minutes prior to cabazitaxel
  - diphenhydrAMINE 50 mg IV and ranitidine 50 mg IV in 50 mL over 20 minutes (compatible up to 3 hours when mixed in bag)

TREATMENT:

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

Drug	Dose	BC Cancer Administration Guideline
cabazitaxel	25 mg/m²	IV in 250 mL NS over 60 min (use non-DEHP 0.2 micron in-line filter)
predniSONE*	10 mg daily (or 5 mg bid)	PO

*Alternate steroid dosing option: May substitute with dexamethasone PO 1.5 mg daily based upon toxicity and patient tolerance

Repeat every 21 days x 10 cycles

Discontinue treatment, if no response after 2 cycles

DOSE MODIFICATIONS:

1. **Hematological**

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
greater than or equal to 1.5	and	greater than or equal to 90	100%
1.0 to less than 1.5	or	70 to less than 90	75%
less than 1.0	or	less than 70	delay

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Hypersensitivity**: Reactions are common with cabazitaxel. They can occur within minutes of initiation of a cabazitaxel infusion. Patients should be closely observed for reactions, especially during the first and second infusions. Premedications with antihistamine, corticosteroid and H2 antagonist are recommended prior to each treatment to reduce incidence and severity of reactions. For severe hypersensitivity reactions, cabazitaxel treatment should be stopped. Refer to BC Cancer Hypersensitivity Guidelines.
3. **Hepatic Dysfunction**: cabazitaxel 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 (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 (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.

4. **Renal Toxicity**: No dosage adjustment is necessary for patients with renal impairment

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

References:

1. de Bono JS, Oudard S, Ozguroglu M, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. Lancet 2010; 376(9747):1147-54.
2. de Wit R, de Bono J, Stenberg CN, et al. Cabazitaxel versus abiraterone or enzalutamide in metastatic prostate cancer. N Eng J Med 2019;381:2506-18.

Appendix: Prostate Cancer Funding Algorithm