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

Protocol Code: *UGUPABI*

Tumour Group: *Genitourinary*

Contact Physician: *Dr. Christian Kollmannsberger*

ELIGIBILITY:

Patients must have:

- metastatic castration resistant prostate cancer who are either:
  - chemotherapy naïve
    OR
  - have received prior chemotherapy containing DOCEtaxel, and
- A BC Cancer "Compassionate Access Program" (CAP) approval prior to treatments

Patients should have:

- ECOG performance status 0-2
- Life expectancy greater than 3 months

Note:

- Patients can receive either enzalutamide (UGUPENZ) or abiraterone (UGUPABI) in metastatic castration resistant disease but not sequential use of these agents.

EXCLUSIONS:

Patients must not have:

- Active or symptomatic viral hepatitis or chronic liver disease
- History of adrenal dysfunction
- Clinically significant heart disease (LVEF less than 50% at baseline)
- Previously received abiraterone (GUMCSPABI), enzalutamide (GUMCSPENZ), apalutamide (GUMCSPAPA), or darolutamide with DOCEtaxel (UGUMCSPDD) for metastatic castrate sensitive disease
- Previously received apalutamide (UGUPAPA), enzalutamide (UGUNMPENZ) or darolutamide (UGUNMPDAR) for non-metastatic castration resistant disease

CAUTION:

- Bilirubin greater than 1.5 x ULN, ALT greater than 2.5 x ULN
- Uncontrolled hypertension

TESTS:

- Baseline: CBC & Diff, total bilirubin, ALT, alkaline phosphatase, creatinine, random glucose, sodium, potassium, PSA, testosterone
- Baseline if clinically indicated: total protein, albumin, GGT, LDH, TSH, calcium, MUGA scan or echocardiogram
- Cycles 1 to 3, every 4 weeks: CBC & Diff, total bilirubin, ALT, alkaline phosphatase, creatinine, random glucose, sodium, potassium, blood pressure, PSA
- Cycles 1 to 3, every 2 weeks: potassium, ALT, alkaline phosphatase, total bilirubin, blood pressure

- Cycles 4 onward, before each physician visit: CBC & Diff, ALT, alkaline phosphatase, total bilirubin, creatinine, random glucose, sodium, potassium, blood pressure, PSA
- If clinically indicated: total protein, albumin, TSH, calcium, LDH, GGT, testosterone, MUGA scan or echocardiogram

TREATMENT:

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

Drug	Dose	BCCA Administration Guideline
abiraterone	1000 mg	PO daily
predniSONE*	10 mg daily or 5 mg twice daily OR 5 mg daily**	PO daily

* Dexamethasone may be substituted for patient or physician preference, based upon toxicity and patient tolerance. When substituting dexamethasone for predniSONE the dose is:

- PredniSONE 10 mg PO daily: dexamethasone 1.5 mg PO daily.
- PredniSONE 5 mg PO daily: dexamethasone 0.5 mg PO daily

**More mineralocorticoid side effects were observed with the lower dose of predniSONE

One cycle consists of 4 weeks (30 days).

For cycles 1 to 3: Dispense 30 day supply with each physician visit.

For cycles 4 onwards: Dispense 90 day supply with each physician visit.

Treat until disease progression or unacceptable toxicity.

DOSE MODIFICATIONS:

1. Hepatic dysfunction:

Bilirubin		ALT	Dose
Less than or equal to ULN – 1.5 x ULN	and	Less than or equal to ULN to 2.5 x ULN	100%
1.5 – 3 x ULN	and	2.5 – 5 x ULN	100% Monitor liver tests at least weekly until grade 1 (Bilirubin less than 1.5 x ULN, ALT less than 2.5 x ULN)
greater than 3 x ULN	or	greater than 5 x ULN	Hold abiraterone. Monitor liver tests at least weekly until grade 1 (Bilirubin less than 1.5 x ULN, ALT less than 2.5 x ULN) Reduce dose of abiraterone by 250 mg and resume only after liver tests less than or equal to grade 1

ULN = upper limit of normal

2. Hypokalemia Management:

Hypokalemia has been observed and should be aggressively managed. Serum potassium should be monitored closely in patients who develop hypokalemia.

Serum potassium (mmol/L)	Grade of Hypokalemia	Action	Further Action or Maintenance
Low potassium or History of hypokalemia		Weekly (or more frequent) laboratory electrolyte evaluations.	Titrate dose to maintain potassium greater than 3.5 mmol/L and less than 5.0 mmol/L (greater than 4.0 mmol/L recommended)
less than 3.5 – 3.0	Grade 1	Initiate oral or IV potassium supplementation. Consider monitoring magnesium and replacement if needed.	Titrate dose to maintain potassium greater than 3.5 mmol/L and less than 5.0 mmol/L (greater than 4.0 mmol/L recommended)
less than 3.5 – 3.0 Symptomatic	Grade 2	Withhold abiraterone until potassium corrected. Initiate oral or IV potassium supplementation. Consider monitoring magnesium and replacement if needed.	Titrate dose to maintain potassium greater than 3.5 mmol/L and less than 5.0 mmol/L (greater than 4.0 mmol/L recommended)
less than 3.0 – 2.5	Grade 3	Withhold abiraterone until potassium corrected. Initiate oral or IV potassium and cardiac monitoring. Consider monitoring magnesium and replacement if needed.	
less than 2.5	Grade 4	Withhold abiraterone until potassium corrected. Initiate oral or IV potassium and cardiac monitoring. Consider monitoring magnesium and replacement if needed	

PRECAUTIONS:

1. **Fluid retention:** Fluid retention can occur due to mineralocorticoid excess caused by compensatory adrenocorticotropic hormone (ACTH) drive. The administration of predniSONE will help reduce incidence and severity of fluid retention.
2. **Hypertension:** Patients with hypertension should exercise caution while on abiraterone. Rigorous treatment of blood pressure is necessary, since abiraterone can cause a rapid onset of high blood pressure. Blood pressure will need to be monitored once every 2 weeks for the first three months of abiraterone therapy. Temporary suspension of abiraterone is recommended for patients with severe hypertension (greater than 200 mmHg systolic or greater than 110 mmHg diastolic). Treatment with abiraterone may be resumed once hypertension is controlled (see also http://www.hypertension.ca).
3. **Renal impairment:** No dosage adjustment is necessary for patients with renal impairment.
4. **Hepatic Dysfunction:** Abiraterone undergoes hepatic metabolism. Hepatic dysfunction (particularly elevated AST and ALT) may occur during the first 3 months after starting treatment so a more frequent monitoring of liver function tests is required (every 2 weeks in the first three months and monthly thereafter).

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, Logothetis CJ, Molina A et al. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med 2011;364 (21):1995-2005.
2. Logothetis C, de Bono JS, Molina A et al. Effect of abiraterone acetate on pain control and skeletal-related events in patients with metastatic castration-resistant prostate cancer post docetaxel: Results from the COU-AA-301 phase III study. J Clin Oncol 29:2011 (suppl; abstr 4520).
3. Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. N Engl J Med 2013;368:138-48.