

# BCCA Protocol Summary for Palliative Therapy For Lymphoma Using Radioimmunotherapy: Tositumomab-Priming for <sup>131</sup>I Tositumomab (BEXXAR®)

**Protocol Code**

*LYRITB*

**Tumour Group**

*Lymphoma*

**Contact Physicians**

*Dr. Tom Pickles  
Dr. Laurie Sehn*

## **ELIGIBILITY:**

Relapsed indolent lymphoma including

- Follicular
- Small lymphocytic
- Lymphoplasmacytic
- Marginal Zone

Transformed lymphoma arising from one of the above indolent histologies (excluding CLL (Richter Transformation), where radioimmunotherapy appears ineffective.)

Meeting the following conditions:

1. third line treatment and
2. less than 25% marrow involvement and
3. less than 25% of the marrow previously irradiated and
4. Platelet count greater than  $100 \times 10^9/L$
5. ANC greater than or equal to  $1.5 \times 10^9/L$

Radiation Oncology consultation. The Radiation oncologist is responsible for determining eligibility, prescribing the Tositumomab and making arrangements with Nuclear Medicine for the radiopharmaceutical administration, and for post-therapy haematological monitoring.

A BCCA "Class II Drug Registration Form" must be submitted.

## **EXCLUSIONS:**

- Non-CD20 lymphoma or
- greater than or equal to 25% marrow involvement or
- greater than or equal to 25% of the marrow previously irradiated or
- Hypocellular marrow - less than 15% bone marrow cellularity or marked reduction in bone marrow precursors or in patients with a history of failed stem cell collection.
- Platelet count less than  $100 \times 10^9/L$  or
- ANC less than  $1.5 \times 10^9/L$
- Pregnancy
- HAMA positive

## **CAUTION:**

- Platelet count  $100-150 \times 10^9/L$  or
- Hypocellular marrow – 15-20% bone marrow cellularity

These patients should be carefully assessed regarding risk-benefit, and may be excluded from therapy or a dose-reduction applied (see below).

**TESTS:**

- Baseline: Bone Marrow biopsy if not recently available, HBsAg and HBcoreAb, TSH
- Before dosimetric dose: CBC & diff, platelets, creatinine, bilirubin, AST, ALT
- Before therapeutic dose: CBC & diff, platelets
- Patients on potassium sparing diuretics should be monitored for hyperkalemia
- Recommended post-therapeutic dose: Weekly CBC & diff, platelets for 12 weeks or until counts recover.

**PREMEDICATIONS:**

- Thyroid protective agents (eg. Lugol's Solution 20 drops PO TID or Potassium Iodide tablets 130 mg PO daily) should be initiated at least 24 hours prior to administration of the Tositumomab dosimetric dose and continued until 2 weeks after administration of the therapeutic dose. Patients should not receive the dosimetric dose if they have not yet received at least three doses of Lugol's Solution. The thyroid protection is most important for the first 5 days. If there is significant toxicity to the Lugol's Solution, its discontinuation should be discussed with the Radiation Oncologist.
- Acetaminophen 650-1000 mg PO pre-Tositumomab
- Diphenhydramine 50 mg PO pre-Tositumomab

**TREATMENT:**

- Patients receive Tositumomab on two occasions (dosimetric dose and therapeutic dose). The dosimetric dose is followed by dosimetric radiolabelled tracer in the Nuclear Medicine department. The therapeutic dose, given 7-14 days later, is followed by the active radioimmunoconjugate in the Nuclear Medicine department.

Drug	Dose	BCCA Administration Guideline
Tositumomab	450 mg x 2 doses, dosimetric dose and therapeutic dose (approximately one week apart)  Pharmacy note: Withdraw amount equal to drug volume (ie 32 mL) from minibag prior to adding Tositumomab.	IV in 50 mL NS over 60 minutes.  Use an in-line 0.22 micron filter or attach a 0.22 micron filter to distal end of IV tubing prior to infusion. The same IV tubing set and filter must be used throughout the entire dosimetric or therapeutic step to avoid loss of drug.  <a href="#">Leave filter in place and cap line for transfer of patient to Nuclear Medicine.</a>
<sup>131</sup> I Tositumomab	This agent will be administered in Nuclear Medicine. Coordination of timing of prior Tositumomab administration is essential, as the <sup>131</sup> I Tositumomab should be given within five hours.	

## DOSE MODIFICATIONS:

### 1. Hematologic:

Platelets (x 10 <sup>9</sup> /L)	<sup>131</sup> I Tositumomab
greater than or equal to 150	100%
100-149	Activity of <sup>131</sup> I calculated to deliver 65 cGy total body irradiation and 35 mg Tositumomab IV over 20 minutes
less than 100	Delay

## PRECAUTIONS:

- Hypersensitivity:** Tositumomab can cause allergic type reactions, such as fever, rigors or chills, sweating, hypotension, dyspnea, bronchospasm and nausea during the IV infusion or within 48 hours of infusion. Reduce the rate of infusion by 50% for mild to moderate infusional toxicity. Stop the infusion for severe toxicity. After resolution of symptoms, the infusion may be resumed with a 50% reduction in the rate of infusion. Fatal cytokine release syndrome can occur (see below). See [BCCA Hypersensitivity Guidelines](#).
- Fatal Cytokine Release Syndrome** has been reported with the allied agent, Rituximab. It usually occurs within 1-2 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.
- Rare Severe Mucocutaneous Reactions:** (similar to Stevens-Johnson Syndrome) have been anecdotally reported. If such a reaction occurs, Tositumomab should be discontinued.
- 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 100 mg/day orally, for the entire duration of therapy 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.

**This regimen is only approved for the BC Cancer Agency Centres (CSI, FVC, VC and VIC). Contact Dr. Dr Tom Pickles or alternate (Nicholas Voss, James Morris) at (604) 877-2730 or 1-800-663-3333 with any problems or questions regarding this treatment program.**

Date activated: 01 Nov 2005

Date revised: 01 Dec 2011 (revised timeframe between dosimetric and therapeutic dose, IV line management)