# Efficacy of Infliximab therapy evaluated by fluorescein angiography

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**Background:** We started using infliximab for Behçet disease in our hospital since 2007 and have observed similar effects on ocular symptoms as previously reported in the literature [1]. The Behçet disease ocular attack score 24 (BOS24 score) proposed by Kaburaki *et al.* [2] is a comprehensive clinical index that assigns scores to ocular symptoms. On the other hand, the severity of retinal vasculitis is an important factor in the prognosis of Behçet disease. In clinical settings, fluorescein fundus angiography (FA) is used to measure the severity of retinal vasculitis. Therefore, we assigned scores to the results of FA before and after the initiation of infliximab therapy and evaluated the severity of retinal vasculitis associated with Behçet disease.

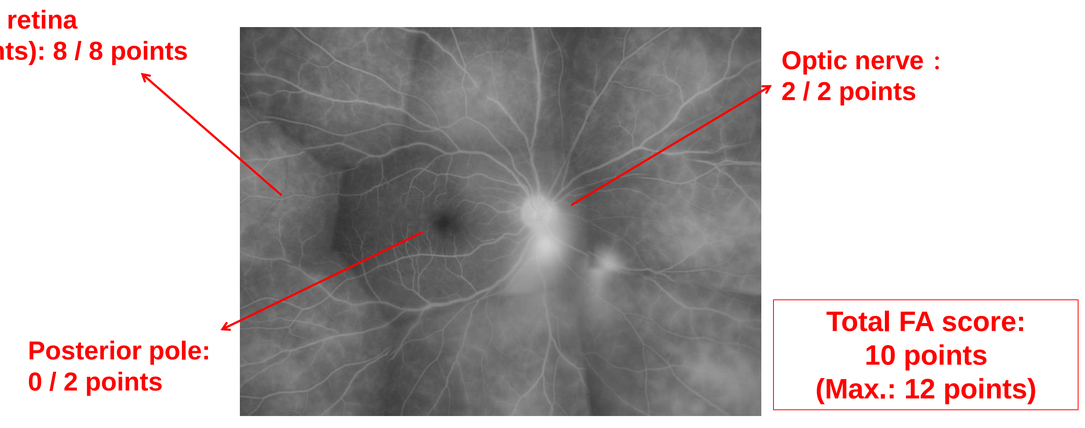
1. Okada AA, et al. Arch Ophthalmol.130. 2012.
2. Kaburaki T, et al. Jpn J Ophthalmol. 58. 2014.

**Patients & Methods:** The present study included 38 outpatients with uveoretinitis associated with Behçet disease, who initiated infliximab therapy between 2007 and 2014 at the Tokyo Medical University Hospital, Department of Ophthalmology. All patients were compatible with the International diagnosis criteria and were followed for 2 years or longer. Initially, Infliximab treatment was initiated as per the protocol at the approved dose of 5 mg/kg administered intravenously at weeks 0, 2, 6, and every 8 weeks thereafter. Other medications (including corticosteroid adrenocortical hormone, cyclosporine, and colchicine) were discontinued prior to the initiation of infliximab therapy in all patients.

***Fluorescein angiography:*** FA scores were determined before treatment and at 2 and 4 years after the initiation of infliximab therapy (pre FA, FA-2Y, and FA-4Y scores, respectively). FA scores were determined in the eye with more severe symptoms or higher turbidity, according to the following criteria: zero to two points for abnormal findings in the optic papilla (two points if there was neovascularization), zero to two points for abnormal findings in the posterior pole (two points if there was neovascularization), and zero to two points for abnormal findings in each quadrant of the peripheral retina (maximum eight points); giving a maximum total score of 12 points (Table 1). The FA images were obtained 2 to 6 minutes after intravenous injection of the fluorescent contrast agent. Image analysis was performed by two masked ophthalmologists. FA score less than 7 was considered “good”, and a score of 7 or higher was considered “poor”. Improvement rate of FA score was calculated as follows: Improvement rate = 1 - post-treatment FA score/pre-treatment FA score × 100%. A rate of 50% or higher was considered as improvement in FA.

**Table 1. Fluorescein angiography (FA) scores**

| Assessment method | Assess the eye with more severe disease |
|---|---|
| | Assess the more easily visualized eye if vitreous opacification is severe |
| **FA assessment** | |
| Optic nerve findings | 0–2 points (neovascularization: 2 points) |
| Posterior pole findings | 0–2 points (neovascularization: 2 points) |
| Peripheral retina findings | 0–8 points (vasculitis in each quadrant: 0–2 points) |




***Behçet disease ocular attack score 24*:** BOS24 were calculated according to the methods reported by Kaburaki *et al.* [2]. We calculated the summation of BOS24 over the 6-month period (BOS24-6M) before initiation of infliximab therapy (BOS24-6M before infliximab therapy = preBOS24-6M) as well as the summation of BOS24 for the last 6 months of 2 years (BOS24-6M 2 years after initiation of infliximab = 2Y BOS24-6M) and 4 years of therapy (BOS24-6M 4 years after initiation of infliximab = 4Y BOS24-6M). Differences between post-treatment and pre-treatment scores were calculated.

***Factors associated with BOS24 and FA score changes in response to infliximab therapy:*** Improvement rates of 2Y BOS24-6M and 4Y BOS24-6M relative to preBOS24-6M were compared. Furthermore, improvement rates in FA-2Y and FA-4Y scores relative to pre FA were also compared. Associations between the improvement in FA score and age, presence of antibodies to infliximab and presence of extraocular symptoms after infliximab initiation were evaluated.

## Results:

**Table1. Patient background**

| | 2 years of IFX treatment | 4 years of IFX treatment |
|---|---|---|
| Number of patient | 38 | 28 |
| Sex (male:female) | 27:11 | 21:7 |
| Mean age (years) | 48.8 ± 13.1 | 47.3 ± 12.1 |
| Mean observation period (years) | 5.4 ± 1.7 | 5.7 ± 1.3 |

**Table2. Changes in BOS24 and FA score before and after infliximab therapy**

| | | | |
|---|---|---|---|
| Subjects followed for at least 2 years (n=38) | PreBOS24-6M | 2Y BOS24-6M | P-value (paired t-test) |
| | 19.1 ± 10.9 | 0.1 ± 0.6 | < 0.0001 |
| | Pre FA score | FA-2Y score | |
| | 9.1 ± 2.7 | 4.7 ± 3.6 | < 0.0001 |
| Subjects followed for at least 4 years (n=28) | PreBOS24-6M | 4Y BOS24-6M | P-value (paired t-test) |
| | 20.0 ± 11.9 | 0.1 ± 0.8 | < 0.0001 |
| | Pre FA score | FA-4Y score | |
| | 9.2 ± 2.8 | 3.4 ± 3.2 | 3.4 ± 3.2 |

**Table3. Improvements in BOS24and FA score after infliximab therapy**

| | Improvement after infliximab therapy |
|---|---|
| 2Y BOS24-6M vs. Pre BOS24-6M (n=38) | All cases (100%) |
| 4Y BOS24-6M vs. Pre BOS24-6M (n=28) | All cases (100%) |
| FA-2Y score vs. Pre FA (n=38) | 20 cases (52.6%) |
| FA-4Y score vs. Pre FA (n=28) | 21 cases (75.0%) |

**Table4. Change in extraocular symptoms after IFX therapy**

| | Before IFX | After IFX |
|---|---|---|
| All extraocular symptoms | 38 cases | 9cases |
| Oral aptha | 38 cases | 2 cases |
| Cutaneous symptoms | 25 cases | 1 case |
| Arthritis | 11 cases | 6 cases |
| Genital ulceration | 7 cases | 1 case |
| Epididymal inflammation | 1 case | No cases |

**Table5. Factors associated with improvements in FA score after 2 and 4 years of IFX therapy**

| After 2 years IFX | Relative factor | P-value |
|---|---|---|
| Improvement rate: 20/38 cases | Pre FA score | < 0.0005 ($\chi^2$ test) |
| | Positive extraocular symptoms | 0.17 ($\chi^2$ test) |
| **After 4 years IFX** | **Relative factor** | **P-value** |
| Improvement rate: 21/28 cases | Pre FA score | 0.42 ($\chi^2$ test) |
| | Positive extraocular symptoms | 0.33 ($\chi^2$ test) |

### Summary of results

- In all subjects, the 2Y and 4Y BOS24-6M was significantly reduced compared to the pre BOS24-6M . Likewise, the FA-2Y and FA-4Y score in all subjects was significantly reduced compared to the pre FA score (Table2).
- In all patients, the BOS24-2Y and BOS24-4Y were improved compared to the preBOS24-6M. The FA-2Y score was improved compared to the pre FA score in 20 patients, while the FA-4Y score was improved in 21 patients (Table3).
- Extraocular symptoms resolved following treatment in 29 patients (Table4).
- Greater improvement in FA-2Y score correlated with lower FA score before initiation of therapy No significant correlation was observed between improvement in FA-2Y score and occurrence or persistence of extraocular symptoms. On the other hand, improvement in FA-4Y score did not correlate significantly with pre FA score, or occurrence or persistence of extraocular symptoms (Table5).

**Conclusions:** Infliximab therapy is effective in reducing both the BOS24 and FA score with respect to the severity of retinal vasculitis. The FA score improved further with longer-term infliximab therapy. Furthermore, the FA score before infliximab therapy, which reflects the initial severity of retinal vasculitis was associated with the FA score after infliximab therapy. Of the 38 patients included in the present study, extraocular symptoms resolved following treatment in 29 patients (76.3%), demonstrating the efficacy of infliximab in treating these symptoms. However, arthritis, oral aphthous ulcers and genital ulcers persisted in some patients, demonstrating individual variation in response to infliximab