ELIGIBILITY:
- Relapsed/refractory Ewing’s sarcoma, rhabdomyosarcoma, intra-abdominal small round blue cell tumour, or neuroblastoma
- ECOG PS 0-2
- Adequate hematologic parameters (ANC greater than or equal to 1.5 x 10^9/L, and platelets greater than or equal to 100 x 10^9 /L).
- Adequate hepatic and renal function

EXCLUSIONS:
- Creatinine clearance less than 40 mL/min. Use with caution in patients with renal dysfunction. See DOSE MODIFICATIONS for reduction in dose in patients with renal dysfunction.
- ECOG PS 3-4

TESTS:
- Baseline: CBC & diff, platelets, creatinine, BUN, bilirubin, ALT, sodium, potassium, phosphate, albumin, urinalysis (r+m)
- Before each treatment cycle (Day 1):
  - CBC & diff, platelets, creatinine, BUN, bilirubin, ALT, sodium, potassium, phosphate, albumin
  - Urinalysis (r+m). Notify physician if patient has hematuria.
- Weekly: CBC & diff, platelets

PREMEDICATIONS:
- ondansetron 8 mg PO prior to treatment
- dexamethasone 8 mg PO/IV prior to treatment
- prochlorperazine 10 mg PO prn
- LORazepam 1 mg PO prn

PREHYDRATION:
- Ensure patient has taken at least 500 mL of fluid prior to each day of therapy; if not, prehydrate daily with NS 500 mL over 30 minutes to 1 hour.
**TREATMENT:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclophosphamide</td>
<td>250 mg/m²/day x 5 days (days 1 to 5)</td>
<td>IV in 100 mL NS over 20 min to 1 hour</td>
</tr>
<tr>
<td><strong>Administer topotecan after cyclophosphamide</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>topotecan</td>
<td>0.5 mg/m²/day x 5 days (days 1 to 5) OR</td>
<td>IV in 25 to 50 mL NS over 30 min</td>
</tr>
<tr>
<td></td>
<td>If filgrastim support available:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.75 mg/m²/day x 5 days (days 1 to 5);</td>
<td>IV in 50 mL NS over 30 min</td>
</tr>
<tr>
<td></td>
<td>please see note below</td>
<td></td>
</tr>
</tbody>
</table>

- Repeat 5-day treatment every 21 days x 4 cycles

**Posthydration:**
- D5-NS at 500 mL over 30 minutes to 1 hour on days 1 to 4 or 5
- Instruct patient to drink 2 L of fluid over 24 hours

**DOSE MODIFICATIONS:**

1. **Hematological:**
   a) on treatment day:

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Dose (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.5 and greater than or equal to 100</td>
<td></td>
<td>treat as per nadir</td>
</tr>
<tr>
<td>less than 1.5 or less than 100</td>
<td></td>
<td>delay until recovery</td>
</tr>
</tbody>
</table>

b) at nadir:

<table>
<thead>
<tr>
<th>ANC (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Dose (both drugs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 0.5 or less than 50</td>
<td></td>
<td>20% dose reduction</td>
</tr>
</tbody>
</table>
2. **Any Grade 3 or 4 toxicity (except nausea):** decrease dose of both drugs by 20% or as clinically indicated.

3. **Renal Dysfunction:**

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

\[
\text{CrCl (mL/min)} = N \times (140-\text{age}) \times \text{weight (kg)} \\
\text{serum creatinine (\(\mu\text{mol/L}\))} \\
\text{where } N = 1.04 \text{ for females and } 1.23 \text{ for males}
\]

**PRECAUTIONS:**

1. **Myelosuppression** is a significant risk. Saylor’s Phase II clinical trial used topotecan 0.75 mg/m²/d x 5 days, with filgrastim support starting Day 6 until adequate neutrophil recovery. There was Grade 3/4 neutropenia in 53% of courses, and 44% of courses were complicated by Grade 3/4 thrombocytopenia.¹ This current protocol uses topotecan 0.5 mg/m²/d x 5 days without filgrastim support. However, if felt appropriate (i.e., dependent on review of prior therapy, renal status, performance status, etc) **AND** if filgrastim support is available, the oncologist may use the Saylor regimen. Fever or other evidence of infection must be assessed promptly and treated aggressively.

2. Advise patients of importance of **adequate oral hydration** prior to and following chemotherapy.

3. Topotecan is a **radiation sensitizing agent.**⁴

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

**REFERENCES:**