BC Cancer Protocol Summary for Treatment of Relapsed or Refractory Peripheral T-Cell Lymphoma (PTCL) with romiDEPsin

Protocol Code: ULYROMI

Tumour Group: Lymphoma

Contact Physician: Dr. Laurie Sehn
Dr. Kerry Savage

ELIGIBILITY:
- Patients with symptomatic relapsed/refractory PTCL with at least one prior treatment
- Use with caution in patients with history of cardiac dysfunction
- Patients are eligible to either romidepsin (ULYROMI) or pralatrexate (ULYPRA)
- A Compassionate Access Program (CAP) approval is required prior to the initiation of treatment (please refer to https://cap.phsa.ca/)

TESTS:
- Baseline (required before first treatment): CBC & diff, platelets, electrolytes, potassium, magnesium, ECG
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2): HBsAg, HBcoreAb
- Before day 1, 8 and 15 of each cycle: CBC & diff, platelets
- Before day 1 of each cycle: electrolytes, potassium, magnesium; note, low potassium and low magnesium must be corrected before starting romiDEPsin

PREMEDICATIONS:
Antiemetic protocol for moderately emetogenic chemotherapy (see protocol SCNAUSEA)

SUPPORTIVE MEDICATIONS:
If HBsAg or HBcoreAb positive, start lamiVUDine 100 mg/day PO for the duration of chemotherapy and for six months afterwards.

TREATMENT:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>romiDEPsin</td>
<td>14 mg/m² on days 1, 8 and 15</td>
<td>IV in 500 mL NS over 4 hours</td>
</tr>
</tbody>
</table>

Repeat each treatment cycle every 28 days. Up to 8 cycles

DOSE MODIFICATIONS:
1. Hematological, day 1, 8 and 15

<table>
<thead>
<tr>
<th>ANC (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>romiDEPsin</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1.0 and greater than or equal to 50</td>
<td>14 mg/m²</td>
<td></td>
</tr>
<tr>
<td>less than 1.0 or less than 50</td>
<td>delay* then 14 mg/m²</td>
<td></td>
</tr>
<tr>
<td>less than 0.5 and febrile (greater or equal to 38.5°C) or less than 25 and requires platelet transfusion</td>
<td>delay* then 10 mg/m²</td>
<td></td>
</tr>
</tbody>
</table>
*delay until ANC greater than or equal to 1.5 x 10^9/L and platelets greater than or equal to 75 x 10^9/L or baseline

2. Non-Hematological Toxicity:

<table>
<thead>
<tr>
<th>Toxicity Grade</th>
<th>1st Event Dose</th>
<th>2nd Event Dose</th>
<th>Subsequent events Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>14 mg/m²</td>
<td>14 mg/m²</td>
<td>14 mg/m²</td>
</tr>
<tr>
<td>2</td>
<td>delay* then 14 mg/m²</td>
<td>delay* then 14 mg/m²</td>
<td>delay* then 14 mg/m²</td>
</tr>
<tr>
<td>3</td>
<td>delay* then 14 mg/m²</td>
<td>delay* then 10 mg/m²</td>
<td>discontinue</td>
</tr>
<tr>
<td>4</td>
<td>delay* then 10 mg/m²</td>
<td>discontinue</td>
<td>n/a</td>
</tr>
</tbody>
</table>

*stop treatment immediately and delay until toxicity resolved to grade 0-1 or baseline

3. Hepatocellular Carcinoma: has not been studied
4. Renal Impairment: has not been studied

PRECAUTIONS:

1. Hepatitis B Reactivation: All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with lamivudine during chemotherapy and for six months afterwards. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy.

2. Infection: Serious infections, sometimes fatal, including pneumonia, sepsis and viral reactivation e.g., Epstein-Barr and hepatitis B (see paragraph above) have occurred during or within 30 days of treatment. Monitor patients with a history of viral infections closely; consider antiviral prophylaxis. The risk of life-threatening infection may be increased in patients who have received prior treatment with antilymphocytic monoclonal antibodies or have bone marrow involvement.

3. QTc prolongation/ECG changes: QTc prolongation has been observed; use caution in patients with a history of QTc prolongation, congenital long QT syndrome, with medications known to prolong the QT interval or with pre-existing cardiac disease. For these patients obtain baseline and periodic ECG; monitor and correct electrolyte abnormalities.

4. Hyperuricemia and tumour lysis syndrome: Patients at risk of tumour lysis syndrome should have appropriate prophylaxis and be monitored closely. See BC Cancer Drug Manual romidepsin Drug Monograph for more information.

5. CYP3A4 substrate (major): Concomitant therapy with strong or moderate CYP 3A inhibitors may increase romidepsin exposure; avoid if possible. Concomitant use of romidepsin with strong CYP 3A inducers may decrease romidepsin exposure; avoid if possible.

Call Dr. Laurie Sehn, Dr Kerry Savage or tumour group delegate at (604) 877-6000 or 1-800-663-3333

with any problems or questions regarding this treatment program.

References