BC Cancer Protocol Summary for Treatment for Metastatic Castration Sensitive Prostate Cancer using Enzalutamide

Protocol Code: *GUMCSPENZ*

Tumour Group: *Genitourinary*

Contact Physician: *Dr. Christian Kollmannsberger*

ELIGIBILITY:

Patients must have:

- metastatic castration sensitive prostate cancer (mCSPC) who are either:
  - chemotherapy naïve or have received prior chemotherapy containing DOCEtaxel

  AND
  - no prior androgen deprivation therapy (ADT) or have received ADT for not more than 6 months for metastatic castration sensitive prostate cancer (mCSPC) immediately prior to starting current protocol
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Patients should have:

- ECOG performance status 0-2
- Serum potassium greater than 3.5 mmol/L

EXCLUSIONS:

- Patients treated with enzalutamide for mCSPC and develop castration resistant disease are:
  - NOT eligible to receive abiraterone (UGUPABI)

TESTS:

- Baseline: CBC and differential, platelets, creatinine, sodium, potassium, blood pressure
- Patients at risk for electrolyte abnormality and QTc prolongation: ECG
- Each time seen by physician: PSA, blood pressure.
- If clinically indicated: creatinine, sodium, potassium, ECG

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
enzalutamide	160 mg daily	PO

One cycle consists of 4 weeks (30 days) of enzalutamide. Dispense 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 deprivation 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. Armstrong, AJ et al. ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer. J Clin Oncol 2019; 37: 2974-2986
2. Davis ID et al. Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer. N Engl J Med. 2019 Jul 11; 381(2):121-131.