Brolucizumab

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Approved indication: macular degeneration

Beovu (Novartis)
pre-filled syringes and vials containing 120 mg/mL solution

Age-related macular degeneration is a common cause of visual loss. It may be due to atrophy (dry) or choroidal neovascularisation (wet).[1] As the development of blood vessels involves vascular endothelial growth factor A (VEGF-A), this protein is a target for drug therapy. Anti-VEGF treatments for wet age-related macular degeneration include aflibercept and ranibizumab. These drugs are injected into the vitreous humor.

Brolucizumab is a monoclonal antibody which binds to VEGF-A. By preventing VEGF-A from binding to its receptor, brolucizumab should reduce neovascularisation. Only a small volume (0.05 mL) of solution is injected into the vitreous. Very little enters the systemic circulation. Brolucizumab has a systemic half-life of 4.4 days and is eliminated like other proteins. Its pharmacokinetics are unlikely to be affected by liver or kidney disease, or other drugs.

The trials of brolucizumab assessed its effect on the best corrected visual acuity. They enrolled patients who could read between 78 and 23 letters on a retinopathy scale. This vision is approximately equivalent to 20/32 and 20/400 on a Snellen chart.

A phase II trial enrolled patients over the age of 50 years with previously untreated neovascular macular degeneration. The average numbers of letters they could read on the retinopathy scale was 54.8. Participants were given an intravitreal injection of aflibercept (45 patients) or brolucizumab (44 patients) each month for three months followed by an injection every eight weeks. Although the trial continued for 56 weeks, efficacy was assessed at weeks 12 and 16. After 12 weeks visual acuity had improved by 6.89 letters with aflibercept and by 5.75 with brolucizumab. The corresponding mean changes at 16 weeks were 6.62 and 6.04 letters. This met the study criteria for showing that brolucizumab was statistically non-inferior to aflibercept.[2]

Two phase III trials, HAWK and HARRIER, also used aflibercept as an active control in 1082 untreated patients.[3] Like the phase II trial, there was a loading phase of three intravitreal injections, but then brolucizumab was injected every 12 weeks while aflibercept 2 mg was given every eight weeks. Both trials used the recommended dose of brolucizumab 6 mg, but HAWK also tested 3 mg. From a mean baseline visual acuity of 61.2 letters in the HARRIER trial, patients treated with brolucizumab gained an average of 6.9 letters after 48 weeks. This was non-inferior to the gain of 7.6 letters with aflibercept. In the HAWK trial the average best-corrected visual acuity was 60.6 letters. After 48 weeks this improved by 6.1 letters with brolucizumab 3 mg and by 6.6 letters with 6 mg. Again, this was non-inferior to the increase of 6.8 letters with aflibercept. In both trials, when assessed at 16 weeks, there was statistically significantly less disease activity in patients treated with brolucizumab 6 mg (22.7% and 24%) compared with aflibercept (32.2% and 34.5%).[3]

There are risks with injecting an antibody into the eye. In the phase III trials the common adverse effects included conjunctival haemorrhage and pain. There is a risk of uveitis, endophthalmitis and retinal haemorrhage and detachment.[3] Approximately 5% of patients had a reduction in vision of at least 15 letters in the phase III trials, but this outcome was similar with aflibercept. There was an imbalance in cases of uveitis. In one trial it affected 2.2% of the patients given brolucizumab compared with 0.3% of the aflibercept group. Other ocular adverse events include cataract, vitreous detachment and raised intraocular pressure.[3] As treatment involves injecting a protein, some patients will develop hypersensitivity.

There may be benefits if patients only need an intravitreal injection every 12 weeks. However, in the phase III trials many patients had to switch to injections every eight weeks. The proportions who were able to continue brolucizumab 6 mg at 12-week intervals for 48 weeks were 51% and 55.6%.[3] Patients who have no disease activity when assessed after four months of treatment are more likely to be able to remain on a 12-week regimen. Like other intravitreal injections, brolucizumab should not be used concurrently in both eyes.

T manufacturer provided the AusPAR and the product information

REFERENCES

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NEW DRUGS

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, and the European Medicines Agency and the Therapeutic Goods Administration.