BC Cancer Protocol Summary for Treatment of Metastatic Castration-Resistant Prostate Cancer using Olaparib

Protocol Code:	*UGUPOLAP*
Tumour Group:	*Genitourinary*
Contact Physician:	*Dr. Christian Kollmannsberger* *Dr. Krista Noonan*

ELIGIBILITY:

Patients must have:

- Metastatic castration-resistant prostate cancer (mCRPC),
- Deleterious germline and/or somatic mutations in homologous recombination repair genes BRCA 1/2 or ATM
- Progressed on prior ARAT (androgen receptor-axis-targeted) therapy – enzalutamide, abiraterone/predniSONE, apalutamide or darolutamide in the metastatic castration sensitive (mCSPC), nonmetastatic castration-resistant (nmCRPC), or metastatic castration-resistant (mCRPC) prostate cancer setting with or without prior taxane chemotherapy
- A BC Cancer "Compassionate Access Program" (CAP) approval prior to treatment

Patients should have:

- Performance status ECOG 0 to 2

EXCLUSIONS:

Patients must not have:

- Clinical suspicion of myelodysplasia
- Prior treatment with or progression on poly-(ADP ribose) polymerase (PARP) inhibitor for mCRPC (e.g., olaparib or niraparib)

TESTS:

- Baseline: CBC & Diff, creatinine, sodium, potassium, ALT, total bilirubin, alkaline phosphatase
- Baseline if clinically indicated: ECG
- Every four weeks: CBC & Diff, PSA
- If clinically indicated: creatinine, sodium, potassium, ALT, total bilirubin, alkaline phosphatase, total protein, albumin, GGT, LDH, urea
- If clinically indicated: CBC & Diff on Day 14

PREMEDICATIONS:

- Antiemetic protocol for chemotherapy with low emetogenicity (see SCNAUSEA)

Warning: The information contained in these documents are a statement of consensus of BC Cancer professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer's terms of use available at http://www.bccancer.bc.ca/terms-of-use

TREATMENT:

Drug	Starting Dose	BC Cancer Administration Guideline
olaparib	300 mg	PO twice daily (dispense 30 days supply*)

* tablets must be dispensed in original manufacturer containers with supplied desiccant

Repeat every 28 days until disease progression or unacceptable toxicity.

DOSE MODIFICATIONS:

1. **Hematology**

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
Greater than or equal to 1.0	and	Greater than or equal to 100	100% of previous cycle's dose
Less than 1.0	or	Less than 100	Delay until recovery, then re-start at a reduced dose level (see table below).

2. **Renal dysfunction:**
   If CrCl falls between 31 to 50 mL/min, reduce dose to 200 mg PO twice daily. Treatment with olaparib is not recommended if CrCl is less than or equal to 30 mL/min.

3. **Due to Other Toxicities**
   Dose reductions should be made according to the following increments:

Dose level 0 (100%)	Dose level -1	Dose level -2
300 mg PO BID	250 mg PO BID	200 mg PO BID

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Anemia**: In patients with hemoglobin less than 90 g/L, consider correction of anemia prior to beginning/continuing olaparib treatment
3. **Hepatic impairment**: no modifications are required for mild to moderate impairment (Child-Pugh A or B). Use in severe impairment (Child-Pugh C) is not recommended as there is no data.
4. **Drug interactions**: Olaparib is primarily metabolized by CYP3A. Concurrent use of moderate or strong CYP3A inhibitors and strong CYP3A inducers should be avoided. If concurrent use cannot be avoided, dose modification may be required.

Call Dr. C Kollmannsberger or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

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REFERENCES:

1. de Bono J, Mateo J, Fizazi K, et al. Olaparib for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med 2020;382 (22): 2091-2102
2. Hussain M, Mateo J, Fizazi K, et al. Survival with olaparib in metastatic castration-resistant prostate cancer. N Engl J Med. 2020;383(24):2345-2357

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