BC Cancer Protocol Summary for Maintenance Treatment of Relapsed Platinum Sensitive and Responsive Epithelial Ovarian Cancer using Niraparib

Protocol Code:	*UGOOVNIRAM*
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 to 12 weeks of starting niraparib maintenance,
2. High grade serous or endometrioid histology, and
3. BC Cancer Compassionate Access Program (CAP) approval.

Patients are eligible to receive only one line of PARP-inhibitor treatment (GOOVOLAPM or GOOVFOLAM or UGOOVNIRAM or UGOOVFNIRM)
- Unless prior PARP-inhibitor treatment was discontinued for reasons other than progression

EXCLUSIONS:

Patients must 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 niraparib or another PARP-inhibitor. If discontinued for another reason other than progression (e.g. intolerance, patient choice), retreatment may be considered.

TESTS:
- **Baseline:** CBC & diff, platelets, creatinine, sodium, potassium, ALT, bilirubin, alk phos, blood pressure
    - If clinically indicated: tumour marker (CA 125, CA 15-3, CA 19-9, CEA), ECG
- **Every four weeks for the first year (cycles 1 to 12):** CBC & diff, platelets, blood pressure
    - Cycle 1: check CBC & diff, platelets weekly or on Day 14
- **After one year (cycles 12+):** CBC & diff, platelets, blood pressure as clinically indicated
- If clinically indicated: CBC & diff, platelets on Day 14
- If clinically indicated: creatinine, ALT, bilirubin, alk phos, any initially elevated tumour marker

PREMEDICATIONS:

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

TREATMENT:

Drug	Weight	Starting Dose	BC Cancer Administration Guideline
niraparib	Greater than or equal to 58 kg	300 mg	PO once daily
	Less than 58 kg	200 mg	

Repeat every 28 days until disease progression or unacceptable toxicity.

DOSE MODIFICATIONS:

1. Hematology

Platelets (x 10^9/L)		ANC (x 10^9/L)		Hemoglobin (g/L)	Dose
greater than or equal to 100	and	greater than or equal to 1.0	and	greater than or equal to 80	100% of previous cycle's dose
less than 100					First occurrence: Delay until recovery, then re-start at same dose. Discontinue if counts do not recover within 28 days. If platelet count was less than 75 x 10^9/L, re-start at reduced dose level (see table below).
					Second occurrence: Delay until recovery, then re-start at a reduced dose level (see table below). Discontinue if counts do not recover within 28 days.
		less than 1.0			Delay until recovery to greater than or equal to 1.5 x 10^9/L, then re-start at a reduced dose level (see table below). Discontinue if counts do not recover within 28 days.
				less than 80	Delay until recovery to greater than or equal to 90 g/L, then re-start at a reduced dose level (see table below). Discontinue if counts do not recover within 28 days.

2. Due to Other Toxicities

Dose reductions should be made according to the following increments:

Starting Dose	**300 mg**	**200 mg**
Dose level -1	200 mg	100 mg
Dose level -2	100 mg*	Discontinue

* If further dose reduction is necessary, discontinue niraparib

3. Hepatic impairment:
For moderate hepatic impairment, reduce starting dose by one level. Use in severe impairment (Child-Pugh C) is not recommended as there is no data.

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 niraparib treatment
3. **Hypertension**: Hypertension and hypertensive crisis have been reported and may occur with first dose. Monitor blood pressure and heart rate regularly for the first year of treatment, then as clinically indicated. Hypertension should be clinically managed with antihypertensive medications and niraparib dose adjustment as needed.
4. **Renal impairment**: no modifications are required for mild to moderate impairment. Use in severe impairment (CrCl < 30 mL/min) is not recommended as there is no data.

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:

1. Mirza MR, Monk BJ, Herrstedt J, et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. N Engl J Med 2016;375(22):2154-64.
2. GlaxoSmithKline Inc. ZEJULA® product monograph. Mississauga, Ontario; 2 October 2020.
3. GlaxoSmithKline. ZEJULA full prescribing information. Research Triangle Park, NC, USA; May 2021.