BC Cancer Protocol Summary for Treatment of Epithelial Ovarian Cancer Relapsing after Primary Treatment using DOXOrubicin Pegylated Liposomal

Protocol Code	*GOOVLDOX*
Tumour Group	*Gynecologic Oncology*
Contact Physicians	*Dr. Paul Hoskins* *Dr. Mark Heywood*

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., GOOVCATR, GOOVCAD, GOOVCAG, 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., GOOVCARB)
- 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: GOOVTOP, GOOVLDOX, GOOVGEM, GOOVETO, GOOVVIN, GOOVTAX3, GOOVDOC.
- 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:

- Pre-existing cardiomyopathy or congestive heart failure (relative contraindication)
- Premorbid disease affecting ability to tolerate DOXOrubicin pegylated liposomal
- Hepatic dysfunction (see DOSE MODIFICATIONS, below)

TESTS:

- Baseline: CBC with differential, platelets, bilirubin, ALT, Alk Phos, tumour markers (at physician's discretion), imaging for tumour assessment (at physician's discretion)
- Before each treatment: CBC with differential, platelets, tumour markers (at physician's discretion)
- If clinically indicated: creatinine, urea, albumin, ALT, Alk Phos, bilirubin, LDH, protein level, GGT
- If clinically indicated: cardiac function tests: echocardiogram or MUGA scan

PREMEDICATIONS:

- Antiemetic protocol for chemotherapy with low emetogenicity (see SCNAUSEA)

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline	
DOXOrubicin pegylated liposomal	40 mg/m^2	IV in 250 mL D5W (doses greater than or equal 90 mg in 500 mL D5W)	*Initial dose*: at rate of 1mg/min *Subsequent doses, if no prior infusion reaction:* infuse over 1 hour

Repeat every 28 days until disease progression (usual treatment 9 cycles).

DOSE MODIFICATIONS:

1. **Hematological**

ANC (x10^9/L)		Platelets (x10^9/L)	Dose
greater than or equal to 1.0	and	greater than or equal to 100	100%
less than 1.0	or	less than 100	delay until recovery, then proceed with 100% dose
febrile neutropenia			reduce subsequent cycles by 10 mg/m^2

2. **Hepatic**

Total bilirubin (micromol/L)	Dose (mg/m^2)
less than 21	40
21 to 50	30
greater than 50	20

3. **Stomatitis**

Grade	Symptoms	Dose
1	painless ulcers, erythema, or mild soreness	40 mg/m^2
2	painful erythema, edema or ulcers, but can eat	delay until recovered to Grade 1, then continue at 30 mg/m^2
3	painful erythema, edema or ulcers, and cannot eat	delay until recovered to Grade 1, then continue at 30 mg/m^2; or discontinue treatment
4	requires parenteral or enteral support	discontinue treatment

Note: If delay has been necessary due to stomatitis, change of interval to five weeks is recommended.

4. **Palmar-Plantar Erythrodysesthesia (PPE) (Hand-Foot Skin Reaction)**

Grade	Symptoms	Dose

1	mild erythema, swelling or desquamation not interfering with normal daily activities	if no prior Grade 2 or 3 occurrence, proceed at full dose. if prior Grade 2 or 3 occurrence, delay one week; once recovery evident, continue treatment at 30 mg/m^2
2	erythema, swelling or desquamation interfering with but not precluding normal daily activities; small blisters or ulcerations less than 2 cm in diameter	delay one week; once recovery evident, continue treatment at 30 mg/m^2
3	blistering, ulceration or swelling preventing normal daily activities; cannot wear regular clothing	delay one week, and re-assess; consider dexamethasone 2 mg TID until symptoms resolve; if still Grade 3 after a one week delay, discontinue treatment; if resuming, dose at 30 mg/m^2

Note: If delay has been necessary due to PPE, change of interval to five weeks is recommended.

5. **Other Grade 3 or 4 Toxicities**
   Reduce dose by 10 mg/m^2.

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Cardiac Toxicity**: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction.
3. **Extravasation**: DOXOrubicin pegylated liposomal is considered an irritant. Refer to BC Cancer Extravasation Guidelines.
4. **Acute Infusion Reaction**: may occur with first infusion, usually within minutes of starting. Refer to BC Cancer Hypersensitivity Guidelines. *Note: the first step is to stop the infusion*. In subsequent cycles, reactions are rare, but prophylaxis with dexamethasone, diphenhydrAMINE, and famotidine may be used.
5. **Palmar-Plantar Erythrodysesthesia (PPE) (Hand-Foot Skin Reaction)**: See BC Cancer Drug Manual liposomal DOXOrubicin monograph for suggested strategies for preventing or minimizing PPE. Corticosteroids may reduce the incidence of PPE during treatment.[2]

Call Dr. Paul Hoskins, Dr. Mark Heywood or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

REFERENCES:

1. Hoskins P, et al. Identifying patients unlikely to benefit from further chemotherapy: A descriptive study of outcome at each relapse in ovarian cancer. Gynecol Oncol 2005;97(3):862-9.
2. Alberts DS, et al. Efficacy and safety of liposomal anthracycline in phase I/II clinical trials. Sem Oncol 2004;32(Suppl 13):53-90.