

BC Cancer Protocol Summary for Treatment of Low Grade Lymphoma or Chronic Lymphocytic Leukemia with Fludarabine

Protocol Code

LYFLU

Tumour Group

Lymphoma

Contact Physician

Dr. Laurie Sehn

ELIGIBILITY:

- Symptomatic or threatening advanced stage indolent lymphoma (small lymphocytic lymphoma, lymphoplasmacytic lymphoma [formerly Waldenstrom's macroglobulinemia], marginal zone lymphoma or follicular lymphoma) or chronic lymphocytic leukemia

TESTS:

- Baseline (required before first treatment): CBC & diff, serum creatinine, bilirubin, ALT
- 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, HBcoreAb
- Before each treatment: CBC & diff, serum creatinine

PREMEDICATIONS:

- None

SUPPORTIVE MEDICATIONS:

If HBsAg or HBcoreAb positive, start lamiVUDine 100 mg PO daily for the duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
fludarabine	25 mg/m ² /day x 5 consecutive working weekdays (may skip Sat/Sun/holidays)	IV in 100 mL NS over 30 minutes

OR

Drug	Dose	BC Cancer Administration Guideline
fludarabine	40 mg/m ² /day x 5 consecutive days (round dose to nearest 10 mg)	PO Do not chew, break or crush the tablets.

Repeat every 28 days until maximum clinical benefit achieved, usually 4-6 cycles, to a maximum of 8 cycles. For further cycles, undesignated approval is required.

DOSE MODIFICATIONS:

1. Hematologic:

ANC (x 10 ⁹ /L)*		Platelets (x 10 ⁹ /L)*	Dose
less than 1.2	OR	less than 100	Delay until count recovery

*No dose reduction if decreased counts are due to disease.

2. **Renal Dysfunction:** For any patient with a serum creatinine above normal and for all patients above the age of 60 years, a creatinine clearance should be measured or calculated using the following formula:

Estimated creatinine clearance (in mL/minute) =

For men: $[1.23 \times (140 - \text{age in y})(\text{weight in kg})] \div \text{serum creatinine in micromol/L}$

For women: $[1.04 \times (140 - \text{age in y})(\text{weight in kg})] \div \text{serum creatinine in micromol/L}$

Creatinine Clearance (mL/min)	Dose	Actual Dose and Schedule (Note change in number of days)	
		PO	IV
greater than or equal to 70	100%	40 mg/m ² /day x 5 days	25 mg/m ² /day x 5 days
30 to less than 70	50%	32 mg/m ² /day x 3 days	20 mg/m ² /day x 3 days
less than 30	DO NOT USE		

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 fludarabine. The Canadian Blood Service recommends that patients on fludarabine should receive irradiated blood products, effectively eliminating this risk.
3. **Hepatitis B.** The immunosuppression associated with fludarabine may increase the risk of re-activation of hepatitis B. Although the risk of this is probably small, fludarabine should be avoided in patients with known prior hepatitis B (HBsAg positive or anti-hepatitis B antibody positive) unless the clinical situation justifies this increased risk and this has been explained to the patient.
4. **Hepatitis B Reactivation:** All lymphoma patients should be tested for both HBsAg and HBcAb. If either test is positive, such patients should be treated with lamivudine during chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcAb positive. 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.

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.

References:

1. Cheson B, et al. Fludarabine. J Clin Oncol 1991;9:175-88.
2. Johnson S, et al. Multicentre prospective randomised trial of fludarabine versus cyclophosphamide, doxorubicin and prednisone (CAP) for treatment of advanced-stage chronic lymphocytic leukemia. Lancet 1996;347:1432-8.
3. Chin Yee, I et al. The role of fludarabine in intermediate- and high-risk chronic lymphocytic leukemia. Current Oncology 1999;6:90-102.
4. Boogaerts MA, et al. Activity of oral fludarabine phosphate in previously treated chronic lymphocytic leukemia. J Clin Oncol 2001; 22:4252-4258.