FINAL STUDY REPORT

Study Title: A prospective non-randomised exploratory study to assess the safety and efficacy of aflibercept in cystoid macular oedema associated with Retinitis Pigmentosa

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Purpose: This study investigated the safety and efficacy of aflibercept (Eylea; Regeneron, Tarrytown, New York, USA and Bayer Healthcare, Leverkusen, Germany) in patients suffering with cystoid macula oedema (CMO) associated with retinitis pigmentosa (RP-CMO).

Setting: This was a prospective, exploratory, phase II, non-randomised, single-centre, open-label, 1-year, 1-arm clinical trial.

Methods: Participants received intravitreal aflibercept (ivA) every four weeks for the first three months as a loading dose, followed by a treat and extend protocol up to 12 months. Extension from monthly to 6, 8, 10 and 12 week follow up occurred when there was no further reduction in macula oedema compared with the previous visit.

Primary Outcome Measures: (1) To report the efficacy of aflibercept in RP-CMO [Time Frame: baseline to 12 months] via mean Central Macular Thickness (CMT) on Spectral Domain OCT (SDOCT) at 12 months; A participant would be considered a 'responder' if their CMT reduced by at least 11%. (2) To report the safety of aflibercept in RP-CMO [Time Frame: baseline to 12 months] via the documentation of adverse events deemed related to the trial drug.

Results: All 30 patients were recruited within 6 months of study commencement. Twenty-nine patients had 12 month outcome data; with 1 patients' data being carried forward with an intention-to-treat analysis undertaken after early withdrawal from the study due to on-going mental health issues. Data was reported as descriptive due to the small sample size.

Efficacy: Primary outcome assessment demonstrated mean CMT of 413.3 microns at 12 months compared to 458.7 microns at baseline when reporting the group as a whole (responders and non-responders). Analysis of 'responders-only' (n=11) demonstrated mean CMT of 350.3 microns at 12 months compared to 489.8 microns at baseline.

Safety: In this clinical trial the study drug (aflibercept) had previously been subject to extensive investigation in clinical trials with a large amount of safety data available. Throughout the study herein all ocular and non-ocular/systemic adverse events were recorded, with each event assessed by the investigator to determine if additional recording and reporting was required. One ocular SAE was reported during the study period.

- Ocular SAE: One patient reported sub-acute reduction of vision during visit 8. Objective reduction of vision by 14 ETDRS letters was documented and injections immediately discontinued. Outer retinal layer thinning observed on SDOCT was similar to baseline and nil acute observed on microperimetry testing, autofluorescence imaging, SDOCT, or OCT angiography. After taking this into consideration and with knowledge that his non-study eye already had advanced photoreceptor loss, the reduction in vision was considered likely to be secondary to

progression of underlying RP rather than due to the study drug. This patient still attended for their 6 and 12 month follow-up appointments.

Please see the table attached for a summary of ocular and non-ocular adverse events (AE's) and serious adverse events (SAE's) recorded throughout this study.

Conclusion: This study demonstrates that aflibercept can be effective at reducing mean CMT in a third of patients with RP-CMO. The limited sample size precludes establishing definite predictive factors of treatment response. Further investigation into the effect of aflibercept on RP-CMO involving a larger sample of participants would be worthy of consideration.

A manuscript reporting the results of this trial is currently being drafted and will be submitted to a peer-reviewed medical journal. The results will also be presented at national and international scientific meetings.