BCCA Protocol Summary for Treatment of Recurrent/refractory Neuroblastoma, Ewing’s Sarcoma, Osteogenic Sarcoma or Rhabdomyosarcoma with Topotecan/Cyclophosphamide

Protocol Code: SAAVTC
Tumour Group: Sarcoma
Contact Physician: Dr. Meg Knowling

ELIGIBILITY:
- Relapsed/refractory Ewing’s sarcoma, rhabdomyosarcoma, intra-abdominal small round blue cell tumour, or neuroblastoma
- ECOG PS 0-2
- Adequate hematologic parameters (ANC ≥ 1.5 x 10^9/L, and platelets ≥ 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, AST, electrolytes, phosphate, albumin, urinalysis (r+m)
- Before each treatment cycle (Day 1):
  - CBC & diff, platelets, creatinine, BUN, bilirubin, AST, electrolytes, 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 250 ml/m²/h x 1 hour.
TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA 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>topotecan</td>
<td>0.5 mg/m²/day x 5 days (days 1 to 5) OR</td>
<td>IV in 50 mL NS over 30 min</td>
</tr>
<tr>
<td></td>
<td>If filgrastim support available:</td>
<td></td>
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<tr>
<td></td>
<td>0.75 mg/m²/day x 5 days (days 1 to 5); please see note below</td>
<td></td>
</tr>
</tbody>
</table>

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

Posthydration:
- D5-NS at 125 mL/m²/h x 1 to 2 hours on days 1 to 4 or 5

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</td>
<td>and</td>
<td>greater than or equal to 100</td>
</tr>
<tr>
<td>less than 1.5</td>
<td>or</td>
<td>less than 100</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</td>
<td>or</td>
<td>less than 50</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>

CrCl (mL/min) = \( N \times (140 \text{- age}) \times \text{weight (kg)} \)
serum creatinine (µmol/L)
where \( N = 1.04 \) for females and 1.23 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. Meg Knowling 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 May 2014
Date revised: 01 Sep 2015 (Class II requirement deleted)

REFERENCES: