

BCCA Protocol Summary for Treatment of Relapsed/Progressing Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using Gemcitabine

Protocol Code

GOOVGEM

Tumour Group

Gynecologic Oncology

Contact Physician

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PREFACE:

- In platinum sensitive disease: patients will ideally receive doublet therapy consisting of carboplatin plus either a taxane or gemcitabine (e.g., GOOVCA^TR, GOOVCA^DR, GOOVCA^G)
- In platinum resistant disease (i.e., cancer progresses within six months of completing a platinum-containing treatment protocol): patients will ideally receive single agent carboplatin, as it is the least toxic and most convenient choice of the equally efficacious agents available (i.e., GOOVCA^RB)
- In platinum refractory disease (i.e., cancer progresses while being treated with a platinum) choose between available agents based upon toxicity profile and convenience of dosing regimen. Options include: GOOV^TOP, GOOLDOX, GOOVGEM, GOOVETO, GOOVVIN, GOOV^TA^X3, GOOV^DOC. If gemcitabine (GOOVGEM), topotecan (GOOV^TOP) or pegylated liposomal doxorubicin (GOOV^LDOX) is used, only one of these options will be reimbursed in any one patient. Subsequently, if a patient is thought likely to benefit from one of the other two, a request should be submitted to the BCCA Compassionate Access Program (CAP).
- 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 with a taxane or gemcitabine.
- If used at the time of second, or greater, relapse, more than six months benefit to the two preceding chemotherapy regimens must have occurred (i.e., day 1 of treatment N to day of progression on treatment N+1 must be greater than 6 months)¹
- Adequate hematologic, liver and cardiac function
- PS ECOG 3 or better
- A “Class II Drug Registration Form” must be submitted at the time of initiation of treatment (included in BCCA PPPO; separate submission not needed if PPPO used)

EXCLUSIONS:

- Relapse of platinum sensitive disease (i.e., greater than 6 months from end of first-line treatment). See PREFACE, above. Exception: cases of unacceptable toxicity from platinum agent

TESTS:

- Mandatory Baseline tests: CBC, including differential and platelets, creatinine
- Suggested Baseline tests: appropriate tumour markers and imaging study
- In Cycle 1 and in any Cycle in which a dose change has been made: Before treatment on days 1, 8, and 15: CBC, including differential and platelets
- In Cycle 2 and subsequent cycles when no dose change has been made: Before treatment on day 1 only: CBC, including differential and platelets
- Appropriate tumour markers and imaging studies should be repeated as necessary

PREMEDICATIONS:

- Antiemetic protocol for chemotherapy with low to low-moderate emetogenicity (see [SCNAUSEA](#))

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Gemcitabine	800 mg/m ² on day 1, 8, and 15	IV in 250 mL NS over 30 min

Repeat every 28 days until progression or unacceptable toxicity occurs, to a maximum of 6 cycles. To continue beyond six cycles, submit a BCCA Compassionate Access Program (CAP) application.

DOSE MODIFICATIONS:

1. **Hematology:** on day 1 in any cycle; and on day 1, 8 and 15 in cycle 1 and in all cycles in which a dose change has been made

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose
greater than or equal to 1	and	greater than or equal to 100	100%
less than 1	or	less than 100	<i>If day 1:</i> delay until recovery, then proceed at reduced dose of 700 mg/m ² . <i>If day 8:</i> omit dose. If counts recover by day 15 proceed at reduced dose of 700 mg/m ² . <i>If day 15:</i> omit dose. Proceed at reduced dose of 700 mg/m ² with next cycle.

Note: If a recurrence of hematologic count problems occurs despite dose reduction to 700 mg/m²: either (i) discontinue gemcitabine if regimen had been day 1 & 8 only, or day 1 & 15 only; or, (ii) change to day 1 & 8 only, or day 1 & 15 only, if regimen had been day 1, 8, & 15.

2. **Febrile Neutropenia:** decrease subsequent doses to 700 mg/m². If a recurrence of febrile neutropenia occurs despite dose reduction to 700 mg/m²: either (i) discontinue gemcitabine if regimen had been day 1 & 8 only, or day 1 & 15 only; or, (ii) change to day 1 & 8 only, or day 1 & 15 only, if regimen had been day 1, 8, & 15.
3. **Pneumonitis:** discontinue gemcitabine if pneumonitis occurs
4. **Non-Hematologic Toxicities:** may include
 - Mucositis

- Transient truncal rash
- Fatigue
- For Grade 3 toxicity, delay treatment until resolution of symptoms, then resume at 700 mg/m². If dose already reduced, switch to day 1 & 8 only or day 1 & 15 only. If Grade 3 toxicity persists, discontinue gemcitabine.
- For Grade 4 toxicity, discontinue treatment.
- Doses reduced for toxicity should not be re-escalated.

PRECAUTIONS:

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. **Fever and Flu-like Symptoms:** may commonly occur (fever 37%, flu-like symptoms 19%). Use acetaminophen as necessary for comfort.
5. **Drug Interaction – warfarin:** gemcitabine may cause increased anticoagulant effect of warfarin. Monitor INR carefully during and for 1-2 months after gemcitabine therapy; adjust warfarin dose as necessary.

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

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