BC Cancer Protocol Summary for Treatment of Non- Metastatic Castration Resistant Prostate Cancer Using Darolutamide

Protocol Code: *UGUNMPDAR*

Tumour Group: *Genitourinary*

Contact Physician: *Dr. Christian Kollmannsberger*

ELIGIBILITY:

Patients must have:

- Non-metastatic castration resistant prostate cancer (nmCRPC)
  - No radiologic evidence of metastases (negative bone scan, negative CT of pelvis, abdomen, chest) within the last 6 months (exception: pelvic lymph nodes < 2 cm in short axis below the aortic bifurcation)
- No prior chemotherapy for nmCRPC,
- PSA doubling time of less or equal to 10 months, and
- A BC Cancer "Compassionate Access Program" (CAP) request must be approved prior to treatment

Patients should have:

- ECOG performance status 0 to 2

Notes:

- Patients with nmCRPC are eligible to receive any of the following, but not their sequential use:
  - apalutamide (UGUPAPA),
  - darolutamide (UGUNMPDAR), or
  - enzalutamide (UGUNMPENZ)
- Patients who have progressed to metastatic disease on darolutamide (UGUNMPDAR):
  - Are eligible to receive all of the following:
    - DOCEtaxel (GUPDOC),
    - cabazitaxel (GUPCABA), and
    - radium in metastatic CRPC (GUPRAD)
  - Are **NOT** eligible to receive enzalutamide (UGUPENZ) or abiraterone (UGUPABI, UGUPAVOABI, UGUPAVNABI)

EXCLUSIONS:

- Metastatic prostate cancer (exception: pelvic lymph nodes < 2 cm in short axis below the aortic bifurcation)
- Prior treatment for nmCRPC with apalutamide (UGUPAPA) or enzalutamide (UGUNMPENZ)
- Prior chemotherapy for nmCRPC

TESTS:

- Baseline: CBC & Diff, platelets, albumin, total bilirubin, alkaline phosphatase, GGT, INR, ALT, creatinine, sodium, potassium, PSA, testosterone, blood pressure
- Baseline if clinically indicated: ECG
- Each time seen by physician: PSA, blood pressure
- If clinically indicated: albumin, total bilirubin, INR, ALT, creatinine, sodium, potassium, TSH, ECG, HbA1c, calcium, random glucose, testosterone

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
darolutamide	600 mg	PO twice daily

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

Dose Reduction:
Dose level -1: darolutamide 300 mg PO twice 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.

DOSE MODIFICATION:

1. **Hematological and Non-Hematological Toxicities**
   For toxicities greater than or equal to grade 3, reduce dose to 300 mg twice daily or withhold dose until symptoms improve. Dose reduction below 300 mg twice daily is not recommended. Dose may be escalated back to 600 mg twice daily based on tolerance.

2. **Hepatic Impairment**

Hepatic Impairment	Recommended Dose
Mild (Child-Pugh A)	No adjustment
Moderate (Child-Pugh B)	300 mg twice daily
Severe (Child-Pugh C)	Not recommended

3. **Renal Impairment**

Creatinine Clearance (mL/min)	Recommended Dose
greater than 30	No adjustment
15-29	300 mg twice daily
less than 15	Not recommended

PRECAUTIONS:

1. **Rash:** Rash has been reported. It is mostly grade 1-2 with less than 1% reported as grade 3-4. Corticosteroids and antihistamines may be used to treat the rash.
2. **Drug interactions**: Darolutamide is primarily metabolized by CYP3A4. Concomitant administration of darolutamide with strong inducers (e.g., rifampin) or strong inhibitors (e.g., itraconazole) of CYP3A4 may result in change in serum level of darolutamide.

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. Fizazi K, Shore N, Tammela TL, et al. Darolutamide in nonmetastatic, castration-resistant prostate cancer. N Engl J Med 2019;380(13):1235-1246.
2. Bayer Inc. NUBEQA™ darolutamide product monograph. Mississauga, Ontario; 19 Feb 2020.