BC Cancer Protocol Summary for Maintenance Treatment of Newly Diagnosed Platinum Responsive Epithelial Ovarian Cancer using Niraparib

Protocol Code:	*GOOVFNIRM*
Tumour Group:	*Gynecologic Oncology*
Contact Physician:	*Dr. Aalok Kumar*

ELIGIBILITY:

Patients must have:
1. Platinum-responsive ovarian/fallopian tube/peritoneal carcinoma,
    a. Platinum-responsive defined as partial or complete clinical response to platinum treatment,
    b. Completed at least 6 cycles of first-line platinum chemotherapy, and
    c. Last dose of platinum chemotherapy within 12 weeks of starting niraparib maintenance
2. High grade serous or endometrioid histology,
3. Stage III or IV disease (patients may have upfront, interval or delayed debulking surgery), and

Patients are eligible to receive only one line of PARP-inhibitor treatment (GOOVOLAPM or GOOVFOLAM or GOOVNIRAM or GOOVFNIRM)
- 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, or
- Prior bevacizumab (except for patients on bevacizumab at the time of listing of GOOVFNIRM)

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		Baseline Platelet count	Starting dose	BC Cancer Administration Guideline
niraparib	Greater than or equal to 77 kg	and	Greater than or equal to 150 x 10^9/L	300 mg	PO once daily
	Less than 77 kg	or	Less than 150 x 10^9/L	200 mg	

Repeat every 28 days for 3 years (39 cycles).

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. Aalok Kumar or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

REFERENCES:

1. Gonzalez-Martin A, Pothuri B, Vergote I, et al. Niraparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med 2019;381(25):2391-2402.
2. GlaxoSmithKline Inc. ZEJULA® product monograph. Mississauga, Ontario; 2 October 2020.
3. GlaxoSmithKline. ZEJULA full prescribing information. Research Triangle Park, NC, USA; May 2021.