BC Cancer Protocol Summary for Palliative Therapy for Relapsed/Progressing Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using Metronomic Low-Dose Oral Cyclophosphamide

Protocol Code	*GOOVCYCPO*
Tumour Group	*Gynecologic Oncology*
Contact Physician	*Dr. Theresa Chan*

PREFACE:

• In platinum sensitive disease: patients should be considered for doublet therapy consisting of CARBOplatin plus either a taxane, gemcitabine, or DOXOrubin pegylated liposomal (e.g., GOOVCATR, GOOVCAD, GOOVCAG, GOOVPLDC).
• In platinum resistant disease (i.e., progression within six months of completing a platinum containing treatment protocol): patients may be rechallenged with single agent CARBOplatin, as it is the least toxic and most convenient choice of the equally efficacious agents available (i.e., GOOVCARB).
• In platinum refractory disease (i.e., progression while being treated with a platinum): choose between available agents based upon toxicity profile and convenience of dosing regimen. Options include GOOVTOP, GOOLDOX, GOOVGEM, GOOVETO, GOOVVIN, GOOVTAX3, GOOVDOC, GOOVCYCPO.
• Patients who will not benefit from further therapy after second or subsequent rounds of chemotherapy can be identified by the following formula: “day 1 of treatment N to day of progression on treatment N+1 is less than or equal to 6 months.” They should be offered symptomatic management or investigational protocols.

ELIGIBILITY:

- Platinum refractory ovarian, primary peritoneal or Fallopian tube carcinoma
- Platinum resistant ovarian, primary peritoneal or Fallopian tube carcinoma in cases where patient specific concerns dissuade the clinician from selecting single-agent CARBOplatin
- Platinum sensitive ovarian, primary peritoneal or Fallopian tube carcinoma in cases where actual or potential toxicity precludes the use of CARBOplatin or CISplatin alone or in combination
- 2 or more prior lines of non-platinum containing chemotherapy, unless actual or potential toxicity precludes use of these other protocols
- ECOG 2 or better and greater than 3 month life expectancy
- Adequate hematologic and renal function

EXCLUSIONS:

- severe renal dysfunction, creatinine clearance less than 10 mL/min

TESTS:

- Baseline: CBC and diff, platelets, serum creatinine
- Before each treatment: CBC
- If clinically indicated: creatinine, CA125

PREMEDICATIONS:

- Antiemetic protocol for low emetogenic chemotherapy protocols (see SCNAUSEA)

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
cyclophosphamide	50 mg orally once daily continuously	PO

1 cycle = 4 weeks

Repeat every 28 days until disease progression (usual treatment 6 to 9 cycles).
Discontinue if no response after 2 cycles or unacceptable toxicity.

DOSE MODIFICATIONS:

1. **Hematological**

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose (all drugs)
Less than 1.0	or	Less than 100	Delay until recovery

2. **Renal dysfunction**

$$\text{GFR} = \frac{N^* \times (140 - \text{Age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$$

* For males N = 1.23; for females N=1.04

For Cyclophosphamide: Renal failure may lead to reduced excretion of metabolites and increased toxicity. Significant falls in clearance with increased exposure have been documented in patients with renal impairment. Severe renally impaired patients (CrCl less than 10 mL/min) are at particular risk and should be treated at reduced dose and with caution. See BC Cancer Cancer Drug Manual.

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.

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

References:

1. Andre N, Carre M, Pasquier E. Metronomics: towards personalized chemotherapy? Nat Rev Clin Oncol. 2014;11:413–431.
2. Perroud H, Scharovsky G, Rozados V, Alasino C et al. Clinical response in patients with ovarian cancer treated with metronomic chemotherapy. Ecancermedicalscience. 2017,11:723.
3. Ferrandina G, Corrado G, Mascilini F, Malagutiet P at al. Metronomic oral cyclophosphamide (MOC) in the salvage therapy of heavily treated recurrent ovarian cancer patients: a retrospective, multicenter study. BMC Cancer 2014, 14:947-954.
4. Sánchez-Muñoz A, Mendiola C, Pérez-Ruiz E, Rodríguez-Sánchez C et al. Bevacizumab plus low-dose metronomic oral cyclophosphamide in heavily pretreated patients with recurrent ovarian cancer. Oncology. 2010;79:98–104.