

BC Cancer Protocol Summary for the Treatment with Subcutaneous or Intravenous Alemtuzumab for Fludarabine-Refractory B-Chronic Lymphocytic Leukemia (B-CLL) or with Intravenous Alemtuzumab for Previously Untreated T-Prolymphocytic Leukemia (T-PLL)

Protocol Code

LYALEM

Tumour Group

Lymphoma

Contact Physician

Dr. Laurie Sehn, Dr. Alina Gerrie

ELIGIBILITY:

Subcutaneous or intravenous alemtuzumab for patients with previously treated B-CLL and

- Aged 18 years or older
- Have not responded to or had early documented relapse after Fludarabine
- Have received at least one alkylating agent-containing regimen unless 17p deletion (p53 gene).
- Life expectancy of at least 12 weeks
- Rai Stage II, III or IV with symptomatic splenomegaly, lymphadenopathy, or cytopenias related to marrow infiltration or sequestration.
- WHO performance status 0 to 2

Intravenous alemtuzumab for patients with previously untreated T-PLL and

- WHO performance status 0 to 3

Alemtuzumab ceased to be commercially available in 2012. Prescribers must apply for a patient-specific supply of alemtuzumab at least 1 week prior to the scheduled treatment through the Clinigen MabCampath Distribution Program (CDP) by email at medicineaccess@clinigengroup.com

EXCLUSIONS:

- Hypersensitivity reactions to other monoclonal antibody therapies
- HIV seropositivity
- Pregnant or lactating
- New York Heart Association grade III or IV congestive heart failure
- Active systemic infection
- Bulky (greater than 5 cm) adenopathy at any site
- Pre-existing autoimmune cytopenias

TESTS:

- Baseline (required before first treatment): CBC & diff, [total](#) bilirubin, ALT
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with further treatment): serology for HIV, CMV, Varicella and HSV, HBsAg, [HBsAb](#), HBcoreAb
- Weekly: CBC & Diff, CMV-DNA by PCR. CMV-DNA by PCR required on Monday but results not needed to proceed with treatment. **Results must be checked prior to proceeding with treatment on Wednesday.**
(Note: frequency of CBC testing may be increased as per physician decision if ANC less than $0.5 \times 10^9/L$ and platelets less than $50 \times 10^9/L$ and until cytopenia resolves or remains stable for greater than one week.)
- Before each treatment, if cytopenias develop, until stable or resolved (bi or tri-weekly): CBC & Diff
- [If clinically indicated: HBV viral load, ALT \(see protocol SCHBV\)](#)
- Assess clinical response at 4, 8 and 12 weeks

Discontinue after 4 weeks, if progressive disease
 Discontinue if CR is achieved prior to week 12
 Discontinue if no clinical benefit achieved after 8 weeks

- Clinical toxicity assessment for infusion reactions, respiratory/cardiac events, autoimmune complications, bleeding and infection is recommended weekly for at least the first 4 weeks, then as per physician discretion. Laboratory parameters must be reviewed weekly.

PREMEDICATIONS:

To be given prior to IV and SC alemtuzumab to prevent infusion reactions:

- diphenhydrAMINE 50 mg PO prior to alemtuzumab
- acetaminophen 650 mg PO prior to alemtuzumab
- predniSONE 10 mg PO 15 to 30 minutes prior to alemtuzumab for the first two weeks; once a stable dose of alemtuzumab has been established, predniSONE can be omitted and resumed only if needed to control side effects

SUPPORTIVE MEDICATIONS:

Prophylactic Antibiotics (start at week 1 and continue until 2 months after completion of treatment):

- cotrimoxazole 1 DS tab PO 3 times each week
- valACYclovir 500 mg PO BID OR acyclovir 400 mg PO BID

Very high risk of hepatitis B reactivation. If HBsAg or HBcoreAb positive, follow hepatitis B prophylaxis as per [SCHBV](#).

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
alemtuzumab	<p>Administer three times each week. First week doses 3-10-30 mg. Escalate to 10 mg, then 30 mg only if toxicities grade I or II, and improving. Subsequent weeks 30-30-30 mg.</p> <p>If grade III or IV reactions occur, lower dose to maximum tolerated dose (3 or 10 mg) until well tolerated for one week, then resume escalation to maximum of 30 mg/dose.</p> <p>Maximum <u>total</u> weekly dose is 90 mg.</p> <p>If treatment is interrupted for more than 7 days for any reason, re-initiate treatment at 3 mg, and escalate as above</p>	<p>SC (thigh) Or IV in 100 mL NS over 2 hours</p> <p>NOTE: Alemtuzumab is now available in a preservative-free 30 mg/mL vial. (Previously Alemtuzumab was available as a 10 mg/mL ampoule.)</p> <p>New volume for doses, due to new solution strength:</p> <p>3 mg = 0.1 mL 10 mg = 0.33 mL 30 mg = 1 mL</p> <p>Do not shake the vial prior to use. Filtration prior to use is NOT required.</p>

Dosing three times each week, usually Monday, Wednesday, Friday for a maximum of 12 weeks. (Note: Longer duration requires CAP approval.)

Note: 1 week = 1 Cycle.

Patients may self-administer at home after initial training. Evening dosing may decrease side effects.

Note: all doses described in mg regardless of height and weight.

Vitals monitoring:

Immediately before the start of the intravenous treatment, monitor vitals (pulse, respiratory rate and blood pressure). During the infusion, directly observe patient and monitor vitals every 30 minutes until the end of the infusion. Patients should be observed for 1 hour after the dose. Continue vitals monitoring every 30 minutes during the observation period.

For subcutaneous treatment, monitor vitals (pulse, respiratory rate and blood pressure) immediately before the injection. Patients should be observed and vitals taken every 30 minutes for 1 hour after the dose until at least 3 doses at the highest level being given have been monitored. After that, monitoring may be discontinued.

DOSE MODIFICATIONS:

Hematological:

Permanently discontinue treatment if autoimmune hemolytic anemia or immune thrombocytopenia develops during treatment.

ANC (x10 ⁹ /L)	Platelets (x10 ⁹ /L)	Dose
greater than 0.25	And greater than 25	100%
less than 0.25	Or less than 25	First occurrence: hold treatment and resume at same dose when ANC greater than 0.5 and platelets greater than 50 (restart at 3 mg if delay between doses greater than 7 days) Second occurrence: hold treatment and resume at 10 mg when ANC greater than 0.5 and platelets greater than 50. (restart at 3 mg if delay between doses greater than 7 days, and escalate to maximum of 10 mg/treatment) Third occurrence: permanently discontinue treatment
NOTE: If baseline ANC less than 0.5 and/or platelets less than 25 at initiation of therapy: If ANC or platelets decrease to less than 50% of baseline value, hold therapy and resume when ANC and platelets return to baseline values. Restart at 3 mg if delay between dosing greater than or equal to 7 days.		

PRECAUTIONS:

1. **Neutropenia:** fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Need for irradiated blood products:** potentially life-threatening transfusion-related graft-versus-host-disease has been described in patients actively receiving alemtuzumab. The Canadian Blood Service recommends that patients on alemtuzumab should receive irradiated blood products, effectively eliminating this risk.

3. **Infusion related events:** alemtuzumab has been associated with infusion-related events including hypotension, rigors, fever, shortness of breath, bronchospasm, chills and/or rash. In order to prevent infusion reactions, all patients should receive premedication with an oral antihistamine and acetaminophen prior to dosing and monitoring for infusion-related symptoms is recommended. Also, premedication with prednisONE 10 mg orally 15 to 30 minutes before the alemtuzumab for the first two weeks of alemtuzumab, regardless of route of administration, is also recommended. Systemic reactions are significantly less frequent and severe following SC injection. Local skin reactions are common. Escalate dose only if less than or equal to NCI grade II and improving. Meperidine 25 mg IV may be useful for rigors.
4. **Live vaccines:** Patients with any history of lymphoid cancers including chronic lymphocytic leukemia should not be given live vaccines including those receiving alemtuzumab.
5. **CMV-DNA by PCR positive:** Discontinue alemtuzumab treatment, Continue CMV-DNA by PCR testing, and initiate Gancyclovir IV if rising viral load, or symptoms of CMV infection.
6. **Autoimmune cytopenias** – Discontinue therapy in any patient developing autoimmune cytopenias or marrow aplasia. Safety of restarting therapy has not been demonstrated.
7. **Hepatitis B Reactivation:** See [SCHBV protocol](#) for more details.

Call Dr. Laurie Sehn or tumour group delegate at (250) 712-3900 or 1-800-563-7773 with any problems or questions regarding this treatment program.

References:

1. Lundin et al. Phase II trial of subcutaneous anti-CD52 monoclonal antibody alemtuzumab (Campath) as first line treatment for patients with B-cell chronic lymphocytic leukemia (B-CLL). Blood 2002;100:768-73.
2. Keating et al. Therapeutic role of alemtuzumab (Campath IH) in patients who have failed fludarabine: results of a large international study. Blood 2002;99:3554-61.