

BC Cancer Protocol Summary for Treatment of Relapsed/Progressing Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using PAclitaxel

Protocol Code

GOOVTAX3

Tumour Group

Gynecologic Oncology

Contact Physician

GO Systemic Therapy

PREFACE:

- In platinum sensitive disease: patients should be considered for doublet therapy consisting of carboplatin plus either a taxane or gemcitabine or DOXOrubicin pegylated liposomal (e.g., GOOVCA^{TR}, GOOVCA^D, GOOVCA^G, GOOVPLDC)
- 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., GOOVCAR^B)
- 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: GOOVTO^P, GOOLDOX, GOOVGEM, GOOVETO, GOOVVIN, GOOVTAX³, GOOVDO^C. If gemcitabine (GOOVGEM), topotecan (GOOVTO^P) or DOXOrubicin pegylated liposomal (GOOVLDO^X) 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 BC Cancer 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.
- Adequate hematologic, liver and cardiac function
- PS ECOG 3 or better

EXCLUSIONS:

- Peripheral neuropathy Grade 2 or higher (relative contraindication)
- Prior severe arthromyalgia unresponsive to treatment (relative contraindication)

TESTS:

- Baseline: CBC & Diff, total bilirubin, ALT
- Baseline, if clinically indicated: alkaline phosphatase, LDH, GGT, creatinine, sodium, potassium, CA 125, CA 19-9, CA 15-3, CEA, SCC
- Before each treatment: CBC & Diff, total bilirubin, ALT
If clinically indicated: alkaline phosphatase, LDH, GGT, creatinine, sodium, potassium, CA 125, CA 19-9, CA 15-3, CEA, SCC

PREMEDICATIONS:

- **PACLitaxel must not be started unless the following drugs have been given:**
 - 45 minutes prior to PACLitaxel:
 - dexamethasone 20 mg IV in 50 mL NS over 15 minutes
 - 30 minutes prior to PACLitaxel:
 - diphenhydrAMINE 50 mg IV in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)
- additional antiemetics not usually required (see [SCNAUSEA](#))

TREATMENT:

Drug	Starting Dose	BC Cancer Administration Guideline
PACLitaxel	175 mg/m ² *	IV in 250 to 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)

***For patients who have demonstrated an unusual degree of marrow toxicity with previous treatments or who are thought to be at risk of increased toxicity, a reduced initial dose of 155 mg/m² is suggested**

Repeat every 21 days until disease progression (usual treatment 9 cycles).

DOSE MODIFICATIONS:

1. Hematological

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose
greater than or equal to 1.0	and	greater than or equal to 100	175 mg/m ²
less than 1.0	or	less than 100	delay until recovery; resume at 175 mg/m ²

2. **Febrile Neutropenia:** Reduce dose to 155 mg/m² after first occurrence of febrile neutropenia. In the case of a second occurrence, use filgrastim (G-CSF) together with the same dose of paclitaxel, or discontinue paclitaxel.

3. Hepatic Dysfunction

ALT		Total bilirubin	Dose (mg/m ²)
less than 10 x ULN	and	less than or equal to 1.25 x ULN	175
less than 10 x ULN	and	1.26-2 x ULN	135
less than 10 x ULN	and	2.01-5 x ULN	90
greater than or equal to 10 x ULN	or	greater than 5 x ULN	not recommended

ULN = upper limit of normal

3. **Arthralgia and/or myalgia:** If arthralgia and/or myalgia of grade 2 (moderate) or higher is not relieved by adequate doses of NSAIDs or acetaminophen with codeine (e.g., Tylenol #3®), a limited number of studies report a possible therapeutic benefit using:
 - Prednisone 10 mg po bid x 5 days starting 24 hours post-paclitaxel
 - Gabapentin 300 mg po on day before chemotherapy, 300 mg bid on treatment day, then 300 mg tid x 7-10 days
 If arthralgia and/or myalgia persist, reduce subsequent PACLitaxel doses to 135 mg/m² or switch to Docetaxel (GOOVDOC).
4. **Neuropathy:** Dose modification or discontinuation may be required (see BC Cancer Drug Manual).

PRECAUTIONS:

1. **Hypersensitivity:** Reactions are common. See BC Cancer Hypersensitivity Guidelines

<i>mild</i> symptoms (e.g. mild flushing, rash, pruritus)	<ul style="list-style-type: none"> • complete PACLitaxel infusion. Supervise at bedside • no treatment required
<i>moderate</i> symptoms (e.g. moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension)	<ul style="list-style-type: none"> • stop PACLitaxel infusion • give IV DiphenhydrAMINE 25-50 mg and Hydrocortisone IV 100 mg • after recovery of symptoms resume PACLitaxel infusion at 20 mL/hr for 5 minutes, 30 mL/hr for 5 minutes, 40 mL/hr for 5 minutes, then 60 mL/hr for 5 minutes. If no reaction, increase to full rate. • if reaction recurs, discontinue PACLitaxel therapy. Consider use of docetaxel (GOOVDOC) • if no further reaction, and infusion is completed, in subsequent cycles, premedicate with dexamethasone 20 mg 12 and 6 hours prior to paclitaxel, and begin infusion at reduced rate with incremental increases as detailed above.
<i>severe</i> symptoms (i.e. <u>one</u> or more of respiratory distress requiring treatment, generalised urticaria, angioedema, hypotension requiring therapy)	<ul style="list-style-type: none"> • stop PACLitaxel infusion • give IV antihistamine and steroid as above. Add epinephrine or bronchodilators if indicated • discontinue PACLitaxel therapy. Consider use of docetaxel (GOOVDOC)

2. **Extravasation:** PACLitaxel causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Radiation recall reactions:** are occasionally seen.

Contact the GO Systemic Therapy physician at your regional cancer centre or the GO Systemic Therapy Chair with any problems or questions regarding this treatment program.