# Tumour necrosis factor inhibitors improve inflammatory control in eyes with refractory non-infectious uveitis

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## Purpose

There has been a recent rise in the use of biological agents specifically tumour necrosis factor α inhibitors (TNFα) in eyes with non-infectious intermediate, posterior or pan uveitis (NIIPPU) that are refractory to conventional treatment (steroids and other second-line immunosuppressive agents. The aim of this study was to examine the effect of TNFα blockers on visual function and disease control in these uveitides.

## Introduction

Patients with NIIPPU have a significant risk of vision loss due to cystoid macular oedema and scarring (2). Conventional immunosuppression with steroids and second-line agents are not always effective in controlling ocular inflammation and this is due to either lack of efficacy or the development of intolerable side effects which may lead to discontinuation of treatment. TNFα is a potent pro-inflammatory cytokine that plays a key role in induction and maintenance of inflammation (3). Agents that block TNFα have achieved remarkable success in systemic autoimmune disease such as, ankylosing spondylitis and Crohn's disease but their efficacy varies in ocular autoimmune conditions.

## Methods

A retrospective longitudinal study of patients diagnosed with refractory NIIPPU and treated with biologics between 2001- 2016 at Moorfields Eye Hospital, London, UK. The ethical approval for the study is ROAD 16039. All age groups were included in the study if they failed treatment with steroids and at least one second-line immunosuppressive agent and had at least three month follow-up.

## Results

82 patients were included in the study (32 female) (39.02 %), right eye 80 (51.28%). Mean age at the time of diagnosis was 33.9±1.7 years. Length of follow-up after baseline (initiation of biologics) was 4.7±0.4 years. Anatomic types of uveitis were as follows: intermediate uveitis 42 eyes (26.9%) ,posterior uveitis 31 (19.9%) and pan uveitis 83 (53.2%).

## Results

| Etiology | No. of eyes (%) |
|---|---|
| Behcet disease | 51 (32.7) |
| Vasculitis (ANCA+ve and idiopathic) | 8 (5.1) |
| HLA-B27 related uveitis | 25 (16.0) |
| Vogt Koyanagi Harada syndrome | 6 (3.8) |
| Sarcoidosis | 8 (5.1) |
| Systemic lupus erythematosus | 3 (1.9) |
| Serpiginous choroiditis | 2 (1.3) |
| Takayasu vasculitis | 1 (0.6) |
| Punctate inner choroidopathy | 2 (1.3) |
| Rheumatoid arthritis | 4 (2.6) |
| Multifocal choroiditis | 2 (1.3) |
| Idiopathic pan and intermediate uveitis | 32 (20.5) |
| Juvenile idiopathic arthritis | 6 (3.8) |
| Blau syndrome | 2 (1.3) |
| Birdshot chorioretinopathy | 2 (1.3) |
| Intermediate uveitis | 2 (1.3) |

**Table.1** Disease etiologies and corresponding number of eyes

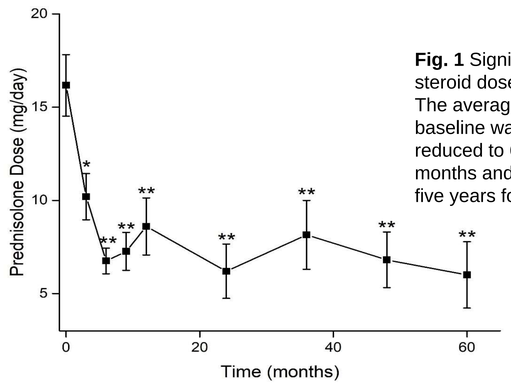


**Fig. 1** Significant reduction in steroid dose after starting biologics. The average prednisolone dose at baseline was 16.4±1.7mg/day reduced to 6.5±0.7mg/day by six months and remained stable up to five years follow-up (p<0.0001).

| Biologic agent | Number of eyes (%) | Time to prednisolone <10mg/day Months, Median (95% CI) |
|---|---|---|
| Infliximab | 76 (48.7) | 6.0 (3.37-8.63) |
| Adalimumab | 60 (38.5) | 3.0 (1.77-4.23) |
| Etanercept* | 4 (2.6) | 6.0 |
| Rituximab | 14 (9.0) | 9.0 (0.68-17.32) |
| Vedolimumab* | 2 (1.3) | 3.0 |

**Table. 2 Adalimumab** patients had a significantly shorter interval for achieving prednisolone dose <10 mg per day compared to **infliximab** patients, the medians were 3 and 6 months respectively (p value = 0.04).

*No CI generated due to small numbers on these biologics.

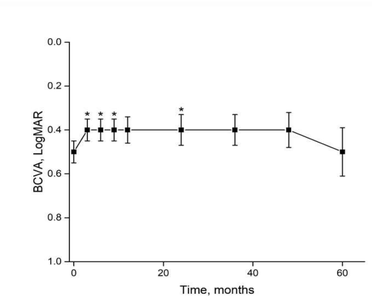


**Fig.2** BCVA improved from 0.5±0.05 LogMAR at baseline to 0.4±0.05 LogMAR at 3 months follow-up (p=0.006) and remained stable during the 60 months follow-up.

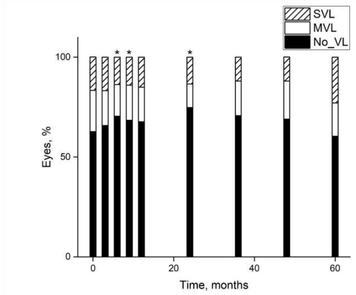


**Fig.3** A significantly greater percent of eyes avoided vision loss on biologics. Percentage of eyes without vision loss (BCVA< 6/12), rose from 62.7% (94 eyes) at baseline to 74.8%, p=0.01, at 24 months follow-up.

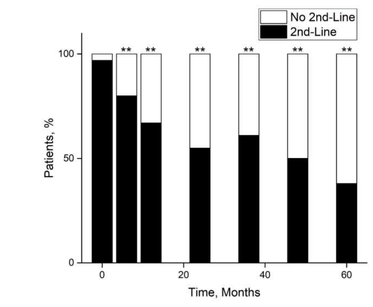


**Fig.4** significant reduction in the proportion of patients receiving 2nd-line immunosuppressive agent at therapeutic dose on biologics. The percentages are 97% at baseline versus 38% at 60 months follow-up p value<0.0001).




**Fig. 5** The average flare-up rate before baseline is 4.6±0.32 flares (1.8±0.14 flares/year), while after biologics this reduced to an average of 1.6±0.22 flares (0.6±0.08 flares/year, p<0.0001). 42.3% of eyes (n=66) had flares after baseline.

## Conclusion

1. Treatment with TNFα blockers results in improved long-term disease control in patients with NIIPPU while maintaining visual function.
2. On biologics a significant reduction in daily steroid dose was achieved after 6 months. Adalimumab patients reached this faster than those on infliximab and steroids reduction was maintained throughout the follow-up time.
3. TNFα reduced the dependence on other immunosuppressive drugs.
4. A significantly lower rate of flare-ups after initiating biologic therapy.

**References**

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2. DICK, A. D., FORRESTER, J. V., LIVERSIDGE, J. & COPE, A. P. 2004a. The role of tumour necrosis factor (TNF-alpha) in experimental autoimmune uveoretinitis (EAU). *Prog Retin Eye Res,* 23**,** 617-37