BC Cancer Protocol Summary for Treatment of Epithelial Ovarian Cancer Relapsing after Primary Treatment Using DOXOrubicin Pegylated Liposomal (CAELYX)

**Protocol Code**
GOOVLDX

**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, GOOVCA, 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, GOOVLDX, 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, 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).

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**Warning:** The information contained in these documents is a statement of consensus of BC Cancer professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient’s care or treatment. Use of these documents is at your own risk and is subject to BC Cancer’s terms of use available at www.bccancer.bc.ca/terms-of-use.
TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOXOrubicin pegylated liposomal (CAELYX)</td>
<td>40 mg/m² IV in 250 mL D5W (doses greater than or equal 90 mg in 500 mL D5W)</td>
<td>Initial dose: at rate of 1mg/min Subsequent doses, if no prior infusion reaction: infuse over 1 hour</td>
</tr>
</tbody>
</table>

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

DOSE MODIFICATIONS:

1. Hematological

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 and greater than or equal to 100</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

less than 1.0 or less than 100 delay until recovery, then proceed with 100% dose

febrile neutropenia reduce subsequent cycles by 10 mg/m²

2. Hepatic

<table>
<thead>
<tr>
<th>Total bilirubin (micromol/L)</th>
<th>Dose (mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 21</td>
<td>40</td>
</tr>
<tr>
<td>21 to 50</td>
<td>30</td>
</tr>
<tr>
<td>greater than 50</td>
<td>20</td>
</tr>
</tbody>
</table>

3. Stomatitis

<table>
<thead>
<tr>
<th>Grade</th>
<th>Symptoms</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>painless ulcers, erythema, or mild soreness</td>
<td>40 mg/m²</td>
</tr>
<tr>
<td>2</td>
<td>painful erythema, edema or ulcers, but can eat</td>
<td>delay until recovered to Grade 1, then continue at 30 mg/m²</td>
</tr>
<tr>
<td>3</td>
<td>painful erythema, edema or ulcers, and cannot eat</td>
<td>delay until recovered to Grade 1, then continue at 30 mg/m²; or discontinue treatment</td>
</tr>
<tr>
<td>4</td>
<td>requires parenteral or enteral support</td>
<td>discontinue treatment</td>
</tr>
</tbody>
</table>

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)**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Symptoms</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mild erythema, swelling or desquamation not interfering with normal daily activities</td>
<td>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/m²</td>
</tr>
<tr>
<td>2</td>
<td>erythema, swelling or desquamation interfering with but not precluding normal daily activities; small blisters or ulcerations less than 2 cm in diameter</td>
<td>delay one week; once recovery evident, continue treatment at 30 mg/m²</td>
</tr>
<tr>
<td>3</td>
<td>blistering, ulceration or swelling preventing normal daily activities; cannot wear regular clothing</td>
<td>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/m²</td>
</tr>
</tbody>
</table>

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/m².

**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 ranitidine may be used.
5. **Palmar-Plantar Erythrodysesthesia (PPE) (Hand-Foot Skin Reaction):** See BC Cancer 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:**