

BCCA Protocol Summary for Adjuvant Therapy of High Risk Malignant Melanoma with High Dose Interferon (HDIFN) Alfa-2b

Protocol Code

SMAJIFN

Tumour Group

Melanoma

Contact Physician

Dr. Kenneth Wilson

ELIGIBILITY:

- **Patients must be under the direct care of an oncologist familiar with interferon therapy and its possible side effects.**
- Palpable node positive melanoma at initial diagnosis or at recurrence, confirmed pathologically, post-regional lymphadenectomy, R0 status (i.e., zero residual disease after surgery ie pathologic complete resection).
- For other indications, Compassionate Access Program (**CAP**) (previously known as the Undesignated Drug Request Process) must be approved.

EXCLUSIONS:

- Microscopic node positive, but palpably negative nodes.
- Sentinel node positive, but palpably negative nodes.
- Patients with distant metastases, or resected distant metastases.
- History of immune/collagen vascular disease.
- Concomitant corticosteroid or immunosuppressive therapy.
- Simultaneous or recent (less than 4 weeks) radiotherapy.
- Hemoglobin less than 100 gm/L, WBC less than $3 \times 10^9/L$, ANC less than $1.5 \times 10^9/L$, or platelet count less than $70 \times 10^9/L$.
- Bilirubin greater than or equal to 35 micromol/L, ALT or AST greater than or equal to 3 times the upper limit of normal, alkaline phosphatase greater than or equal to 3 times the upper limit of normal.
- Elevated serum creatinine.
- History of hypersensitivity to interferon alfa or any component of the injection.
- Significant neuropsychiatric conditions.

TESTS:

- **Baseline:**
 - CBC and differential, platelets, AST, ALT, Alkaline Phosphatase, Total Bilirubin, LDH, TSH, serum creatinine, ECG if pre-existing cardiac condition.
 - CT scan of brain, thorax, abdomen and pelvis are recommended prior to start of high dose interferon.
 - Screening for depression (e.g., using Beck Depression Scale) is recommended,

- especially in patients with high risk of mood disorders.
- Bone scan if clinically indicated from symptoms, chest X-ray, or elevated alkaline phosphatase.
- **During treatment:**
 - Assessment by a physician including mood changes, CBC and differential, platelets, AST, ALT, Alkaline Phosphatase

Weeks 1-4 (Induction phase)	every week
Weeks 5-52 (Maintenance phase)	every 4 weeks

- Chest X-ray: every 6 months

PREMEDICATIONS:

- Acetaminophen 650 mg PO 30 minutes pre- IV Interferon alpha-2b and every 4-6 hours regularly during induction phase (Weeks 1-4)

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Interferon alfa-2b (Induction phase)	20 million units/m ² /day daily for 5 consecutive days per week, for 4 weeks (Weeks 1–4) Dose rounded to nearest million units	IV in 50 mL NS over 20 min, followed by 500 mL NS IV over 30 min to 1 hour
Interferon alfa-2b (Maintenance phase)	10 million units/m ² /day 3 times a week (Monday, Wednesday, and Friday), for 48 weeks (Weeks 5-52.) Dose rounded to nearest million units	Subcutaneous

Note:

- Depending on the patient's performance status and symptoms, a rest period of 2-3 weeks between induction phase (Weeks 1-4) and maintenance phase (Weeks 5-52) may be considered.
- Multi-dose pen for maintenance phase: Once a pen is opened and first used, it should not be used longer than 4 weeks. Up to 48 hours of storage at 15-25°C is permitted during the 4 weeks.

DOSE MODIFICATIONS:

1. Hematology/biochemistry:

ANC (x10 ⁹ /L)		AST or ALT	Dose
less than 0.5	or	greater than 5 X ULN	Delay until recovery: resume at 50% dose . If failure to recover within 4 weeks, discontinue interferon permanently
less than 0.25	or	greater than 10 X ULN	Discontinue permanently

ULN = Upper Limit of Normal range

If intolerance persists after dose reduction, or if ANC decrease to less than 0.25 x10⁹/L, or ALT / AST rises to greater than 10 x upper limit of normal, Interferon alpha-2b should be discontinued.

PRECAUTIONS:

Interferon alfa-2b may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations.

Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many but not all cases these disorders resolve after stopping Interferon alfa-2b therapy.

Call Dr. Kenneth Wilson or tumour group delegate at (250) 519 5572 or 1-800-670-3322 local 5572 with any problems or questions regarding this treatment program.

Date activated: 1 August 2002

Date revised: 1 July 2011 (clarified blood tests, added multi-dose pen stability)

Reference:

1. Kirkwood JM, Ibrahim JG, Sosman JA, et al. High-dose interferon alfa-2b significantly prolongs relapse-free and overall survival compared with the GM2-KLH/QS-21 vaccine in patients with resected stage IIB-III melanoma: results of intergroup trial E1694/S9512/C509801. J Clin Oncol 2001;19(9):2370-80.