

BC Cancer Protocol Summary for Treatment of Advanced Ovarian Cancer in Patients Who Have Progressed or Recurred Following First-line Platinum-based Treatment Using CARBOplatin and Gemcitabine

Protocol Code

GOOV CAG

Tumour Group

Gynecologic Oncology

Contact Physician

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ELIGIBILITY:

Patients must have:

- Histologically proven ovarian, tubal or peritoneal cancer with evidence of recurrence or progression not treatable with surgery or radiation therapy, **and**
- Disease potentially responsive to CARBOplatin, i.e.- no progression while receiving prior platinum therapy
- For other indications, a BC Cancer “Compassionate Access Program” request must be approved prior to treatment.

Patients should have:

- Adequate bone marrow reserve, i.e. ANC greater than or equal to 1.0 and platelets greater than or equal to 100,
- ECOG status 0 to 2, **and**
- Life expectancy greater than or equal to 12 weeks

EXCLUSIONS:

Patients must not have:

- Borderline malignancy,
- Serious concomitant systemic disorder or active infection,
- CNS metastases, **or**
- Age greater than 80 years

TESTS:

- Baseline Tests: CBC **and** differential, **platelets**; serum creatinine; tumour markers (CA-125, CA 15-3, CA 19-9); nuclear renogram or Cockcroft-Gault formula to determine GFR; imaging as necessary to allow response monitoring
- Before each treatment (Days 1 **and** 8): CBC **and** differential, **platelets**
- Before each cycle (Day 1): serum creatinine, elevated tumour markers

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy protocols (see SCNAUSEA) for CARBOplatin

TREATMENT:

Drug	Dose	BC Cancer Administration Guidelines
gemcitabine	800 mg/m ² (maximum dose 2000 mg) Days 1 and 8	IV in NS 250 mL over 30 minutes
CARBOplatin	Day 1 only; <i>after</i> gemcitabine. Dose at AUC = 5* (May increase to AUC = 6* if interval platelet count greater than or equal to 150)	IV in NS 100 to 250 mL over 30 minutes

*Calvert Formula: CARBOplatin dose (mg) = target AUC x (GFR + 25)

Measured GFR (e.g. nuclear renogram) is preferred whenever feasible, *particularly* in circumstances of co-morbidity that could affect renal function (third-space fluid accumulations, hypoproteinemia, potentially inadequate fluid intake, etc.). The lab reported GFR (MDRD formula) may be used as an alternative to the Cockcroft-Gault estimate of GFR; the estimated GFR reported by the lab or calculated using the Cockcroft-Gault equation should be capped at 125 mL/min when it is used to calculate the initial CARBOplatin dose. When a nuclear renogram is available, this clearance would take precedence.

Cockcroft-Gault Formula

$$\text{GFR} = \frac{1.04 \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

Note: The same method of estimation should be used throughout the treatment course (i.e. if lab reported GFR was used initially, this should be used for dosing in all subsequent cycles and not the Cockcroft-Gault estimate).

Repeat every 3 weeks until disease progression (usual treatment 9 cycles). If ongoing response after six cycles and measurable disease persists, consider continuing or switching to GOOVCARB.

DOSE MODIFICATIONS:

A. Gemcitabine Day 8 – hematological toxicity:

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	% of calculated dose
greater than or equal to 1.0	and	greater than or equal to 100	100
less than 1.0	and/or	less than 100	Omit dose, and reduce subsequent cycle by one dose level

Gemcitabine Day 8 – non-hematological toxicity:

NCIC-CTC Grade	Dose
0, 1, 2	100%
3, 4	50% or omit, at physician's discretion

B. Both drugs in subsequent cycles – hematological toxicity:

Delay treatment until ANC greater than or equal to 1.0 and platelets greater than or equal to 100

And reduce by one dose level (see below) if:

- ANC known to be less than 0.5 for greater than 5 days within a cycle
- ANC known to be less than 0.1 for greater than 3 days within a cycle
- Febrile neutropenia occurred
- Platelets less than 50 within a cycle
- Cycle was delayed greater than 1 week due to toxicity
- Day 8 dose was omitted (as per table, above)

C. If no delay, and ANC greater than or equal to 1.0, platelets greater than or equal to 100, and no other toxicity is observed, consider increasing one of the two drugs (but not both in the same cycle) by one dose level (see below).

Drug	Dose Level +1	Dose Level 0	Dose Level -1
gemcitabine	1000 mg/m ² Days 1 & 8	800 mg/m ² Days 1 & 8	700 mg/m ² Days 1 & 8
CARBOplatin	AUC = 5, or 6 if interval platelet count greater than or equal to 150	AUC = 5	AUC = 4

D. Both drugs in subsequent cycles – non-hematological toxicity:

Grade in previous cycle	Dose
3 (except nausea/vomiting)	50%
4	Consider delay or discontinuation

If serum creatinine changes greater than 20% from baseline, consider recalculating CARBOplatin dose using new GFR.

If recovery from toxicities has not occurred after two weeks delay, re-treatment is not recommended.

PRECAUTIONS:

The following toxicities have been reported with CARBOplatin and/or gemcitabine therapy:

1. **Neutropenia.** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Renal Dysfunction.** Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare). Use caution with pre-existing renal dysfunction.
3. **Pulmonary Toxicity.** Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
4. **Transient truncal rash.**
5. **Nausea.**
6. **Mucositis.**
7. **Fatigue.**

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