BC Cancer Protocol Summary for Maintenance Treatment of Relapsed, BRCA-Mutated, Platinum Sensitive and Responsive Epithelial Ovarian Cancer using Olaparib

Protocol Code:	*GOOVOLAPM*
Tumour Group:	*Gynecologic Oncology*
Contact Physician:	*Dr. Jenny Ko*

ELIGIBILITY:

Patients must have:

1. Platinum-sensitive recurrent ovarian/fallopian tube/peritoneal carcinoma,
    a. Platinum sensitive defined as partial or complete response to platinum retreatment,
    b. Two or more prior lines of platinum chemotherapy and in radiologic (complete or partial) response to the most recent platinum based therapy,
    c. Recurrence should be greater than four months from previous line of platinum-based chemotherapy, and
    d. Last dose of platinum chemotherapy retreatment within 8 weeks of starting olaparib maintenance,
2. High grade serous or endometrioid histology, and
3. Germline or somatic *BRCA* mutation.

Patients are eligible to receive only one line of PARP-inhibitor treatment (GOOVOLAPM or GOOVFOLAM or GOOVNIRAM or GOOVFNIRM)

EXCLUSIONS:

Patients should not have:

- Performance status ECOG 3 or worse (unless related to chemotherapy toxicity and expected to improve),
- Clinical suspicion of myelodysplasia,
- Platinum resistance,
    - progression while on platinum-based therapy,
    - progression within four months of last platinum dose, or
- Prior progression on olaparib or another PARP-inhibitor. If discontinued for another reason other than progression (e.g. intolerance, patient choice), retreatment may considered.

TESTS:

- Baseline: CBC & diff, platelets, creatinine, sodium, potassium, ALT, bilirubin, alk phos.
    - If clinically indicated: tumour marker (CA 125, CA 15-3, CA 19-9, CEA), ECG.
- Every four weeks: CBC & diff, platelets.
    - If clinically indicated: creatinine, ALT, bilirubin, alk phos, any initially elevated tumour marker.
- If clinically indicated: CBC & diff, platelets on Day 14

PREMEDICATIONS:

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

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 31-50 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 BID	250 mg BID	200 mg 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. Jenny Ko or tumour group delegate at (604) 851-4710 or 1-877-547-3777 with any problems or questions regarding this treatment program.

REFERENCES:

Pujade-Lauraine E, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Oncol 2017;18(9):1274-84.