Commentary: Anti-vascular endothelial growth factor therapies in vitreo-retina practice: Biosimilars versus biologics

The advent of intravitreal vascular endothelial growth factor (anti-VEGF) therapy has radically improved the anatomical and visual outcomes of neovascular age-related macular degeneration (NVAMD), diabetic macular edema (DME), and retinal venous occlusions (RVO).[1] The first anti-VEGF medication approved for clinical use was pegaptanib sodium (Macugen, EyeTech Pharmaceuticals).[2] Subsequently, we have three other drugs (Ranibizumab, Aflibercept, and Brolicizumab)[3] and the off-label Bevacizumab.[3]

All these agents are Biologics, which are therapeutic agents containing protein from living organisms. Development of Biologics takes 10–15 years and involves huge investment and therefore these medications are expensive and involve a huge financial burden on patients especially in the treatment of chronic diseases like Wet NVAMD and DME. The need for continuous treatment, frequent monitoring, and periodic injections have posed a challenge in terms of patient compliance and cost of treatment in a developing country like India where a vast majority of patients are not covered by health insurance.

In this context, Biosimilars form a genuine option in vitreo-retina practice. Biosimilars are molecules different from Biologics but similar in pharmacokinetics to the innovative molecule. They are supposed to have comparable efficacy and safety to the originator molecule. The cost of manufacturing a biosimilar is only 1/10th of a biologic and therefore the end product would be 30% cheaper than the originator molecule.

Razumab (Intas Pharmaceuticals) became the first biosimilar to Ranibizumab and it received approval in the year 2015.[4] Most of the practicing retina specialists initially were cautious in their use of Razumab. They were concerned about the safety and efficacy of the drug. Unlike the originator which had undergone multiple randomized controlled trials, the biosimilar does not have strong evidence about its safety and efficacy prior to its regulatory approvals. Razumab was approved after a retrospective multicenter clinical trial in 103 patients with NVAMD.[5] This obviously creates an element of uncertainty among practicing clinicians about the efficacy and safety. Subsequently, the RE-ENACT study which was again a retrospective analysis of 561 patients with NVAMD, DME, and RVO shared favorable anatomical and functional results.[6] Therefore over the last few years, Razumab has maintained a constant performance in terms of its safety and efficacy and this is reflected in its increased acceptance among retinologists in our country.[7]

Globally there are various other biosimilars to anti-VEGF agents in the pipeline both for Ranibizumab and Aflibercept. With the success of Razumab, it is obvious that similar such molecules will gain easier acceptance from clinicians. There is a strong possibility therefore towards a shift towards biosimilars provided they are competitively priced.[8] However, it is important for pharmaceutical companies in their race to enter this growing competitive market to follow stringent systems in preapproval clinical trials and ensure safety and efficacy. Regulatory bodies also should create sensitive parameters before giving approval. This will also allow stiff pricing of the biologics in this growing segment of the pharmaceutical industry.

Giridhar Anantharaman

Giridhar Eye Institute, Cochin, Kerala, India

Correspondence to: Dr. Giridhar Anantharaman, Giridhar Eye Institute, Cochin, Kerala, India.
E-mail: giridhareye@gmail.com

References

1. Rosenfeld PJ, Brown DM, Heier JS, Boyer DS, Kaiser PK, Chung CY, *et al*; MARINA Study Group. Ranibizumab for neovascular age-related macular degeneration. N Engl J Med 2006;355:1419-31.
2. Gragoudas ES, Adamis AP, Cunnigham ET Jr., Freinsod M, Guyer DR. Pegatanib for neovascular age-related macular degeneration. N Engl J Med 2004;351:2805-16.
3. Schmidt-Erfurth U, Kaiser PK, Korobelnik JF, Brown DM, Chong V, Nguyen QD, *et al*. Intravitreal aflibercept injection for neovascular age-related macular degeneration: Ninety-six-week results of the VIEW studies. Ophthalmology 2014;121:193-201.
4. Sharma A, Kumar N, Kuppermann BD, Bandello F, Loewenstein A. Understanding biosimilars and its regulatory aspects across the globe: An ophthalmology perspective. Br J Ophthalmol 2020;104:2-7.
5. Sharma S, Khan M, Chaturvedi A; RE-ENACT 2 Study Investigators Group. A multicenter, retrospective study (RE-ENACT 2) on the use of Razumab (world's first biosimilar Ranibizumab) in wet age-related macular degeneration. Ophthalmol Ther 2020;9:103-14.
6. Sharma S, Khan MA, Chaturvedi A; RE-ENACT Study Investigators Group. Real-life clinical effectiveness of Razumab (world's first biosimilar Ranibizumab) in wet age-related macular degeneration, diabetic macular oedema, and retinal vein occlusion: A retrospective pooled analysis. Int J Ophthalmol Eye Res 2018;6:377-83.
7. Sharma A, Reddy P, Kuppermann BD, Bandello F, Lowenstein A. Biosimilars in ophthalmology: "Is there a big change on the horizon?" Clin Ophthalmol 2018;12:2137-43.
8. Sheth JU, Stewart MW, Khatri M, Gupta SR, Chawla S, Rajendran A, *et al*. Changing trends in the use of anti-vascular endothelial growth factor (anti-VEGF) biosimilars: Insights from the Vitreoretinal Society of India Biosimilars of Anti-VEGF Survey. Indian J Ophthalmol 2021;69:352-6.

Access this article online	
Quick Response Code:	Website: www.ijo.in
	DOI: 10.4103/ijo.IJO_40_21

Cite this article as: Anantharaman G. Commentary: Anti-vascular endothelial growth factor therapies in vitreo-retina practice: Biosimilars versus biologics. Indian J Ophthalmol 2021;69:358-9.