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

Protocol Code: *UGUPAPA*

Tumour Group: *Genitourinary*

Contact Physician: *Dr. Christian Kollmannsberger*
Dr. Daniel Khalaf

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 apalutamide (UGUPAPA):
- 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)

EXCLUSIONS:

Patients must not have:

- Metastatic prostate cancer (exception: pelvic lymph nodes < 2 cm in short axis below the aortic bifurcation)
- Prior treatment with enzalutamide (UGUNMPENZ) or darolutamide (UGUNMDAR) in nmCRPC
- Prior chemotherapy for nmCRPC
- Uncontrolled hypertension (systolic blood pressure greater than 160 mmHg or diastolic greater than 95 mmHg)

TESTS:

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

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
apalutamide	240 mg	PO once daily (dispense each 30-day supply in original container)

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

Dose reduction:
Dose level -1: apalutamide 180 mg PO daily
Dose level -2: apalutamide 120 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.

DOSE MODIFICATION:
Rash management:

Grade	Management
1	Continue apalutamide at current dose. Initiate topical steroid cream AND oral antihistamine
2	May continue apalutamide, or hold at treating physician's discretion Initiate topical steroid cream AND oral antihistamine If symptoms improve to equal or less than grade 1, restart apalutamide at same dose (240 mg PO daily)
≥ 3	Hold apalutamide Initiate topical steroid cream AND oral antihistamine Consider short course oral steroid If symptoms improve to equal or less than grade 1, restart apalutamide at same dose (240 mg PO daily), or reduced dose by one dose level (180 mg PO daily) If toxicity recurs at Grade 3 or higher, reduce dose by one dose level (180 mg PO daily or 120 mg PO daily).

PRECAUTIONS:

1. **Rash:** Rash is reported in 25% of patients on apalutamide. It is commonly described as macular or maculopapular in presentation and has a median onset within 3 months. It typically resolves after 2 months. Corticosteroids and antihistamines have been used to treat the rash (see rash management table).

2. **Hypothyroidism:** Grade 1-2 hypothyroidism is reported in up to 22% of patients receiving apalutamide. Median onset is 4 months. Monitor TSH throughout treatment and initiate thyroid replacement as indicated.
3. **Falls and fractures:** Falls and fractures have been associated with apalutamide. Mechanism unknown. Fractures have been reported within one month and up to 32 months after treatment initiation.
4. **Drug interactions**: CYP2C8 inhibitors (e.g. gemfibrozil) and CYP 3A4 inhibitors (e.g. ketoconazole) may increase the serum level of apalutamide.
5. **Seizures:** Seizures have been reported in patients on apalutamide. Onset of 12-16 months after treatment initiation. Use cautiously in patients with a history of seizures or other predisposing factors. Permanently discontinue apalutamide in patients who develop a seizure during treatment.
6. **Hypertension:** Apalutamide may result in an increased blood pressure. This rarely leads to discontinuation or dose modification, but may require antihypertensive treatment. Monitor blood pressure frequently.

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. Smith MR, Saad F, Chowdhury S, et al. Apalutamide treatment and metastasis-free survival in prostate cancer. N Engl J Med 2018; 378(15):1408-1418.
2. Janssen Inc. ERLEADA™ apalutamide product monograph. Toronto, Ontario; 3 July 2018