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 PO daily for the duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
romiDEPsin	14 mg/m^2 on days 1, 8 and 15	IV in 500 mL NS over 4 hours

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

DOSE MODIFICATIONS:

1. **Hematological, day 1, 8 and 15**

ANC (x10^9/L)		Platelets (x10^9/L)	romiDEPsin
greater than or equal to 1.0	and	greater than or equal to 50	14 mg/m^2
less than 1.0	or	less than 50	delay* then 14 mg/m^2
less than 0.5 and febrile (greater or equal to 38.5ºC)	or	less than 25 and requires platelet transfusion	delay* then 10 mg/m^2

Warning: The information contained in these documents are 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

*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:

Toxicity Grade	1st Event Dose	2nd Event Dose	Subsequent events Dose
0-1	14 mg/m^2	14 mg/m^2	14 mg/m^2
2	delay* then 14 mg/m^2	delay* then 14 mg/m^2	delay* then 14 mg/m^2
3	delay* then 14 mg/m^2	delay* then 10 mg/m^2	discontinue
4	delay* then 10 mg/m^2	discontinue	n/a

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

3. **Hepatic Impairment**: 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 continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive. 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 inducer 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

1. Coiffier B, et al. results from a pivotal, open-label, phase II study of romidepsin in relapsed or refractory peripheral T-cell lymphoma after prior systemic therapy. J Clin Oncol 2012;30:631-6.
2. Coiffier B, et al. Romidepsin for the treatment of relapsed/refractory peripheral T-cell lymphoma: pivotal study update demonstrates durable responses. J Hematol Oncol 2014;7:11.
3. Piekarz RL, et al. Phase 2 trial of romidepsin in patients with peripheral T-cell lymphoma. Blood 2011;117(22):5827-34.
4. Crump M, et al. Gemcitabine, dexamethasone, and cisplatin in patients with recurrent or refractory aggressive histology B-cell non-Hodgkin lymphoma: a Phase II study by the NCIC-CTG. Cancer 2004;101(8):1835-42.

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