BC Cancer Protocol Summary for Treatment of Metastatic Castration Sensitive Prostate Cancer Using Darolutamide

Protocol Code:	*GUMCSPDAR*
Tumour Group:	*Genitourinary*
Contact Physician:	*GU Systemic Therapy*

ELIGIBILITY:

Patients must have:

- metastatic castration sensitive prostate cancer (mCSPC),
- No prior systemic therapy for prostate cancer. Previous androgen deprivation therapy (ADT) is permitted if patient received:
  - Less than 6 months of ADT for mCSPC immediately prior to starting this protocol, and
  - no ADT for adjuvant treatment of non-metastatic prostate cancer within 1 year of starting this protocol

Patients should have:

- Good performance status

Notes:

- Patients with mCSPC are eligible to receive any of the following, but not their sequential use:
  - apalutamide (GUMCSPAPA),
  - abiraterone (GUMCSPABI),
  - darolutamide (GUMCSPDAR),
  - darolutamide with DOCEtaxel (UGUMCSPDD), or
  - enzalutamide (GUMCSPENZ)
- Patients treated with darolutamide for mCSPC who develop castration resistant disease are NOT eligible to receive abiraterone (UGUPABI, UGUPAVOABI, UGUPAVNABI) or enzalutamide (UGUPENZ)

TESTS:

- Baseline: CBC & Diff, 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:

Androgen deprivation therapy per protocol GUPADT should be maintained, unless prior bilateral orchiectomy.

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

- Discontinue antiandrogen (e.g., bicalutamide), if used as part of combined androgen blockade prior to initiation of darolutamide.
- Dispense a 90-day supply of darolutamide with each physician visit.
- Treat until disease progression or unacceptable toxicity.

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

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.

Contact the GU Systemic Therapy physician at your regional cancer centre or the GU Systemic Therapy Chair with any problems or questions regarding this treatment program.

REFERENCES:

1. Saad F, Vjaters E, Shore N et al. Darolutamide in Combination with Androgen-Deprivation Therapy in Patients With Metastatic Hormone-Sensitive Prostae Cancer From the Phase III ARANOTE Trial. J Clin Oncol 2024; 42(36): 4271-4281.
2. Darolutamide (NUBEQA) Canada's Drug Agency (CDA-AMC) Reimbursement Recommendation. Canadian Journal of Health Authorities. November 2025; 5(11): 1-10.