# BC Cancer Protocol Summary for Treatment of BRCA-Mutated High-Risk Early Breast Cancer using Olaparib

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| ***Protocol Code:*** | *UBRAJOLA* |
| ***Tumour Group:*** | *Breast* |
| ***Contact Physician:*** | *Dr. Nathalie LeVasseur* |

## ELIGIBILITY:

Patients must have:

- High-risk early stage* HER2-negative breast cancer with deleterious or suspected deleterious germline *BRCA 1/2* mutation (patients must have confirmation of germline BRCA mutation before treatment is initiated),
- Received prior chemotherapy,
- Olaparib initiated within 12 weeks of completion of last treatment (surgery, chemotherapy, or radiation), and
- BC Cancer "Compassionate Access Program" request approval prior to treatment

* Definition of high-risk early stage patients:

- Triple negative breast cancer**:
  - Patients treated with upfront surgery and adjuvant chemotherapy who have either node positive disease or pT ≥2 cm, or
  - Patients treated with neoadjuvant chemotherapy followed by surgery and have residual invasive disease (other than DCIS) in the breast and/or in resected lymph nodes (non-pCR)
- Hormone receptor (HR)-positive, HER2-negative breast cancer:
  - Patients treated with upfront surgery and adjuvant chemotherapy and have 4 or more involved lymph nodes, or
- Patients treated with neoadjuvant chemotherapy followed by surgery and have residual disease in breast and/or in resected lymph nodes (non-PCR) and CPS + EG Score 3 or higher. Neoadjuvant Therapy Outcomes Calculator for CPS + EG Score located at: https://www3.mdanderson.org/app/medcalc/

** Patients are eligible if:

1. HER2 negative:
   - HER2 IHC 0 to 1, or
   - HER2 IHC 2 with FISH negative,

   and
2. ER negative:
   - Less than 1% of ER positive cells, and
   - ER Allred score 0 to 2 out of 8

- Regardless of PR results
- All other cases including ER-low requests require approval via BC Cancer Compassionate Access Program (CAP)

Notes:

- Concurrent adjuvant endocrine therapy may be used at physician's discretion
- Olaparib (UBRAJOLA) use after capecitabine (BRAJCAP) is funded
- Patients are eligible to receive one of the following, but not their sequential use: olaparib (UBRAJOLA) or pembrolizumab (BRAJPEM)
- Patients are eligible to receive one of the following, but not their sequential use: olaparib (UBRAJOLA) or abemaciclib (UBRAJABEAI/UBRAJABET)
- Concurrent adjuvant CDK 4/6 inhibitor is **not** funded
- Concurrent olaparib with pembrolizumab is **not** funded

**EXCLUSIONS**:

Patients must not have:

- Metastatic breast cancer,
- HER-2 positive disease, or
- Myelodysplastic syndrome or acute myeloid leukemia

**TESTS:**

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

**PREMEDICATIONS:**

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

**TREATMENT:**

| Drug | Dose | BC Cancer Administration Guideline |
|---|---|---|
| olaparib | 300 mg twice daily<br>(Total daily dose = 600 mg) | PO<br>(dispense 30 days supply*) |

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

Repeat every 28 days, continuously for up to 1 year of treatment, unless 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 reduced dose level |

### 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. 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. Nathalie LeVasseur or tumour group delegate at (604) 930-2098 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

## REFERENCES:


1. Tutt ANJ, Garber JE, Kaufman B, et al.; OlympiA Clinical Trial Steering Committee and Investigators. Adjuvant Olaparib for Patients with *BRCA1*- or *BRCA2*-Mutated Breast Cancer. N Engl J Med. 2021 Jun 24;384(25):2394-2405.
2. Geyer CE Jr, Garber JE, Gelber RD, et al.; OlympiA Clinical Trial Steering Committee and Investigators. Overall survival in the OlympiA phase III trial of adjuvant olaparib in patients with germline pathogenic variants in BRCA1/2 and high-risk, early breast cancer. Ann Oncol. 2022 Dec;33(12):1250-1268.
3. CADTH: Olaparib (Lynparza) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies 2023; 3(3):1-23.