

# BCCA Protocol Summary for Therapy of Chronic Myeloid Leukemia Using Interferon and Cytarabine

**Protocol Code** *CMLIFNCYT*

**Tumour Group** *Leukemia/BMT*

**Contact Physician** *Dr. John Shepherd*

## ELIGIBILITY:

- Chronic Myeloid Leukemia (CML). This should be considered standard therapy for patients who are not candidates for sibling donor stem cell transplant. Eligibility for ongoing studies should be checked with a member of the Leukemia/BMT Program before starting therapy

## EXCLUSIONS:

- Patients with a known history of adverse reactions to interferon or cytarabine
- Patients who are being considered for therapy with STI571 on the randomized study
- Patients whose Philadelphia chromosome status is not known; peripheral blood testing by pcr for the bcr/abl translocation is not sufficient to follow interferon/cytarabine therapy

## TESTS:

- Baseline: bone marrow examination and formal cytogenetics
- Before each treatment: CBC and differential
- If clinically indicated: Hepatic and renal function

## PREMEDICATIONS:

Pre-medication is not required routinely, however, many patients experience intense flu-like symptoms from interferon and use of acetaminophen is usually necessary to ameliorate these. It is advisable for patients to undergo formal instruction in how to inject both interferon and cytarabine and discuss ways to minimize interferon side effects before starting on the injections.

## TREATMENT:

- Chemotherapy doses for both drugs should be calculated on the basis of the actual or corrected body weight and BSA, whichever is lower.
- Most patients will tolerate interferon if it is started at a lower dose and escalated over the first 1-3 weeks. Usual recommended starting dose is 25% of target dose.
- Interferon and cytarabine should not be mixed or injected at the same site.

| Drug                              | Dose  | BCCA Administration Guideline |
|-----------------------------------|---|-------------------------------|
| Alfa Interferon                   | 5 million units/m <sup>2</sup> per day              | By subcutaneous injection     |
| Cytarabine (cytosine arabinoside) | 20 mg/ m <sup>2</sup> per day for 10 days per month | By subcutaneous injection     |

Patients who do not have evidence of **hematological response** to therapy by 6 months should be reconsidered as the toxicity of treatment may outweigh benefit at that point. **Cytogenetic responses** will virtually always start to occur by 12 months of treatment, and therapy in patients with no evidence of cytogenetic response by 12 months should also be reconsidered

#### DOSE MODIFICATIONS:

1. **Hematological:** The aim of this therapy is suppression of the bone marrow. An attempt should be made to maintain a white cell count of 2-5 x 10<sup>9</sup>/L. Prior to each course of cytarabine, the white cell count should be greater than 2, the neutrophil count greater than 1.5 x 10<sup>9</sup>/L, and the platelet count greater than 100 x 10<sup>9</sup>/L. Absolute dose reduction guidelines cannot be given as they will vary from patient to patient. Consultation with a member of the Leukemia/BMT group is suggested if counts are of concern.
2. **Interferon side effects:** These can often be managed by dose timing or use of acetaminophen. Side effects to be aware of include depression, irritability, weight loss, asthenia, hair loss and hypothyroidism. If a patient develops any of these, full assessment is recommended and the drug may need to be held or discontinued.

#### PRECAUTIONS:

1. **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Depression:** As noted above, this may be a significant problem with interferon. Patients and their partners should be questioned about symptoms of depression and interferon held or discontinued if this becomes apparent. Suicides have been reported in patients who became depressed on interferon.
3. **Hypersensitivity:** Reactions are uncommon with interferon. Small sub-cutaneous nodules at injection sites are common and may be itchy. Patients should be reassured about these.
4. **Oral Ulceration:** Cytarabine may cause oral ulcers; if these persist after one or two cycles, the dose should be reduced by 25-50% and the patient reassessed.

**Call Dr. M. Barnett, J. Shepherd, or any member of the Leukemia/BMT Program of BC at (604) 875-4863 or (604-875-5000 24 hours via Vancouver General Hospital paging) with any problems or questions regarding this treatment program.**

Date activated: 01 Nov 2000

Date last revised: 01 May 2009 (unsafe abbreviations and symbols replaced)

### **References:**

1. Guilhot F, Chastang C, Michallet M, et al. Interferon alfa-2b combined with cytarabine versus interferon alone in chronic myelogenous leukemia. *NEJM* 1997;337:223-9.
2. Silver R, Woolf S, Hehlmann R, et al. An evidence based analysis of the effect of busulfan, hydroxyurea, interferon, and allogeneic bone marrow transplantation in treating the chronic phase of chronic myeloid leukemia: Developed for the American Society of Hematology. *Blood* 1999;94:1517-1536.
3. Sawyers C. Chronic Myeloid Leukemia. *NEJM* 1999;340:1330-1340.