

# BCCA Protocol Summary for Treatment of Relapsed/Progressing Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using **doxorubicin liposomal (Pegylated)**

**Protocol Code**

GOOVLDOX

**Tumour Group**

Gynecologic Oncology

**Contact Physicians**

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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<sup>TR</sup>, GOOVCA<sup>DR</sup>, GOOVCA<sup>G</sup>)
- 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<sup>RB</sup>)
- 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<sup>P</sup>, GOOVLDOX, GOOVGE<sup>M</sup>, GOOVET<sup>O</sup>, GOOVVI<sup>N</sup>, GOOVTA<sup>X3</sup>, GOOVDO<sup>C</sup>. If gemcitabine (GOOVGE<sup>M</sup>), topotecan (GOOVTO<sup>P</sup>) or pegylated liposomal doxorubicin (GOOVLDOX) 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 less than 6 months)<sup>1</sup>
- 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., less than 6 months from end of first-line treatment). See PREFACE, above. Exception: cases of unacceptable toxicity from platinum agent
- Pre-existing cardiomyopathy or congestive heart failure (relative contraindication)
- Premorbid disease affecting ability to tolerate pegylated liposomal doxorubicin
- Hepatic dysfunction (see DOSE MODIFICATIONS, below)

## TESTS:

- Baseline: CBC with differential, platelets, liver function test (LFT) panel, total bilirubin, 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), LFT panel (at physician's discretion)
- If clinically indicated: cardiac function tests: echocardiogram or MUGA scan

## PREMEDICATIONS:

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

## TREATMENT:

Drug	Dose	BCCA Administration Guideline	
doxorubicin liposomal (CAELYX®)	40 mg/m <sup>2</sup>	IV in 250 mL D5W (doses greater than or equal 90 mg should be diluted in 500 mL D5W)	<i>Initial dose:</i> at rate of 1mg/min <i>Subsequent doses, if no prior infusion reaction:</i> 1 hour infusion duration

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. Hematological

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Dose
greater than or equal to 1	and	greater than or equal to 100	100%
less than 1	or	less than 100	delay until recovery, then proceed with 100% dose
febrile neutropenia			reduce subsequent cycles by 10 mg/m <sup>2</sup>

### 2. Hepatic

Total bilirubin (micromol/L)	Dose (mg/m <sup>2</sup> )
less than 21	40
21-50	30
greater than 50	20

### 3. Stomatitis

Grade	Symptoms	Dose
1	painless ulcers, erythema, or mild soreness	40 mg/m <sup>2</sup>
2	painful erythema, edema or ulcers, but can eat	delay until recovered to Grade 1, then continue at 30 mg/m <sup>2</sup>
3	painful erythema, edema or ulcers, and cannot eat	delay until recovered to Grade 1, then continue at 30 mg/m <sup>2</sup> ; 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 <sup>2</sup>
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 <sup>2</sup>
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 <sup>2</sup>

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<sup>2</sup>.

## PRECAUTIONS:

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

**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.**

Date activated: 1 July 2007

Date revised: 1 Jun 2011 (drug name clarified, infusion duration reformatted)

**REFERENCES:**

1. Hoskins P, Gyn Oncol 97, 862-869, 2005
2. Alberts DS, Sem in Onc 32(Suppl13) 53-90, 2004