Ranibizumab

Ranibizumab (trade name **Lucentis** among others) is a monoclonal antibody fragment (Fab) created from the same parent mouse antibody as bevacizumab. It is an anti-angiogenic that has been approved to treat the "wet" type of age-related macular degeneration (AMD, also ARMD), a common form of age-related vision loss.

Its effectiveness is similar to that of bevacizumab.[2][3] Its rates of side effects also appear similar.[4] However, ranibizumab typically costs $2,000 a dose, while the equivalent dose of bevacizumab typically costs $50.[5][6][7][8]

Ranibizumab was developed by Genentech and is marketed in the United States by Genentech and elsewhere by Novartis,[9] under the brand name Lucentis.

1 Pharmacology

Ranibizumab is a monoclonal antibody that inhibits angiogenesis by inhibiting Vascular endothelial growth factor A, a mechanism similar to Bevacizumab.[10]

2 Medical uses

It is often used for age-related wet macular degeneration. Its effectiveness is similar to that of bevacizumab[2][11] and aflibercept.[12]

3 Side effects

A 2014 Cochrane review did not find a difference between bevacizumab and ranibizumab in deaths or total severe side effects when used for macular degeneration.[4] There; however, was not a lot of evidence and thus this conclusion is not that certain.[4]

Ranibizumab does appear to result in a lower risk of stomach and intestinal problems.[4] It is also associated with a low rate of eye related side effects.[13]

The most common side effects in clinical trials were conjunctival haemorrhage, eye pain, vitreous floaters, increased intraocular pressure, and intraocular inflammation.

Although there is a theoretical risk for arterial thromboembolic events in patients receiving VEGF-inhibitors by intravitreal injection, the observed incidence rate was low (< 4%) and similar to that seen in patients randomized to placebo.

Serious adverse events related to the injection procedure occurred with an incidence rate of less than 1% and included endophthalmitis, retinal detachment, and traumatic cataracts. Other serious ocular adverse events observed among ranibizumab-treated patients (incidence rate < 1%) included intraocular inflammation and blindness.[14]

4 Interactions

No significant interactions are known.[15]

5 Administration

The drug is injected intravitreally (into the vitreous humour of the eye) once a month. If monthly injections are not feasible, the regimen may be reduced to 1 injection every 3 months after the first 4 months.[1]

Dosing every 3 months is linked to a loss of approximately 5 letters (1 line) in visual acuity for the following 9 months as compared with dosing on a monthly basis. Large phase 3 clinical trials (MARINA and ANCHOR) which randomized patients with wet macular degeneration showed that 95% of ranibizumab-treated patients maintained visual acuity compared with 62% of those administered placebo ($P < .01$) at 1 year; moreover, up to 40% demonstrated an improvement in vision of at least 3 lines. Vision maintenance and loss were defined as a loss of less than 15 letters and a gain of 15 or more letters in visual acuity, respectively, as measured using the Early Treatment of Diabetic Retinopathy eye chart.[16]

Similar results were found in a randomized controlled trial of patients suffering from macular edema caused by central retinal vein occlusion. Participants injected once a month for 6 months showed a gain of approximately 13 to 15 letters in visual acuity, measured using the Early Treatment of Diabetic Retinopathy eye chart.[17][18]

6 Marketing issues

On November 3, 2010, *The New York Times* reported that Genentech began offering secret rebates to about

300 ophthalmologists in an apparent inducement to get them to use more ranibizumab rather than their less expensive bevacizumab. This may have been in anticipation of the results of the CATT clinical trial,[6] which was sponsored by the National Eye Institute, and compared the relative safety and efficacy of ranibizumab and bevacizumab in treating AMD. In 2008, bevacizumab cost Medicare only $20 million for about 480,000 injections, while ranibizumab cost Medicare $537 million for only 337,000 injections.[19] A small study showed no superior effect of ranibizumab versus bevacizumab in direct comparison.[20] The initial results of the larger Comparison of Age-related Macular Degeneration Treatments Trials (CATT) trial were published in the *New England Journal of Medicine* in May 2011.[6] The trial showed that the two drugs "had equivalent effects on visual acuity when administered according to the same schedule;" however, serious adverse events were more common in the bevacizumab arm of the trial.

The results of several subsequent head-to-head trials of the two anti-VEGF treatments were later published, and the overall results reinforced CATT's findings. The two therapies performed equally at restoring visual acuity according to a 2012 meta-analysis,[21] and also in the IVAN trial, alone and in the investigators' meta-analysis pooling its own results with CATT's.[22] A 2012 meta-analysis focused specifically on safety issues concluded that the rates of several adverse events were higher with bevacizumab, although the absolute rates of ocular serious adverse events were low with both therapies: ocular adverse events were about 2.8 times as frequent with bevacizumab than with ranibizumab, and "The proportion of patients with serious infections and gastrointestinal disorders was also higher." The authors concluded that " clinicians and patients should continue to carefully weigh-up the benefits and harms when choosing between the two treatment options. We also emphasize the need for studies that are powered not just for efficacy, but for defined safety outcomes based on the signals detected in this systematic review"[3]

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8 External links

- Official website Genentech

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