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

Protocol Code: GOOVTOP
Tumour Group: Gynecologic Oncology
Contact Physician: Dr. Paul Hoskins

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, GOOVCLAD, GOOVCAE, 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., GOOVCRAB)
- 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, GOOLDOX, GOOVGEM, GOOVETO, GOOVVIN, GOOVEX3, GOOVDRC.
- 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:
- Creatinine clearance less than 40 mL/min. See DOSE MODIFICATIONS for reduced starting dose in patients with renal dysfunction

TESTS:
- Baseline: CBC & diff (including platelets), creatinine, tumor marker (at physician’s discretion), imaging for tumour assessment (at physician’s discretion)
- Before each cycle on day 1: CBC & diff (including platelets), tumor markers (at physician’s discretion)
- Days 8 and 15 first cycle only (except if dose modification made): CBC & diff (including platelets) to determine nadir levels
- In future cycles, if clinically indicated: creatinine

PREMEDICATIONS:
- Antiemetic protocol for chemotherapy with low to low-moderate emetogenicity (see SCNAUSEA)
TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>BC Cancer Administration Guideline</th>
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<tbody>
<tr>
<td>topotecan</td>
<td>1.25 mg/m²/day x 5 days (days 1-5)*</td>
<td>IV in 50 mL NS over 30 minutes</td>
</tr>
</tbody>
</table>

Repeat 5-day treatment every 21 days until disease progression (usual treatment 9 cycles).

* In heavily pre-treated patients, suggested starting dose is 1 mg/m²/day x 5 days

DOSE MODIFICATIONS:

1. Hematological:
   (a) on treatment day:
   - ANC (x 10^9/L) and Platelets (x 10^9/L) and Dose
     - greater than or equal to 1.0 and greater than or equal to 100: treat as per nadir
     - less than 1.0 and/or less than 100: delay until recovery

   (b) at nadir:
   - ANC (x 10^9/L) and/or Platelets (x 10^9/L) and Dose
     - less than or equal to 0.5 and/or less than or equal to 75: ↓ by 0.25 mg/m²/day

   (c) Febrile neutropenia: decrease dose by 0.25 mg/m²/day. In the case of a second occurrence, use filgrastim (G-CSF) and maintain the same dose level, or discontinue topotecan treatment.

2. Any Grade 3 or 4 toxicity (except nausea): decrease dose by 0.25 mg/m²/day

3. Renal Dysfunction:

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Topotocan Dose</th>
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<tbody>
<tr>
<td>greater than or equal to 40</td>
<td>100%</td>
</tr>
<tr>
<td>20-39</td>
<td>50%</td>
</tr>
<tr>
<td>less than or equal to 20</td>
<td>not recommended</td>
</tr>
</tbody>
</table>

   CrCl in mL/min = 1.04 x (weight in kg)(140 - age in years)

   SCr in micromol/L

PRECAUTIONS:

1. Neutropenia: Fever or other evidence of infection must be assessed promptly and treated aggressively.

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