BC Cancer Protocol Summary for Palliative Therapy for Metastatic Castration Resistant Prostate Cancer Using Enzalutamide

Protocol Code: *UGUPENZ*

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
- 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

Notes:

- Patients treated with abiraterone for metastatic castration sensitive disease (GUMCSPABI) are eligible to receive enzalutamide (UGUPENZ) for metastatic castration resistant disease
- 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:

- Previously received enzalutamide (UGUNMPENZ), apalutamide (UGUPAPA) or darolutamide (UGUNMPDAR) for non-metastatic castration resistant disease
- Previously received enzalutamide (UGUMCSPENZ), apalutamide (UGUMCSPAPA), or darolutamide with DOCEtaxel (UGUMCSPDD) for metastatic castration sensitive disease

CAUTION:

- Uncontrolled hypertension

TESTS:

- Baseline: CBC & Differential, platelets, creatinine, sodium, potassium, PSA, testosterone, blood pressure
- Baseline if clinically indicated: ECG
- Each time seen by physician: PSA, testosterone, blood pressure.
- If clinically indicated: creatinine, sodium, potassium, ECG

TREATMENT:

Drug	Dose	BCCA Administration Guideline
enzalutamide	160 mg daily	PO

One cycle consists of 4 weeks (30 days) of enzalutamide. Dispense a 90 day supply with each physician visit. Treat until disease progression or unacceptable toxicity.

Dose reduction:
Dose level -1: enzalutamide120 mg PO daily
Dose level -2: enzalutamide 80 mg PO daily

Androgen ablative therapy (e.g., LHRH agonist, LHRH antagonist) should be maintained. Discontinue other antiandrogen (e.g., bicalutamide), if used as part of combined androgen blockade.

PRECAUTIONS:

1. **QT prolongation:** Enzalutamide is associated with QTc prolongation. It should be used with caution in patients with a known history of QT prolongation, risk factors for torsade de pointes (e.g. hypokalemia) or patients who are taking medications known to prolong the QT interval.
2. **Seizure:** Enzalutamide is associated with an increased risk of seizure, with a greater risk of seizure at daily doses higher than 160 mg. Seizures resolved after treatment cessation.
3. **Hypertension:** Enzalutamide is associated with increased blood pressure in approximately 7% of patients. Hypertension rarely leads to discontinuation or dose modification, but may require antihypertensive treatment. Blood pressure will need to be monitored once every 2 weeks for the first three months of enzalutamide therapy. Temporary suspension of enzalutamide is recommended for patients with severe hypertension (greater than 200 mmHg systolic or greater than 110 mmHg diastolic). Treatment with enzalutamide may be resumed once hypertension is controlled.
4. **Drug interactions**: CYP2C8 inhibitors (e.g. gemfibrozil) may increase the serum level of enzalutamide. Consider reducing enzalutamide to 120 mg or 80 mg once daily in patients who must be co-administered with a strong CYP2C8 inhibitor.

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. Scher HI, Fizazi K, Saad F, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med 2012;367(13):1187-1197.
2. Beer TM, Armstrong DE, Rathkopf Y, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med 2014;371:424-33.