DRAFT Document for comment

YoBro: a Yorkshire Retina Society suggested pathway for the use of Brolucizumab during the COVID-19 pandemic

Authors: Louise Downey, Helen Devonport, Martin McKibbin, Faruque Ghanchi

The Yorkshire Retina Society welcomes the EMA approval of brolucizumab as a treatment for neovascular age-related macular degeneration (nAMD). Data from the Hawk and Harrier clinical trials have confirmed that, when administered 8 or 12 weekly after the loading phase, brolucizumab is non-inferior to aflibercept, administered every 8 weeks. The potential for 12 weekly dosing is expected to help reduce the number of patient visits and injections. This is particularly important during the recovery phase of the COVID19 pandemic when capacity for intra-vitreal injections has been reduced significantly by the need to maintain social distancing. Given the added incidence of intra-ocular inflammation with brolucizumab, the authors propose the following guidance as minimum standard for clinical care pathways for patients with nAMD:

- Eye clinics planning to introduce brolucizumab as a treatment option should have capacity to monitor nAMD disease activity with visual acuity testing and OCT imaging and a triage system to help identify complications

- Baseline assessment at the point of commencing treatment with brolucizumab should include the standard clinical history and examination, as for all anti-VEGF drugs, and specific questions to identify a history of prior intra-ocular inflammation. Supplementary usage of wide-field retinal imaging is also helpful to document the absence of any previously undetected retinal vascular pathology, including vasculitis

- Clinical staff should also use a red flag questionnaire after each brolucizumab injection to identify signs and symptoms suggestive of intra-ocular inflammation. Patients with positive symptomatology would then be further screened with slit-lamp examination supported with widefield retinal imaging if deemed appropriate.

- The use of customised patient information, with clear information on contacting the local eye clinic in the event of a problem, should be provided.

- In the treatment of eyes that are already receiving another intra-vitreal agent but which require ≤8 weekly treatment, 6mg brolucizumab is a new treatment option. Before switching treatment, clinicians will need to discuss the perceived advantages and the added risk of intra-ocular inflammation.

    - Eyes with controlled or inactive disease: Offer 6mg brolucizumab and extend the most recent follow-up interval by an additional 2 weeks for the subsequent visit.

    - Eyes with stable vision but persistent disease activity: Offer 6mg brolucizumab but maintain the follow-up interval as before for the subsequent visit until better control of disease activity is observed. At this point, the treatment interval may be extended.

    - Eyes with unstable disease activity and/or worsening vision despite monthly therapy: Offer 6mg brolucizumab in a loading phase of 3 * monthly injections followed by adjusted extension of treatment intervals in a treat and extend pathway.

- For treatment naïve eyes, brolucizumab is a new option, especially when there is no history of prior intra-ocular inflammation and good visual acuity in the fellow eye. Prior to starting brolucizumab, other treatment options should be discussed. Visual acuity testing, OCT imaging +/- widefield imaging should be performed at baseline. A loading phase of 3 * monthly injections should be given, with the follow-up interval extended to 8 weeks. Visual acuity testing, OCT imaging and the red flag questionnaire should be completed at every visit.

    - Eyes with persistent disease activity at week 16, based on visual acuity, OCT imaging and symptoms, should remain on an 8 weekly treatment interval.

- For eyes with inactive disease at week 16, the treatment interval may be extended towards 12 weekly intervals using a Treat and Extend protocol to facilitate individualised patient dosing

- When the red-flag questionnaire is suggestive of new intra-ocular inflammation, slit lamp examination +/- widefield imaging are recommended and the planned injection should be deferred.

- Inflammation that predominantly affects the anterior chamber may be treated with topical steroids +/- mydriatics. Close monitoring is required to ensure a good therapeutic response and to confirm resolution of inflammation.

- When the inflammation predominantly affects the posterior segment, widefield imaging +/- FFA may be helpful to identify signs of retinal vasculitis. Oral steroids may be indicated but the possible diagnosis of infective endophthalmitis must also be considered. Further brolucizumab treatment should be withheld in cases with retinal vasculitis/vascular occlusion.