Chronic Model of Uveitis in Rabbit: Efficacy of Triamcinolone Acetonide

Yann Quentric [1], S. Antonelli [1], V. Mauro [1], N. Cimbolini [1], L. Feraille [1], P-P. Elena [1]

(1) *Iris Pharma, La Gaude, France.* - www.iris-pharma.com - info@iris-pharma.com

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Purpose

Uveitis is an intraocular inflammation that partly or totally affects the iris, ciliary body and choroid, whose causes are not always known and may be varied: ocular trauma or systemic diseases of genetic, immune or infectious origin. Uveitis can be acute as acute anterior uveitis, or chronic. During chronic uveitis, the untreated and prolongated inflammation can spread and affect other ocular structures, as lens, vitreous, retina, optic nerve, leading to cataract, glaucoma, macular oedema, and leads to loss of vision.

In this study we suggest using a model of chronic uveitis in rabbits induced by *Mycobacterium tuberculosis* antigen to test efficacy of corticostreroid treatement. This preclinical model will be amenable to evaluate compounds and medical devices in persistent uveitis that require long term treatment.

Methods

Twenty adult New Zealand albino rabbits were preimmunized by subcutaneous injection of *Mycobacterium tuberculosis* antigen H37Ra (10 mg – 0,5 ml Mineral oil) on day 1 (1).
Uveitis was induced by intravitreal injection of antigen prepared from H37Ra (2,5 µg in 50 µl of saline solution) in all preimmunized animals on day 15. Induction was immediately followed by a single intravitreal injection of triamcinolone acetonide (TAA), 2 mg, or saline solution (Vehicle). A second H37Ra 2,5 µg intravitreal challenge was performed in both groups two weeks after the first challenge, without additional treatment.
Clinical signs of uveitis in anterior chamber and vitreous were scored by slit lamp observation twice a week after the challenges, then weekly for 2 months.
At the end of the study (week 10), eye globes were collected and examined by histology (hematoxylin/eosin/safran staining).

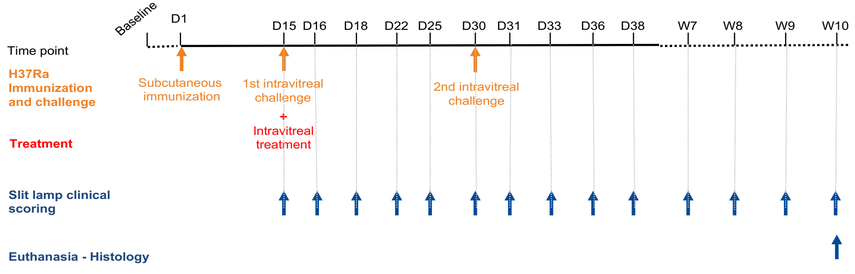
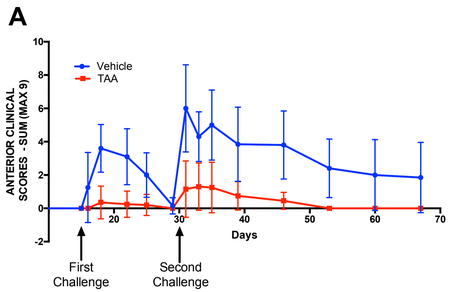


Figure 1: Study design

(1) G J. Jaffe, C-S Yang, Xi-C Wang, S W. Cousins, R P. Gallemore, P Ashton. Ophthalmology 1998;105:46-56
(2) S. Eperon, K. Balaskas, J. Vaudaux, and Y. Guex-Crosier . Curr Eye Res. 2013 Mar;38(3):405-12.

Results



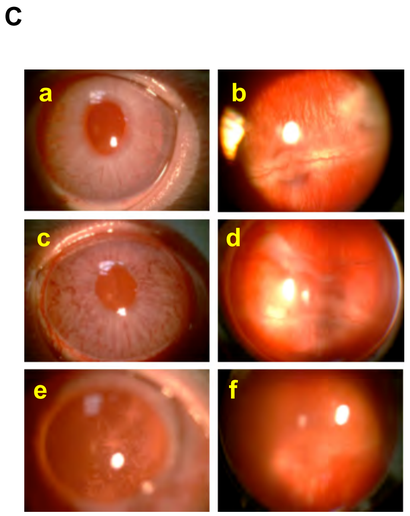


Figure 2: Slit lamp scoring of inflammation
(A) Anterior chamber: adapted scale from G.J Jaffe *et.al (1)* and *S. Eperon et.al (2)*, iris congestion and aqueous cell density (0: none, 1: mild, 2: moderate, 3: severe), additionnal scores were attribuated for absence (0), or presence (1), of fibrin, of synechiae and for normal (0), abnormal (1) iris dilation (maximum score = 9).
(B) Posterior chamber: vitreous opacity from 0 to 4 (Nussenblatt scale), absence (0) presence (1) of floating bodies in the vitreous, of deposits on lens, and normal (0), abnormal (1) fundus (retinal detachment, oedema, retinal tear…) (maximum score = 7).
(C) Typical slit lamp pictures of anterior segment (left row) and fundus (right row) one week after the second challenge for: TAA treated rabbits **(a)** and **(b)**, and Vehicle treated rabbits **(c)**, **(d)**, **(e)** and **(f)**.

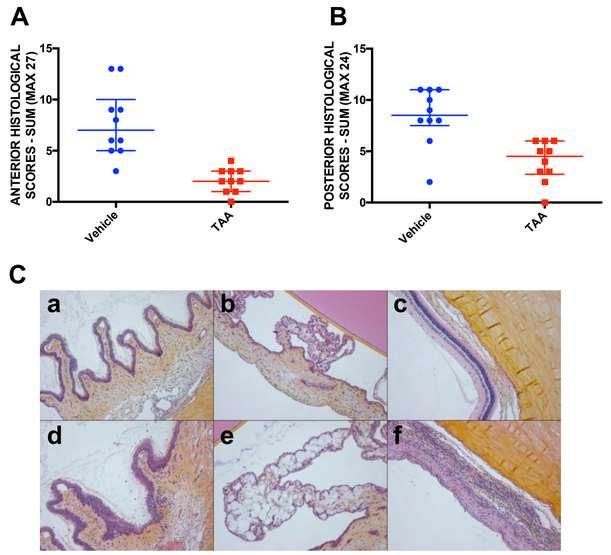


Figure 3: Histological evaluation
Grading of inflammation was performed on ocular sections (0: none, 1: mild, 2: moderate, 3: severe). Sum score data are presented - in **(A)** for the anterior part of the eye (corneal layers, conjuntivae/limbus, iris, ciliary body); - in **(B)** for the posterior part from the lens to the sclera including vitreous, retina and choroid.
(C) Typical pictures of histological section for: TAA treated rabbits: ciliary body **(a),** iris **(b)**, retina-choroid **(c)**, and Vehicle treated rabbits **(d)**, **(e)**, **(f)** respectively.

Clinical signs of uveitis were observed in two days after the first intravitreal challenge in vehicle treated rabbits. Slit lamp examination revealed inflammatory state in the anterior chamber with cells infiltration, iritis, and haze in the vitreous *(Fig-2-C-c, d, e and f, for illustration).* The second challenge induced a stronger and more sustained inflammatory response. TAA treatment significantly reduced inflammation all along the study. Histological analysis indicated signs of panuveitis in the Vehicle treated animals: inflammation of the iris and ciliary body with exudate in aqueous humor (*Fig-3-C-d, e*), degenerative vitreous with fibrous material and inflammatory cells, cells infiltration in the retina and in the optic nerve head and some retinal detachment or disorganization of retinal layers (*Fig-3-C-f*). TAA treated animals showed less cells infiltration and a preserved retina (*Fig-3-C-a, b, c)*.

Conclusion

Here was presented an experimental model of chronic uveitis in rabbit where a single administration of TAA reduced inflammation. This rabbit model of chronic anterior and posterior uveitis can be used to test efficacy of long-term treatment and delivery devices, due to the appropriate size of rabbit eye.