BC Cancer Protocol Summary for Treatment of Relapsed CNS Lymphoma using Temozolomide

Protocol Code	*LYTEM*
Tumour Group	*Lymphoma*
Contact Physician	*Dr. Diego Villa*

ELIGIBILITY:

Patients must have:
- Relapsed/refractory primary or secondary central nervous system (CNS) lymphoma, with or without systemic lymphoma, and
- Progression on prior treatment with high-dose methotrexate (e.g., LYHDMRTEM) and/or radiation, or
- Previously untreated primary or secondary CNS lymphoma not suitable for treatment with high-dose methotrexate/and or radiation per provider discretion

Patients should have:
- ECOG 3 or less

EXCLUSIONS:

Patients must not have:

CAUTIONS:

- Creatinine greater than 1.5 x upper limit of normal
- Significant hepatic dysfunction

TESTS:

- Baseline: CBC & Diff, ALT, total bilirubin, creatinine
- 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, HBsAb, HBcoreAb
- Baseline if clinically indicated: random glucose (recommended for patients on dexamethasone)
- Prior to Day 1 of each cycle: CBC & Diff, ALT, total bilirubin
- If clinically indicated: creatinine, sodium, potassium, magnesium, calcium, random glucose, HBV viral load, HBsAg (see protocol SCHBV)

PREMEDICATIONS:

- ondansetron 8 mg given 30 minutes prior to each dose of temozolomide

Warning: The information contained in these documents are a statement of consensus of BC Cancer Agency 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

SUPPORTIVE MEDICATIONS:

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

TREATMENT:

Drug	Dose*	BC Cancer Administration Guideline
temozolomide	150 mg/m^2 once daily x 5 days (Days 1 to 5)	PO

* refer to Temozolomide Suggested Capsule Combination Table for dose rounding

- Dose may be increased to 200 mg/m^2 for the second cycle if no significant hematologic, hepatic or other toxicity is noted (see below)
- Repeat every **4 weeks** until disease progression or unacceptable toxicity

DOSE MODIFICATIONS:

1. **Hematological**

Day 1:

ANC (x10^9/L)		Platelets (x10^9/L)	Dose
Greater than or equal to 1.5	and	Greater than or equal to 100	100%
Less than 1.5	or	Less than 100	Delay*

* follow CBC weekly and re-institute temozolomide at 100 mg/m^2 if ANC recovers to greater than 1.5 x 10^9/L and platelets recover to greater than 100 x 10^9/L within 3 weeks

- Note: Dose reductions below 100 mg/m^2 are not permitted. Temozolomide should be discontinued for repeat Grade 3 or 4 hematologic toxicity (ANC less than 1.0 x 10^9/L, platelets less than 50 x 10^9/L) at the 100 mg/m^2 dose.

Warning: The information contained in these documents are a statement of consensus of BC Cancer Agency 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

2. **Renal Dysfunction:**

Serum Creatinine (micromol/L)	Dose
Less than or equal to 2 x upper limit of normal	100%
Greater than 2 x upper limit of normal	Reduce to 100 mg/m^2*

* discontinue if no resolution of renal dysfunction at this dose

3. **Hepatic Dysfunction:**

Total bilirubin (micromol/L)		ALT	Dose
Less than 25	or	Less than or equal to 2.5 x ULN	100%
25 to 85	or	2.6 to 5 x ULN	Reduce one dose level**
Greater than 85	or	Greater than 5 x ULN	Delay***

** Dose levels are 200 mg/m^2, 150 mg/m^2 and 100 mg/m^2

*** Follow LFTs weekly and re-institute temozolomide at 100 mg/m^2 if total bilirubin recovers to less than 85 micromol/L and ALT recovers to less than 5 x ULN

- Note: Dose reductions below 100 mg/m^2 are not permitted. Temozolomide should be discontinued for repeat total bilirubin greater than 85 micromol/L and repeat ALT greater than 5 x ULN

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Thrombocytopenia:** can occur during treatment. See dose modifications, above.
3. **Hepatitis B Reactivation:** See SCHBV protocol for more details.

Call Dr. Diego Villa or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Makino K, Nakamura H, Hide T, Kuratsu J. Salvage treatment with temozolomide in refractory or relapsed primary central nervous system lymphoma and assessment of the MGMT status. J Neurooncol. 2012 Jan;106(1):155-60.
2. Reni M, Zaja F, Mason W, Perry J, et al. Temozolomide as salvage treatment in primary brain lymphomas. Br J Cancer. 2007 Mar 26;96(6):864-7.

Warning: The information contained in these documents are a statement of consensus of BC Cancer Agency 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