BC Cancer Protocol Summary for Treatment of Mycosis Fungoides and Sézary Syndrome with Mogamulizumab

Protocol Code	*ULYMOGA*
Tumour Group	*Lymphoma*
Contact Physician	*Dr. Kerry Savage*

ELIGIBILITY:

Patients must have:

- Mycosis fungoides or Sézary syndrome,
- Advanced stage (stage IB to IVB),
- At least one prior systemic therapy, and
- BC Cancer "Compassionate Access Program" request approval prior to treatment

Patients should have:

- Good performance status
- Access to a treatment centre with expertise in managing rare immunotherapy mediated toxicities and rash management of mogamulizumab

EXCLUSIONS:

Patients must not have:

- Active or untreated CNS metastases

CAUTIONS:

- Significant cardiac disease [Class III or IV New York Heart Association (NYHA) heart failure],
- Active, known, or suspected autoimmune disease,
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

TESTS:

- Baseline (required before first treatment): CBC & Diff, creatinine, total bilirubin, ALT, alkaline phosphatase
- 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, HBsAb, HBcoreAb
- Baseline if clinically indicated: albumin, calcium, magnesium, phosphate, uric acid, random glucose, ECG, chest x-ray
- Cycle 1, Day 15: CBC & Diff, creatinine, ALT, total bilirubin (no tests required for Cycle 1 Days 8 and 22)
- Prior to Day 1 of each cycle: CBC & Diff, creatinine, ALT, total bilirubin
- If clinically indicated: sodium, potassium, alkaline phosphatase, albumin, calcium, magnesium, random glucose, HBV viral load (see protocol SCHBV), chest x-ray, ECG

- Dermatologic evaluation: intermittent dermatologic evaluation for rash (see Dose Modifications and Precautions)
- Weekly telephone nursing assessment for signs and symptoms of side effects while on treatment (optional)

PREMEDICATIONS:

- Prior to Cycle 1 Days 1 and 8:
  - diphenhydrAMINE 50 mg PO/IV 30 minutes prior to treatment
  - acetaminophen 650 mg PO 30 minutes prior to treatment
  - hydrocortisone 100 mg IV 30 minutes prior to treatment

- If prior infusion reaction, prior to each subsequent dose:
  - diphenhydrAMINE 50 mg PO/IV 30 minutes prior to each treatment
  - acetaminophen 650 mg PO 30 minutes prior to each treatment
  - hydrocortisone 100 mg IV 30 minutes prior to each treatment

- Antiemetics are not usually required

SUPPORTIVE MEDICATIONS:

- Moderate risk of hepatitis B reactivation. If HBsAg or HBcoreAb positive, follow hepatitis B prophylaxis as per SCHBV.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
mogamulizumab	**CYCLE 1:** 1 mg/kg on Days 1, 8, 15, 22	IV in 100 mL NS over 60 minutes using a 0.2 micron in-line filter†
	CYCLES 2 onward: 1 mg/kg on Days 1 and 15	

† Observe patient for 60 minutes after the first infusion and for 30 minutes after the second and third infusion. Observation period not required after 3 consecutive treatments with no reaction.

Repeat every 28 days until disease progression or unacceptable toxicity.

Vitals monitoring:

- For cycles requiring observation period, vitals before start of infusion and as required. Vital signs for subsequent cycles as required

DOSE MODIFICATIONS:

- No specific dose modifications. Toxicity managed by treatment delay and other measures
- For toxicities other than dermatologic toxicity and infusion-related reactions, see SCIMMUNE protocol

1. **Dermatologic toxicity[3]:**

- For rash Grade 1 or higher, consider supportive management as needed:
  - Group 1 (Super-high potency) topical steroids (e.g., clobetasol 0.05% ointment or cream BID),
  - Antihistamine or other agent for pruritus (e.g., loratadine, gabapentin, doxepin, mirtazapine)
- For Grade 2 or higher rash, consider oral steroids (e.g., predniSONE 0.5 to 1 mg/kg/day or equivalent). Biopsy suggested to distinguish disease progression versus mogamulizumab-associated rash.

Grade	Toxicity	Management
1	Rash covering less than 10% BSA, which may or may not be associated with symptoms of pruritus, burning, tightness	▪ Continue mogamulizumab ▪ Consider biopsy and referral to dermatology
2	Rash covering 10 to 30% BSA, which may or may not be associated with symptoms of pruritus, burning, or tightness; associated with psychosocial impact; limiting instrumental ADL; rash covering more than 30% BSA with or without mild symptoms	▪ Hold mogamulizumab ▪ Biopsy and referral to dermatology recommended ▪ Treat rash as clinically appropriate, including administering at least 2 weeks of topical corticosteroids, until rash improves to Grade 1 or less, then ▪ Restart mogamulizumab at previous dose
3	Rash covering more than 30% BSA with moderate or severe symptoms; limiting self-care ADL; antibiotics indicated	
4	Life-threatening consequences; rash covering any % BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection with IV antibiotics indicated	Discontinue
Stevens Johnson Syndrome (SJS) or Toxic epidermal necrolysis (TEN)		▪ Hold if SJS or TEN suspected until SJS and TEN excluded and cutaneous reaction is Grade 1 or less ▪ Dermatology consult suggested

2. **Infusion-related reactions:**

- Refer to SCDRUGRX for management guidelines.

Grade	Toxicity	Mogamulizumab Dose
1	Mild transient reaction	▪ Interrupt infusion and treat symptoms ▪ After symptoms resolve, restart at 50% of previous rate ▪ Administer premedication with diphenhydramine, acetaminophen, and hydrocortisone for subsequent infusions ▪ If reaction recurs after restarting and is unmanageable, discontinue
2	Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS, narcotics, IV fluids); prophylactic medications indicated for 24 hrs or less	
3	Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	
4	Life-threatening consequences; urgent intervention indicated	Discontinue

PRECAUTIONS:

1. **Infusion-related reactions** are reported during treatment with mogamulizumab and can be life threatening. Most reactions occur during or shortly after the first infusion, but can occur with subsequent infusions. The most commonly reported symptoms include chills, nausea, fever, tachycardia, rigors, headache, and vomiting. Premedication with diphenhydramine and acetaminophen is suggested for the first mogamulizumab infusion in all patients. Infusions should be interrupted for any grade reaction and symptoms treated. Permanently discontinue mogamulizumab for life-threatening reactions. When restarting the infusion after symptoms resolve, the infusion rate should be reduced by at least 50%. Premedication with diphenhydramine, acetaminophen, and hydrocortisone should be used for all subsequent infusions. If symptoms recur and are unmanageable, discontinue mogamulizumab. For additional management of infusion-related reactions, see BC Cancer Protocol SCDRUGRX Management of Infusion-Related Reactions to Systemic Therapy Agents.
2. **Dermatologic toxicity**: Rash (including drug eruption) is one of the most common adverse reactions associated with mogamulizumab. The affected areas and appearance vary. The more common presentations include papular or maculopapular rash, morbilliform rash, and lichenoid, spongiotic, or granulomatous dermatitis, but other presentations such as scaly plaques, pustular eruptions, folliculitis, and non-specific dermatitis are also reported. Life threatening

dermatologic toxicity, including Stevens-Johnson syndrome and toxic epidermal necrolysis, has been reported with mogamulizumab. Onset of dermatologic toxicity is variable. Monitor for rash throughout the treatment course. Management of dermatologic toxicity includes topical corticosteroids plus either interruption or permanent cessation of mogamulizumab depending on the severity of the toxicity. Following a moderate to severe reaction, mogamulizumab may be restarted after at least 2 weeks of topical steroids, if the rash has improved to Grade 1 or better. Mogamulizumab should not be restarted following a life-threatening reaction. Skin biopsy may be required to distinguish drug eruption from disease progression.

3. **Infections** including fatal and serious pneumonia, cellulitis, and sepsis are reported in patients treated with mogamulizumab. Fever or other evidence of infection must be assessed promptly and treated aggressively.
4. **Bone marrow suppression** including leukopenia, anemia, thrombocytopenia, neutropenia and lymphocytopenia (including CD4 lymphocytes) may occur. Monitor throughout treatment.
5. **Immune-mediated complications** have been reported with mogamulizumab. Grade 3 or higher reactions have included myositis, myocarditis, polymyositis, hepatitis, pneumonitis, and Guillain-Barre syndrome. Systemic immunosuppressants may be necessary to manage symptoms and mogamulizumab should be held or discontinued as appropriate. Patients with a history of autoimmune disease may experience a worsening of their pre-existing condition during treatment with mogamulizumab and this should be considered prior to commencing mogamulizumab. New onset hypothyroidism (Grade 1 or 2) has been reported rarely, and can be managed with observation or levothyroxine if required. See BC Cancer Protocol SCIMMUNE.
6. **Graft versus host disease exacerbation** and **complications of allogeneic hematopoietic stem cell transplantation (HSCT)** are reported in patients who received allogeneic HSCT after mogamulizumab. These include acute or steroid-refractory graft versus host disease (GVHD) and transplant-related death. A higher risk has been reported if mogamulizumab was last administered within 50 days prior to HSCT. Follow patients closely for early evidence of transplant-related complications after mogamulizumab therapy.
7. **Hepatitis B Reactivation**: See SCHBV protocol for more details.

Call 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. Kim YH, Bagot M, Pinter-Brown L, et al; MAVORIC Investigators. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial. Lancet Oncol. 2018 Sep;19(9):1192-1204.
2. CADTH Review Mogamulizumab (Poteligeo) CADTH Reimbursement Recommendation. Canadian Journal of Health Technologies August 2022; 2(8): 1-19.
3. Musiek ACM, Rieger KE, Bagot M, et al. Dermatologic Events Associated with the Anti-CCR4 Antibody Mogamulizumab: Characterization and Management. Dermatol Ther (Heidelb). 2022 Jan;12(1):29-40.