**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/day PO for the duration of chemotherapy and for six months afterwards.

**TREATMENT:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>fludarabine</td>
<td>25 mg/m²/day x 5 consecutive working weekdays (may skip Sat/Sun/holidays)</td>
<td>IV in 50 to 100 mL NS over 20 to 30 minutes</td>
</tr>
</tbody>
</table>

OR

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>BC Cancer Administration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>fludarabine</td>
<td>40 mg/m²/day x 5 consecutive days</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>(round dose to nearest 10 mg)</td>
<td>Do not chew, break or crush the tablets.</td>
</tr>
</tbody>
</table>

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**:

<table>
<thead>
<tr>
<th>ANC (x $10^9$/L)*</th>
<th>Platelets (x $10^9$/L)*</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 1.2 OR</td>
<td>less than 100</td>
<td>Delay until count recovery</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Dose</th>
<th>Actual Dose and Schedule (Note change in number of days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 70</td>
<td>100%</td>
<td>PO 40 mg/m²/day x 5 days IV 25 mg/m²/day x 5 days</td>
</tr>
<tr>
<td>30 to less than 70</td>
<td>50%</td>
<td>PO 32 mg/m²/day x 3 days IV 20 mg/m²/day x 3 days</td>
</tr>
<tr>
<td>less than 30</td>
<td></td>
<td>DO NOT USE</td>
</tr>
</tbody>
</table>

**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 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.

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**:  