BCCA Protocol Summary for the Treatment of Lymphoma with Single Agent riTUXimab

**Protocol Code**
LYRITUX

**Tumour Group**
Lymphoma

**Contact Physician**
Dr. Laurie Sehn

**ELIGIBILITY:**
- Follicular lymphoma progressive despite alkylating agents and purine analogues (fludarabine or cladribine)
- Newly diagnosed (within 6 months) asymptomatic advanced stage follicular lymphoma not requiring systemic chemotherapy
- Post-transplant lymphoproliferative disease
- Thrombocytopenia secondary to proven lymphocytic neoplasm
- Four treatments with riTUXimab will be reimbursed by BCCA. For further treatments, a “CAP Request” must be approved.

**TESTS:**
- Baseline (required before first treatment): CBC & diff, platelets, creatinine, bilirubin, AST, ALT, alkaline phosphatase, LDH
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with further treatment): HBsAg, HBcoreAb
- Before treatment #1 and #4: CBC & diff, platelets

**PREMEDICATIONS:**
(Note: patients should bring their own supply)
- Diphenhydramine 50 mg PO q 4 h during the IV infusion
- Acetaminophen 650 to 1000 mg PO q 4 h during the IV infusion
- Transfuse as needed to keep hemoglobin greater than 90 g/L, platelets greater than 20 x 10⁹/L

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

**TREATMENT:**

<table>
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<tr>
<th>Drug</th>
<th>Dose</th>
<th>BCCA Administration Standard</th>
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<tbody>
<tr>
<td>riTUXimab**</td>
<td>375 mg/m²</td>
<td>IV in 250 to 500 mL NS (to maintain concentration range between 1 to 4 mg/mL) over 3 to 8 hours* (dose may be divided equally into 2 x 250 mL NS)</td>
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Repeat weekly x 4 doses.

*Start the (first dose) initial infusion at 50 mg/h and, after 1 hour, increase by 50 mg/h every 30 minutes until a rate of 400 mg/h is reached. The subsequent infusions may start at 100 mg/h and be increased by 100 mg/h every 30 minutes until a rate of 400 mg/h is reached. Development of an allergic reaction may require a slower infusion rate. See hypersensitivity below.

** The risk of cytokine release syndrome is low but is increased when the peripheral blood lymphocyte count is greater than 30 to 50 x 10⁹/L. While there is no requirement to withhold riTUXimab based on
lymphocyte count, clinicians may wish to pre-medicate patients with high tumour burden with steroids prior to riTUXimab infusion or omit the riTUXimab from the first cycle of treatment.

DOSE MODIFICATIONS:

None.

PRECAUTIONS:

2. Hypersensitivity: riTUXimab can cause allergic type reactions during the IV infusion such as hypotension, wheezing, rash, flushing, alarm, pruritus, sneezing, cough, fever or faintness. For first dose, patients are to be under constant visual observation during all dose increases and for 30 minutes after infusion is completed. For all subsequent doses (#2 to 4), constant visual observation is not required. Vital signs are not required unless symptomatic. Because transient hypotension may occur during infusion, consider withholding antihypertensive medications 12 hours prior to riTUXimab infusion. If an allergic reaction occurs, stop the infusion and the physician in charge should determine a safe time and rate to resume the infusion. A reasonable guideline is as follows. After recovery of symptoms, restart riTUXimab infusion at one infusion rate below the rate at which the reaction occurred and continue with escalation of infusion rates on the appropriate schedule above. If the infusion must be stopped a second time, restart after clearance of symptoms, at one infusion rate lower and continue at that rate without further escalation. Fatal cytokine release syndrome can occur (see below). See BCCA Hypersensitivity Guidelines.

3. Fatal Cytokine Release Syndrome has been reported. It usually occurs within 1 to 2 hours of initiating the first infusion. Initially, it is characterized by severe dyspnea (often with bronchospasm and hypoxia) in addition to fever, chills, rigors, urticaria and angioedema. Pulmonary interstitial infiltrates or edema visible on chest x-ray may accompany acute respiratory failure. There may be features of tumour lysis syndrome such as hyperuricemia, hypocalcemia, acute renal failure and elevated LDH. For severe reactions, stop the infusion immediately and evaluate for tumour lysis syndrome and pulmonary infiltration. Aggressive symptomatic treatment is required. The infusion can be resumed at no more than one-half the previous rate once all symptoms have resolved, and laboratory values and chest x-ray findings have normalized. The risk of cytokine release syndrome is low but is increased when the peripheral blood lymphocyte count is greater than 30 to 50 x 10^9 /L. While there is no requirement to withhold riTUXimab based on lymphocyte count, clinicians may wish to pre-medicate patients with high tumour burden with steroids prior to riTUXimab infusion or omit the riTUXimab from the first cycle of treatment.

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

5. Rare Severe Mucocutaneous Reactions: (similar to Stevens-Johnson Syndrome) have been anecdotally reported. If such a reaction occurs, riTUXimab should be discontinued.

6. 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.

7. Gastrointestinal Obstruction or Perforation: There have been rare reports of gastrointestinal obstruction or perforation, sometimes fatal, when riTUXimab is given in combination with other chemotherapy, occurring 1 to 12 weeks after treatment. Symptoms possibly indicative of such complications should be carefully investigated and appropriately treated.

Call Dr. Laurie Sehn 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 Aug 1998

Date revised: 1 Mar 2017 (Eligibility updated)