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Bevacizumab Biosimilars:

Studies Show Efficacy, Safety

The biologic Avastin® (bevacizumab) is often used, off-label, in the treatment of wet age-related macular degeneration. A number of biosimilars have been developed and are widely used for this same purpose. Studies, including those described here, have shown the biosimilars' safety and efficacy.

A 2017 study at various eye care centers in India was conducted to evaluate the efficacy and safety profile of intravitreal injection of a bevacizumab biosimilar, Zybev, for different retinal neovascular conditions. The biosimilar injections, 108 in total, were administered for wet age-related macular degeneration, diabetic macular edema, and retinal vein occlusion. Of the 108 eyes, 47 had diabetic macular edema, 32 had wet age-related macular degeneration, and 29 had macular edema secondary to retinal vein occlusion.(1)

The study concluded that the intravitreal injection of the bevacizumab biosimilar "was well tolerated over a period of one month with improvement in best corrected visual acuity (BCVA) and central macular thickness (CMA)."(1) In the discussion of the study, the researchers state that more prospective, randomized studies with repeat injections and larger sample sizes are warranted to evaluate the long-term efficacy and safety of the biosimilar.(1)

The study also concluded: "This short-term retrospective analysis suggests this biosimilar can be effective and safe in the management of various retinal neovascular conditions as well."(1)

A second study including 351 patients (385 eyes) at Farabi Eye Hospital, Tehran, Iran, September 2018 to February 2019, examined the use of the intravitreal injection of the bevacizumab biosimilar Stivant®. The study reported the relative safety of Stivant® and also its efficacy in consistent improvement of central macular thickness in patients and an improved best corrected visual acuity in a portion of patients.(2)

The study included 234 eyes with diabetic macular edema, 87 eyes with age-related macular degeneration, and 64 eyes with macular edema secondary to retinal vein occlusion. The biosimilar was injected in the eyes in three consecutive months and changes in central macular thickness and best corrected visual acuity were measured at baseline and monthly including one month after the third injection. "Our limited experience showed that the intravitreal injection of Stivant® was well tolerated," the researchers stated in their conclusion. The researchers called for a randomized clinical trial to evaluate the efficacy of Stivant® compared with the reference drug.(2)

A third study conducted in Iran and published in the Journal of Ophthalmic and Vision Research, set out to evaluate the safety of the bevacizumab biosimilar Stivant® in New Zealand albino rabbits using electrophysiological and histological analysis. In the study, both eyes of 41 rabbits were injected with 0.1mL of Stivant®. One control group of 14 rabbits received injections of the reference drug; the second control group of three rabbits received saline injections. The results stated: "No significant difference was observed in a-and b-wave amplitudes and latency after intravitreal Stivant® injection between baseline and different time points. Moreover, there was no statistically significant difference in wave amplitudes and latency between the Stivant® and control groups." The study concluded that the biosimilar Stivant® "did not appear to be toxic to the retina in albino rabbits." The results suggest that Stivant® "could be a safe and inexpensive alternative to intravitreal bevacizumab."(3)

At the American Society of Retina Specialists meeting in 2018, results were reported on a prospective, consecutive case series including 22,276 eyes that received Razumab, a Lucentis® biosimilar, and 2,237 eyes that received Zybev, a bevacizumab biosimilar. Patients in the study were treated for a variety of retinal vascular diseases, including choroidal neovascularization secondary to age-related macular degeneration, retinal vein occlusion, and diabetic macular edema.(4)

"Our data confirms that both these biosimilars are effective and safe. These could become the new safe, low-cost therapies for retinal diseases in the future," stated the physician leading the study. (4)

"Patients in the Zybev group experienced a statistically significant improvement in logMAR vision of 0.68 at baseline to 0.56 at 3 months ($P < .05$)." No serious ocular or systemic adverse events were reported, though 11 eyes in the Razumab group and four eyes in the Zybev group experienced intraocular inflammation.(4).

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(2) Mirshahi, A. M.D., Lashay, A. M.D., et. al., Journal of Ophthalmic and Vision Research, Intraocular Injection of Stivant® (A Biosimilar to Bevacizumab): A Case Series, Intraocular Injection of Stivant® (A Biosimilar to Bevacizumab): A Case Series (nih.gov)

(3) Lashay. A. M.D., Faghihi, H. M.D., et. al., Journal of Ophthalmic and Vision Research, Safety of Intravitreal Injection of Stivant, a Biosimilar to Bevacizumab, in Rabbit Eyes, https://pubmed.ncbi.nlm.nih.gov/32864065/

(4) Linneihan, R., Heilio, Ocular Surgery News, Biosimilars for Bevacizumab and Ranibizumab Show Promise for Retinal Diseases, https://www.healio.com/news/ophthalmology/20180726/biosimilars-for-bevacizumab-and-ranibizumab-show-promise-for-retinal-diseases