## Low dose and dose escalating therapy of interferon alfa-2a in the treatment of refractory and sight-threatening Behçet's uveitis

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Despite aggressive treatment with conventional immunosuppressive agents a group of patients with uveitis due to Behçet's disease (BD) still experience relapses of uveitis. This particular group of BD patients with refractory and sight threatening uveitis represents a challenge to the ophthalmologist. For the last 5 years we have been utilizing interferon alfa-2a (IFN-α-2a) in such cases. The use of IFN-α-2a in Behçet's uveitis has been reported. (1-6) However, there is no consensus about the ideal dosing and duration of the treatment for Behçet uveitis. In addition, side-effects some of which are frequent and dose dependent may limit the use of this agent. The use of a low dose regimen may be expected to have fewer side-effects. We utilize a regimen that involves starting IFN-α-2a in a low dose and increasing the dose in a dose escalating manner in case uveitis relapses occur.

A treatment protocol that aimed to utilize a minimum dose of IFN-α-2a (Roferon®-A, Roche Pharmaceuticals, USA) was adjusted prior to the initiation of the study. Schematic illustration of the treatment protocol is shown in Figure 1. For the induction of IFN-α-2a therapy IFN-α-2a was given 3 million international units (IU) subcutaneously (sc) daily for 14 days. Maintenance of IFN-α-2a was achieved with 3 million IU 3x/week sc. Any relapse required increase of the dose of IFN-α-2a, in a sequence of 4.5, 6 and 9 million IU 3x/week sc. To take rapid control over the intraocular inflammation during a relapse periocular or systemic corticosteroids were also utilized along with increase of the dose of IFN-α-2a. After control of intraocular inflammation was achieved the dose of systemic corticosteroids were rapidly tapered to a maximum of 10 mg per day prednisone equivalent or discontinued.

From December 2005 to December 2007 a total of 16 patients (12 male/4 female) with a median age at presentation of 27 years (range: 21-38 years) were recruited to the prospective study. All had severe, refractory and sight-threatening uveitis due to BD. Refractory and sight threatening uveitis due to BD was defined as presence of intraocular inflammation involving the posterior segment either in the form of posterior or panuveitis and failing to respond to one or more conventional immunosuppressive agents.

For this preliminary report, we have set our outcome measures as control of intraocular inflammation with quiescence while on maintenance therapy of IFN-α-2a, rate of ocular relapses in per patient-year (PY) before and after initiation of IFN-α-2a therapy and as the ability to taper off systemic corticosteroids, with a ≤10 mg prednisone equivalent daily dose being considered as a successful taper. We evaluated visual acuity in terms of improvement of visual acuity as described before (7). Accordingly, IFN-α-2a was able to control intraocular inflammation with quiescence in all patients. Uveitis relapse rate decreased from 3.66/PY before to 1.04/PY after initiating IFN-α-2a. Systemic corticosteroids were either discontinued or tapered-off to ≤10mg/day prednisone equivalent in all patients during maintenance. Improvement of visual acuity occurred in 56.6% of eyes. No side effect required manipulation of the dose or discontinuation of IFN-α-2a therapy.

A low dose of IFN-α-2a therapy in the treatment of uveitis associated with BD has been described (5, 6). We have previously reported the differences between the two regimens elsewhere (8).

We conclude that lower doses of IFN-α-2a is able to control intraocular inflammation in patients with severe Behçet uveitis. This approach also has the advantage of avoiding some of the potential side effects that occur with higher doses. However, a partial response or unresponsiveness can be managed with increasing the dose of interferons with a dose-escalation regimen as described here.

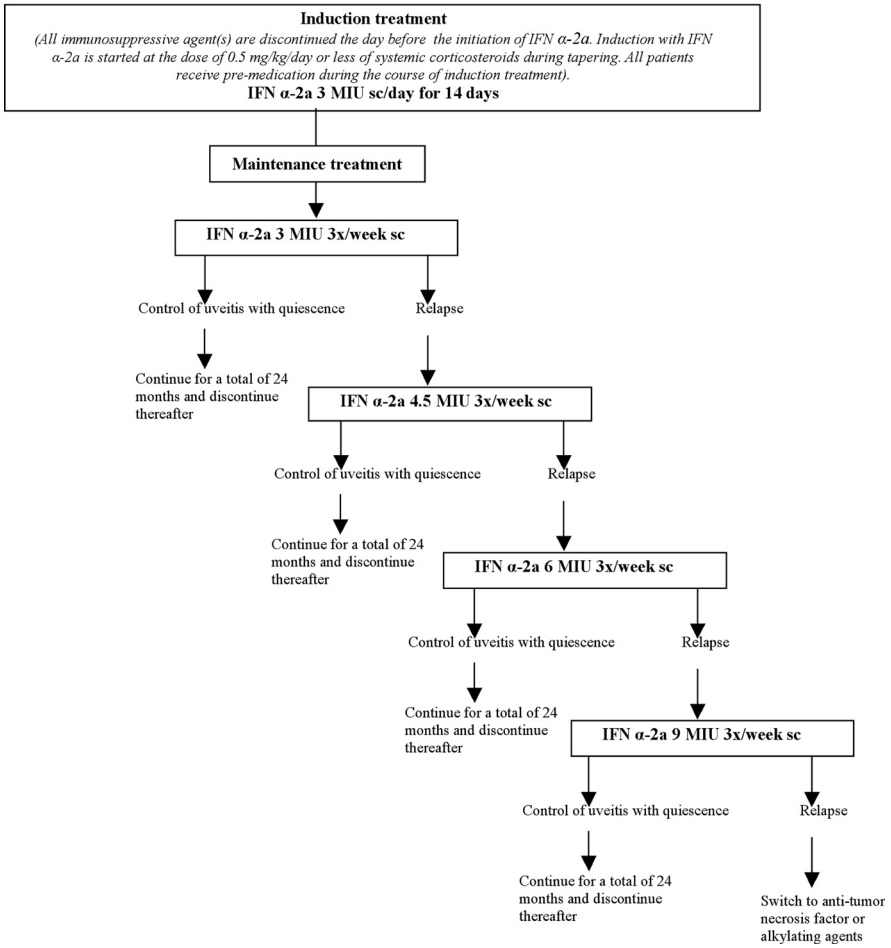


**Fig. 1.** Flow chart for induction and maintenance treatment of IFN-α-2a.

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### References

1. KÖTTER I, ZIERHUT M, ECKSTEIN AK *et al.*: Human recombinant interferon alfa-2a for the treatment of Behçet's disease with sight threatening posterior or panuveitis. *Br J Ophthalmol* 2003; 87: 423-31.
2. KÖTTER I, GUNAYDIN I, ZIERHUT M *et al.*: The use of interferon alpha in Behçet disease: Review of the literature. *Semin Arthritis Rheum* 2004; 33: 320-35.

3. TUGAL-TUTKUN I, GUNEY-TEFEKLI E, URGANCIOGLU M: Results of interferon-alfa therapy in patients with Behçet uveitis. *Graefes Arch Clin Exp Ophthalmol* 2006; 244: 1692-5.
4. HAMURYUDAN V, OZYAZGAN Y, FRESKO I *et al*.: Interferon alfa combined with azathioprine for the uveitis of Behçet's disease: an open study. *Isr Med Assoc J* 2002; 4: 928-30.
5. WECHSLER B, BODAGHI B, HUONG DL *et al*.: Efficacy of interferon alfa-2a in severe and refractory uveitis associated with Behçet's disease. *Ocul Immunol Inflamm* 2000; 8: 293-301.
6. GUEUDRY J, WECHSLER B, TERRADA C *et al*.: Long-term efficacy and safety of low-dose interferon alpha-2a therapy in severe uveitis associated with Behçet disease. *Am J Ophthalmol* 2008; 146: 837-44.
7. JABS DA, NUSSENBLATT RB, ROSENBAUM JT, STANDARDIZATION OF UVEITIS NOMENCLATURE (SUN) WORKING GROUP: Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol* 2005; 140: 509-16.
8. ONAL S, KAZOKOGLU H, DIRESKENELI H, YAVUZ S: Low-dose interferon alfa-2a therapy in severe uveitis associated with Behçet disease. *Am J Ophthalmol* 2009; 147: 1109-10.