Prospective exploratory study to assess the safety and efficacy of aflibercept in cystoid macular oedema associated with retinitis pigmentosa

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ABSTRACT

Aims: To study the safety and efficacy of intravitreal aflibercept (Eylea) (ivA) for retinitis pigmentosa-associated cystoid macular oedema (RP-CMO) at 12 months via mean central macular thickness (CMT) and reported adverse events.
Methods: A prospective, exploratory, phase II, non- randomised, single-centre, open-label, 1-arm clinical trial involving 30 eyes of 30 patients. Serial ivA was given via loading dose (three injections) followed by treat and extend protocol over 12 months.
Results: Twenty-nine out of 30 (96.7%) patients completed 12 months of follow-up. No statistically significant reduction of CMT or visual acuity (VA) improvement was demonstrated overall. Eleven out of 29 (37.9%) participants were considered as 'responders' with at least an 11% reduction of CMT at 12 months on spectral domain optical coherence tomography compared with baseline. A reduction of CMT by mean (SD) 28.1% (12.9 %) was observed in responders at 12 months. No statistically significant corresponding improvement in best corrected VA was seen. No clinically significant adverse events were deemed secondary to ivA.
Conclusion: Serial ivA is safe and effective in patients with RP-CMO reducing CMT in 37.9% of patients. Responders demonstrate anatomical response after their first injection. Longer duration of CMO does not negatively affect response to anti-VEGF.

INTRODUCTION

- Toxic products released from the degenerating retina contribute to RP-CMO formation in 10%–50% of patients with RP.
- Anti-VEGF acts by reversing VEGF dependent proliferation, cell migration and delocalisation of tight junction proteins.
- There are several reports of variable effects of anti-VEGFs in RP-CMO.

Outcome measures

1. The safety of aflibercept in RP-CMO via the documentation of adverse events (AEs).
2. The efficacy of aflibercept in RP-CMO via mean CMT on SD-OCT at 12 months after baseline.

METHODS

1. Loading phase:
IvA was administered every 4 weeks for the first 3-months

2. Treat and extend protocol:
IvA administered for up to 12 months, with monthly follow ups.

Baseline Evaluation and Follow up

- Baseline visual function and intraocular pressure measured
- Best corrected VA, colour vision, contrast sensitivity and SD-OCT measured each visit.
- Microperimetry and fundus autofluorescence at 6-month and 12-month visits.
- Extension to 6, 8, 10 and 12 week follow-up, if there was no reduction in macular oedema.

RESULTS

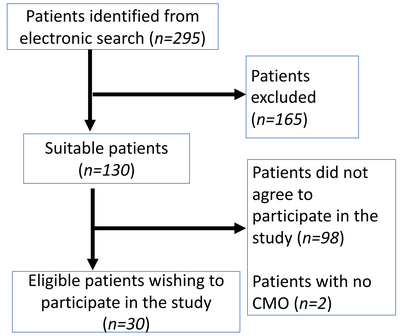


Figure 1
Flow chart describing patient selection methodology.

Study Participants

- Twenty-nine out of 30 (96.7%) patients completed 12 months of follow-up.
- 4 to 11 injections per patient were given over the 12 month study.

Safety

- No clinically significant adverse events secondary to ivA.
- Serial injections were well-tolerated.

Efficacy

- No statistically significant reduction of CMT or visual acuity (VA) improvement was demonstrated overall.
- 11 out of 29 (37.9%) participants were deemed 'responders', with at least an 11% reduction of CMT at 12 months on SD-OCTA from baseline.

Responders vs Non-responders

- Baseline characteristics were similar between responders and non-responders.
- Responders achieved reduction in CMO after their first injection ('early-responder'). There were no 'late-responders'.
- A reduction of CMT by mean (SD) 28.1% (12.9 %) was observed in responders at 12 months (*Figure 3*).
- No statistically significant improvement in best corrected VA was observed in responders (*Figure 4*).

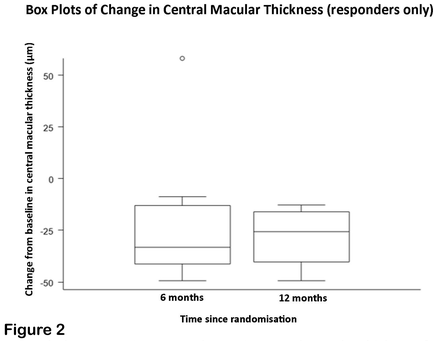


Figure 2
A graph demonstrating mean change in central macular thickness from baseline to 6 months post-baseline, and baseline to 12 months post-baseline in responders only (n=11).

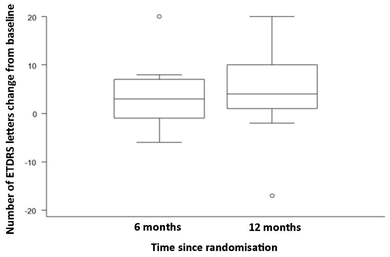


Figure 3
A graph demonstrating mean change in best corrected visual acuity from baseline to 6 months post-baseline, and baseline to 12 months post-baseline in responders only (n=11).

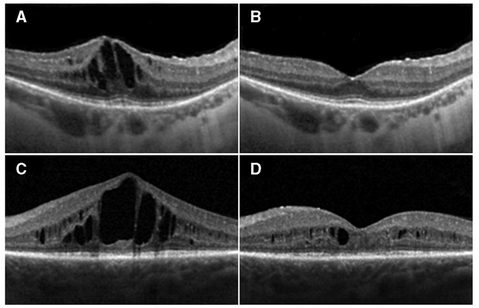


Figure 4
Two representative examples of responders: (A) and (C) show spectral domain optical coherence tomography (SDOCT) baseline images of two study participants. (B) and (D) are SDOCT images taken at 1 month post-first aflibercept injection in the same two participants, respectively.

Conclusions

- Serial ivA is safe and effective in patients with RP-CMO reducing CMT in 37.9% of patients.
- Responders demonstrate anatomical response after their first injection.
- Longer duration of CMO does not negatively affect response to anti-VEGF.
- More trials are needed- study with patients naive to other treatment modalities, shorter history of CMO and relatively intact photoreceptor layer at baseline. Larger cohort, inclusion of a control arm, blinding, and randomisation.