

Anti-VEGF Biosimilars for Retinal Diseases Survey 2023- India (Bio-INDAS)

by the International Retinal Biosimilar Study (Inter-BIOS) Group in Collaboration with the
Vitreoretinal Society of India (VRSI)

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Conflicting Interest:

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The Vitreo Retina Society of India (VRSI) performed its last biosimilar survey in January 2020, when the only ranibizumab biosimilar molecule available was Razumab.^[1] The purpose of present survey was to understand practice patterns in the setting of multiple ranibizumab biosimilar choices.^[2-4] This survey was conducted between July 29, 2023, and August 18, 2023 supplemental material (survey questions). A total of 231 ophthalmologists responded with response rate of 53.5%. There was a good mix of respondents including physicians in private practice (31.2%) corporate hospitals (27.7%), group practitioners (16.5%), charitable hospitals (15.2%) and medical colleges (9.5%). The majority of the respondents were retina specialists (83.5%, n=193) and the minority were comprehensive ophthalmologists (16.5%). Most of the respondents were male (65.1%) and the mean age of the respondents was 44.7±21.3 years. Most of the respondents were in practice for more than 5 years (78.7%). Responses were received from ophthalmologists practicing in 24 states (total of 28 states). (Figure 1A)

Results

Awareness about biosimilar ranibizumab

The majority (95.2%) of the ophthalmologists were aware of all the ranibizumab biosimilars available in India.

Usage of Originator Vs Biosimilar Ranibizumab in India

Biosimilar ranibizumab was the most common ranibizumab administered with 50-100 % usage in 51% respondents whereas the proportion of originator usage was below 25% in the majority of practices (62.8%). (Figure 1B)

Molecule preference

The majority (80.1%) of the respondents listed Razumab as their first preference followed by Ranieyes (7.8%), Oceva (5.2%), Ranizurel (4.8%) and Visumab (2.2%). (Figure 2A)

Perception of Efficacy of Originator Vs Biosimilar Ranibizumab in India

The majority of respondents (74.5%) felt that the biosimilar and originator ranibizumab were equally efficacious. (Figure 2B)

Perception of Safety of Originator Vs Biosimilar Ranibizumab in India

The majority of respondents (73.6%) felt that both the biosimilar and originator ranibizumab were equally safe. (Figure 2C)

Affordability and access

The primary reason for biosimilar usage was reduced cost to the patients (88.7%).

Fair pricing of biosimilar ranibizumab

The majority of the respondents (89.6%) stated that a fair purchase price of the drug should be between INR 5000 to INR 7000 (at present approximately 60-85 USD). Furthermore, the majority of respondents shared that a purchase price of INR 5000- INR 7000/- would completely replace off-label bevacizumab (Avastin, Genentech, USA) use in their practice.

Conclusion

With three biosimilars of ranibizumab already approved by the DCGI,^[2] this survey sheds light on many areas related to biosimilar anti-VEGF usage in India. It summarizes that in India, anti-VEGF biosimilars have become the major proportion of overall anti-VEGF usage for the majority of clinicians (for 3 in 4 patients' clinicians prefer to use biosimilar anti-VEGF). This could be due to a number of reasons: the availability of more than one anti-VEGF biosimilar leading to further price reduction that is affordable to a larger population; low acceptance and use of cheaper off label bevacizumab due to lack of compounding pharmacies and occurrence of cluster endophthalmitis, and still high prices of on label anti-VEGFs. Clinicians are overall satisfied with the safety and efficacy of these molecules.

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Reference

1. 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 Feb;69(2):352-356.
2. Sharma A, Kondo M, Iwahashi C, Parachuri N, Kumar N, Bandello F et al. Approved biosimilar ranibizumab-a global update. Eye (Lond). 2023 Feb;37(2):200-202.
3. Sharma A, Kumar N, Parachuri N, Bandello F, Kuppermann BD, Loewenstein A. Biosimilars for Retinal Diseases: An Update. Am J Ophthalmol. 2021 Apr;224:36-42.
4. Sharma A, Kumar N, Kuppermann BD, Francesco B, Lowenstein A. Ophthalmic biosimilars: Lessons from India. Indian J Ophthalmol. 2019 Aug;67(8):1384-1385.

Legends

- Figure 1A- Sample Characteristics
- Figure 1B- Proportion of biosimilar and innovator use in clinicians practice
- Figure 2A- Clinicians preference of biosimilar ranibizumab molecules
- Figure 2B- Efficacy of biosimilar ranibizumab Vs innovator ranibizumab
- Figure 2C- Safety of biosimilar ranibizumab Vs innovator ranibizumab
- Supplemental material- Survey questions

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