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ORIGINAL RESEARCH

Biosimilars for retinal diseases: United States-Europe awareness survey (Bio-USER – survey)

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ABSTRACT

Purpose: To assess the awareness of biosimilar intravitreal anti-VEGF agents among retina specialists practicing in the United States (US) and Europe.

Methods: A 16-question online survey was created in English and distributed between Dec 01, 2021 and Jan 31, 2022. A total of 112 respondents (retinal physicians) from the US and Europe participated.

Results: The majority of the physicians (56.3%) were familiar with anti-VEGF biosimilars. A significant number of physicians needed more information (18.75%) and real world data (25%) before switching to a biosimilar. About one half of the physicians were concerned about biosimilar safety (50%), efficacy (58.9 %), immunogenicity (50%), and their efficacy with extrapolated indications (67.8 %). Retinal physicians from the US were less inclined to shift from off-label bevacizumab to biosimilar ranibizumab or on-label bevacizumab (if approved) compared to physicians from Europe (p=0.0001). Furthermore, physicians from the US were more concerned about biosimilar safety (p=0.0371) and efficacy compared to Europe (p= 0.0078).

Conclusions: The Bio-USER survey revealed that while the majority of retinal physicians need additional information regarding the safety, efficacy and immunogenicity when making clinical decisions regarding their use. Retinal physicians from US are more comfortable in continuing to use off-label bevacizumab compared to physicians from Europe.

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Bio-USER; survey; awareness; Anti-VEGF; retina; biosimilar; ophthalmology; United States; europe

1. Introduction

Biosimilars are biological products that demonstrate high similarity to an already-approved originator biologic. For regulatory approval, a biosimilar must demonstrate no clinically meaningful differences in quality, safety, and efficacy [1]. Unlike generics that are essentially of identical chemical composition to the original, biosimilars have a more complex biologic composition and therefore are not identical to the original and therefore require a series of clinical trials to validate their safety and efficacy versus the originator. The United States Food and Drug Administration (US-FDA) and European Medical Agency (EMA) recently approved two biosimilar anti-vascular endothelial growth factor (anti-VEGF) of originator ranibizumab (Lucentis, Genentech, USA) for the management of retinal diseases [2–5]. There are many other biosimilar molecules of ranibizumab and aflibercept in the final phase of clinical trials at the time of writing this manuscript. Approval of aflibercept (Eylea, Bayer/Regeneron, USA) biosimilars is expected between 2023 and 2025 [6].

Although ophthalmic biosimilars are new to the field of ophthalmology, their availability is widespread in other areas of medicine. Biosimilars of numerous molecules, such as recombinant human growth hormone (rhGH), erythropoietin, filgrastim, insulin, follitropin, infliximab, and etanercept are widely and safely administered for various systemic diseases [7].

Patients often turn to healthcare professionals as a source of information related to newer medicines. Hence, it is important to understand the awareness regarding these molecules amongst clinicians. Only when clinicians are well acquainted with biosimilars can they effectively counsel patients. When generic drugs first became available in the United States in the 1980s, physicians required a clear understanding of this new

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class of drugs before they were comfortable prescribing them to patients [8]. Similarly, it is expected that physicians will also comprehensive understanding of biosimilars before they feel comfortable offering these new treatment options to their patients. Some of the authors of this manuscript (AS, NK, NP, FB, AL, CR, and BDK) studied the various aspects of biosimilars in ophthalmology [9–15].

The Biosimilars for Retinal Diseases- United States-Europe Awareness Survey (Bio-USER – Survey) was designed to assess the awareness of biosimilar anti-VEGF agents among clinicians practicing in the United States and Europe due to the availability of US-FDA and EMA approved biosimilars. The results of the Bio-USER survey may be of value to better prepare clinicians and industry about gaps in knowledge of ophthalmic biosimilar molecules for clinical use.

2. Methods

A 16-question survey was created in English. This questionnaire was developed after reviewing similar surveys that were utilized for systemic biosimilars [16–18]. Questions were modified to extract relevant information from retina physicians and phrased in a neutral manner. These tailored questions were reviewed and agreed upon by a panel of 3 experts (AS, NK, NP) with experience in biosimilars for retinal diseases. Responses were obtained from retina physicians including faculty, private practitioners, and fellows practicing in the United States and Europe. Retina physicians were shortlisted through a multistage sampling. Personal communication with the chair of ophthalmology institutions in the United States and Europe was made to refer the survey to the retinal physicians in their department. During the survey, primary respondents were encouraged to share it with their colleagues practicing retina to reach the final list of 200 retinal physicians. No specific database was used. Consent was obtained from participants after informing them about the purpose of the survey and how their responses will be used with protection of confidential information. The survey did not require any medical record review or patient interaction therefore institutional review board approval was not required.

The online questionnaire was hosted at Google Forms (Google, CA, USA;). The survey was sent via e-mail, WhatsApp, and LinkedIn between 1 December 2021 and 31 January 2022. Two reminders were sent to those who did not respond. No remuneration was provided to the respondents.

The survey examined a range of topics that were deemed important to understand the awareness of retinal physicians about biosimilars. The survey was also designed to gather information about retina physicians' intent to use biosimilars in their practice and the impact of cost. The widespread use of cost-effective, compounded, off-label bevacizumab makes ophthalmology unique compared to other specialties. However, questions were also included about on-label bevacizumab. Results are presented in the form of descriptive statistics, table, and bar charts. Most responses are reported as nominal data. Data was analyzed using Excel (Microsoft, Richmond, USA). To identify differences regarding the awareness of biosimilars between the United States and European participants, data on key parameters were analyzed comparing the two groups. Fisher's exact test was used to understand differences on parameters between the United States and Europe and between the faculty, private practitioners and members in training.

3. Results

The survey invitation was sent to 200 retinal physicians (100 from the United States and 100 from Europe). A total of 112 retinal physicians responded (US: n = 55, Europe: n = 57) to the survey (response rate = 56%).

3.1. Sample characteristics

There was a mix of respondents with the majority of the responders having an academic faculty position (64.2%, n = 72) followed by private retinal practitioners (17.8%, n = 20) and retina trainees (17.8%, n = 20). The majority of the responders were males (69.6%, n = 78) and mean age of the respondents was 44.7 ± 11.3 years (Table 1). Differential demographic data between the United States and Europe is presented in Table 2.

3.2. Familiarity with the anti-VEGF biosimilars

Although the majority [56.25% (n = 63)] of the physicians were familiar with anti-VEGF biosimilars, only 35.7% (n = 40) acknowledged a complete understanding, while 6.25% (n = 7) of physicians reported only hearing about biosimilars and 1.78% (n = 2) reported no knowledge whatsoever. Most of the responding physicians [64.2% (n = 72)] desired educational information about the safety, efficacy, and performance for a better understanding of anti-VEGF biosimilars. Furthermore, 23.2% (n = 26) of physicians expressed the need for more information regarding guidelines for use of a biosimilar vs the originator molecule. Although, more than half of the respondents [69.6% (n = 78)] acknowledged that biosimilar anti-VEGFs have similar efficacy, safety, and purity compared to originator anti-VEGF, 16% (n = 18) believed that they were less safe than the originator. A small minority [8.9% (n = 10)] responded that they did not know about efficacy and

Table 1. Overall demographic information.

Total Respondents	112 (56%)
U.S. respondents	55
Europe respondents	57
Faculty	64.2%
Private Practitioners	17.8%
Members in training	17.8%
Sex (Male Vs Female)	69.6%/30.4%
Mean Age (Years)	44.7±11.3

Table 2. Differential demographic information.

	US	Europe
Faculty	25	47
Private Practitioners	18	2
Member in training	12	8
Sex (Male vs Female)	74.5%/25.4%	64.9%/35.08%
Mean Age (Years)	43.7±10.7	45.6±12.0

safety comparisons and 5.3% (n = 6) thought that biosimilars were not as efficacious compared to the originator anti-VEGF. Most respondent [91% (n = 102)] agreed that the major advantage of biosimilars over originators was lower pricing. When asked about the examples of originator anti-VEGF drugs (i.e. ranibizumab, aflibercept), most [78.5% (n = 88)] correctly answered. However, when asked about the recently FDA- and EMA-approved ranibizumab biosimilar, only 45.5% (n = 51) of physicians were aware. Finally, although more than half of the physicians [63.3% (n = 71)] correctly responded that biosimilars and generic medications were not the same, 21.4% (n = 24) still considered them to be the same, and 14.2% (n = 16) indicated that they didn't know enough to answer this question (Figure 1).

3.3. Incorporation of biosimilars into clinical practice

When asked if the respondents would be willing to switch their patients from originator to biosimilar ranibizumab if biosimilar ranibizumab becomes available at a lower cost, roughly one-third of respondents [36.6% (n = 41)] wanted more information before making a decision. 34.8% (n = 39) were willing to make a switch. A minority [11.6% (n = 13)], were not in favor of switching despite the lower cost. When asked if a lower cost ranibizumab biosimilar would prompt a shift of cases from off-label bevacizumab to the biosimilar, roughly one-third of the physicians [31.25% (n = 35)] were willing to make such a switch. However, significant number of physicians wanted to have more information [18.75% (n = 21)] and real-world data [25% (n = 28)] before making a switch in therapy. One-third of the physicians, [33% (n = 37)] responded that they would make a switch if the patients were unable to pay. Similar number of physicians [31.25% (n = 35)] chose an option where they would let the patient choose the drug, either originator or biosimilar, for treatment. A very small number of clinicians [15.17% (n = 17)] responded that they would initiate treatment with a ranibizumab biosimilar (Figure 2).

3.4. Concerns regarding biosimilar anti-VEGF

More than one-half of the respondent physicians [56.25% (n = 63)] were concerned about the quality of a biosimilar anti-VEGF. Similarly, about one-half of the respondents were slightly concerned about the safety [50% (n = 56)], efficacy [58.9% (n = 66)] and immunogenicity [50% (n = 56)] and their efficacy in extrapolated indications [67.8% (n = 76)]. Among these parameters, the major concern was regarding safety [21.4% (n = 24)] and immunogenicity [25% (n = 28)]. (Figure 3)

3.5. Awareness of on-label bevacizumab

Most of the physicians [50% (n = 56)] were under the mistaken impression that ONS-5010 (Lytenava from Outlook Therapeutics) is a biosimilar of bevacizumab. And many of them [40.1% (n = 45)] were amenable to prescribing bevacizumab if it receives FDA approval (Figure 4).

3.6. United States vs *Europe*

To understand differences between the United States and Europe, all survey questions were analyzed separately, revealing a few major differences. Retinal physicians in the United States were more aware of the originator molecules compared to Europe (p = 0.0107). Although retinal physicians from both groups had expressed reservations regarding the safety and efficacy of biosimilars, more physicians from the United States expressed concern compared to physicians from Europe, with respect to safety (p = 0.0371) and efficacy (p = 0.0078). Most interestingly, when asked whether lower cost ranibizumab biosimilar would prompt a shift from off-label bevacizumab to FDA-approved low-cost ranibizumab biosimilars, physicians from Europe were much more in favor compared to physicians from the United States (p = 0.0001). Similarly, when asked if they would use on-label bevacizumab (ONS-5010) instead of off-label bevacizumab with FDA approval, physicians from Europe were more in favor compared to physicians from the United States (p = 0.00002) (Figure 5).

3.7. Faculty vs private practitioners vs member in training

To understand differences among faculty vs private practitioners vs members in training, all survey questions were analyzed separately, revealing a few major differences. Faculty and private practitioners had no significant difference except on one question entitled 'If On label bevacizumab (ONS-5010/Lytenava from Outlook Therapeutics) receives FDA approval, will you use it instead of off-label bevacizumab (Avastin)' Private practitioners needed more scientific information compared to respondents at faculty position (p = 0.0451). The majority of the differences were noticed between members in training and faculty or private practitioners, such as members in training did not have a complete understanding of biosimilars (p = 0.0194) and some of them have never heard of them (p = 0.0090) when compared to the faculty. Furthermore, some of the members in training had the wrong impression that Razumab (Intas Pharmaceuticals, Ahmedabad, India) is an FDA and EMA-approved ranibizumab biosimilar (p = 0.0481) when compared to the faculty. In most of the questions, members in training needed more scientific information about biosimilars before making a decision such as switching from originator to biosimilar ranibizumab if its cost-effective (p = 0.0327), shifting from off-lable bevacizumab to low-cost biosimilar ranibizumab (p = 0.0153) and willing to use on label bevacizumab (if approved) instead of off-label bevacizumab (p = 0.0167)

4. Discussion

With the two biosimilars of ranibizumab already approved by the FDA and EMA, many other biosimilars of originator ranibizumab (Lucentis) and aflibercept (Eylea) are on the horizon, and many other innovative therapies are in the pipeline [2–4], retinal physicians will have a wider choice of anti-VEGF medicines to treat common retinal conditions. Consequently, they need additional education to make informed treatment

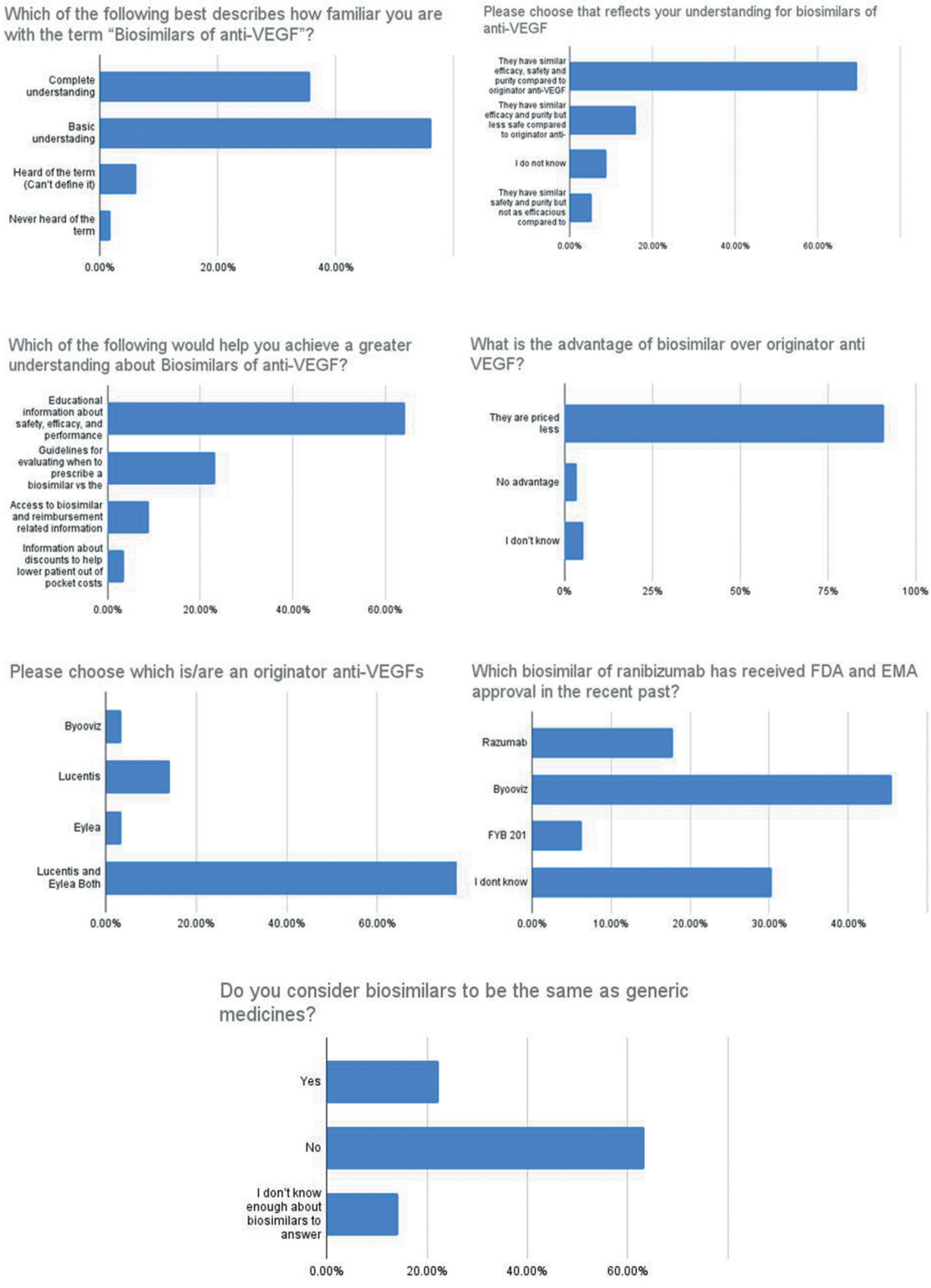

Figure 1. The response related to familiarity with the anti-VEGF biosimilars.

decisions. Cardinal Health recently performed a survey on awareness and perspective regarding the role of biosimilars in ophthalmology [16]. Cardinal Health surveyed community-based retina specialists in the United States (n = 37). They found that more than half (55%) of the respondents had read research on biosimilars but were not familiar with the specifics, such as manufacturing, approval processes, and clinical trial design. The Bio-USER survey revealed similar findings with more than one-half of the physicians reporting only a basic understanding of biosimilars while very few indicated

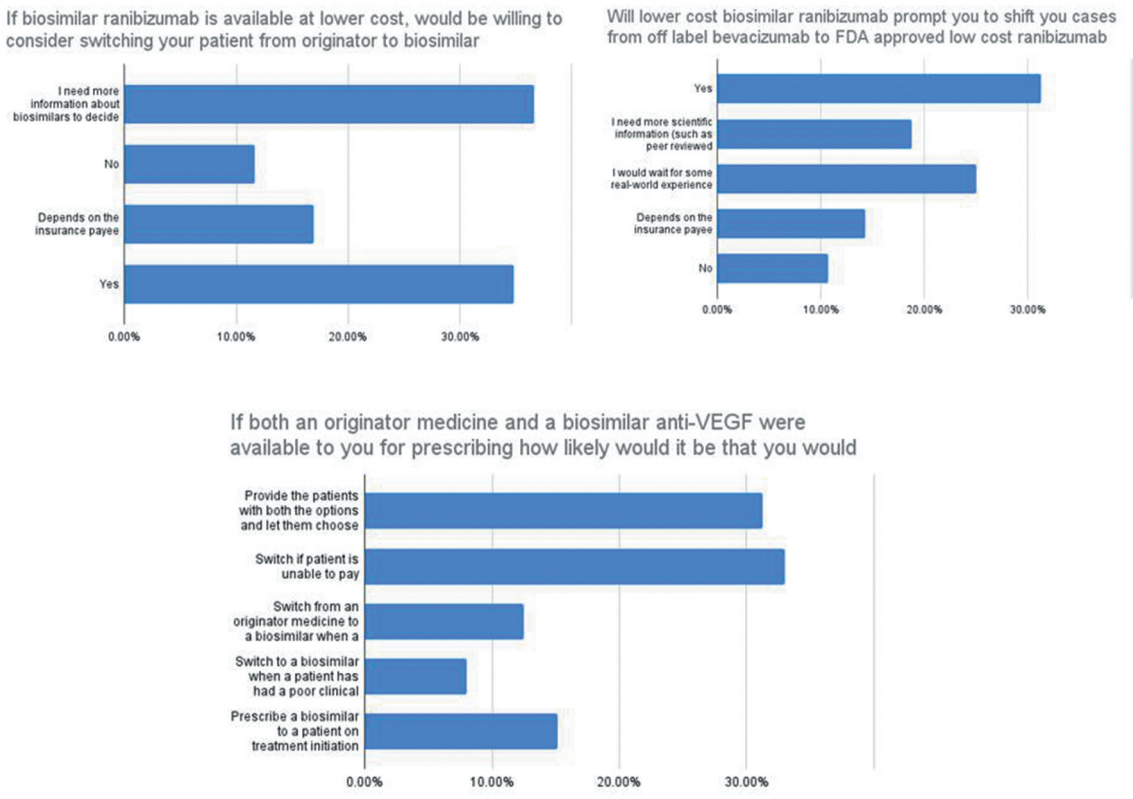

Figure 2. Responses related to incorporation of biosimilars into clinical practice.

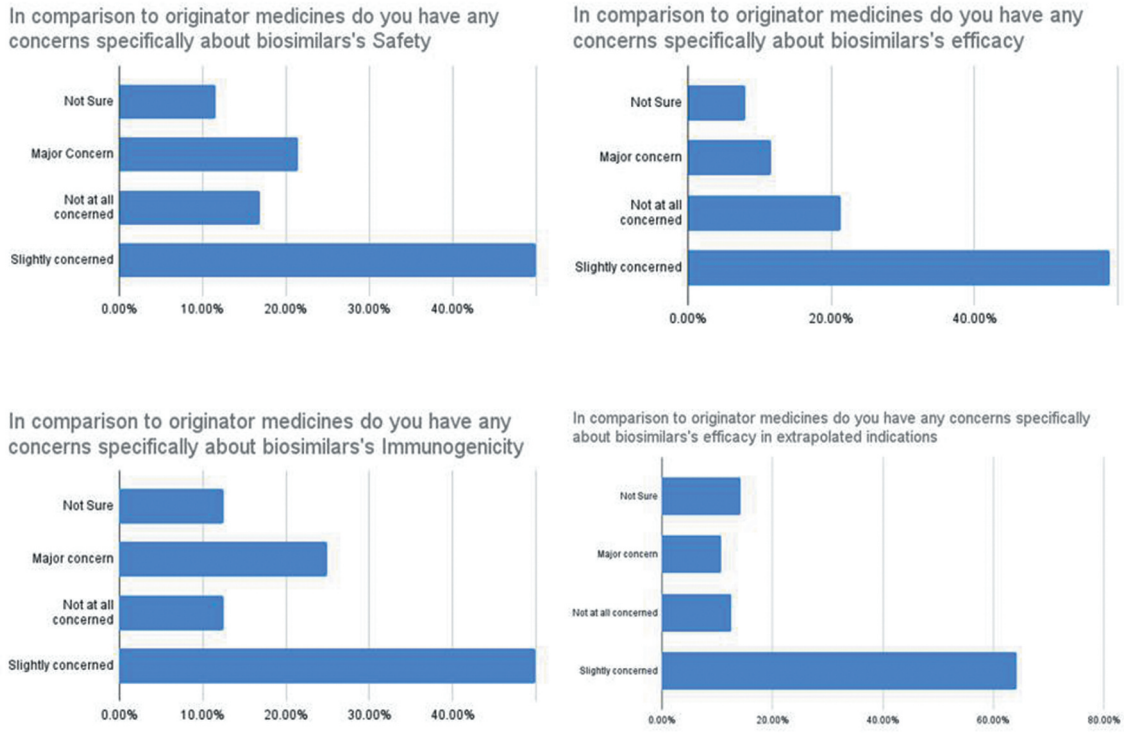

Figure 3. Responses related to concern about biosimilar anti-VEGF.

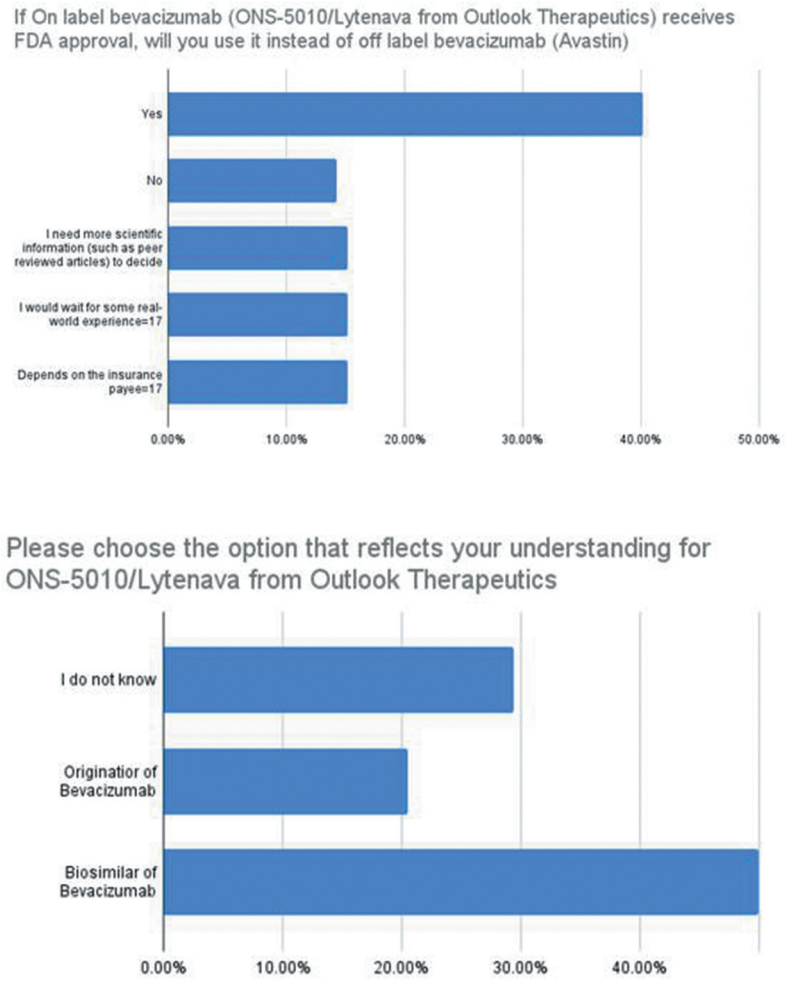

Figure 4. Responses related to awareness of on-label bevacizumab.

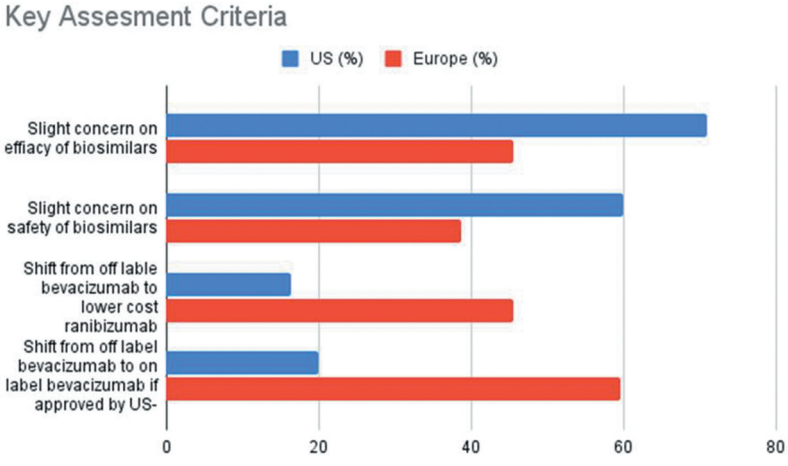

Figure 5. Key differences between retinal physicians from the United States and Europe.

sufficient knowledge relating to these molecules. In contrast to the Cardinal Health survey, our Bio-USER survey reported fewer retinal physicians who were completely ignorant about biosimilars. This could be due to the fact that the Cardinal Health survey was conducted before the approval of ranibizumab-nuna (Byooviz, Samsung Bioepis, South Korea/Biogen, USA) and the Bio-USER survey (reported herein) was conducted after the approval. Importantly, the results of ranibizumab-nuna phase 3 trials were presented at the American Academy of Ophthalmology Annual Meeting in 2021 [19], which explains the increased awareness about biosimilar anti-VEGFs medications among retina specialists.

However, many of the respondents were still not aware that Byooviz is an FDA- and EMA-approved biosimilar of ranibizumab. Interestingly, some of the retinal physicians (19%) in our survey responded that Razumab (approved in India) is FDA and EMA approved which is not true. This may relate to the availability of literature on Razumab over the past 7 years as it was the first biosimilar of originator ranibizumab (Lucentis) approved in 2015 for clinical use but limited to use only in India [20].

In our Bio-USER survey, a majority of the respondents were not willing to switch their patients from an originator ranibizumab to a biosimilar ranibizumab without more information on biosimilars including guidelines. Only a few retinal physicians reported the willingness to initiate treatment with a biosimilar at this time. This shows that cost is not the primary motivating consideration for physicians in making a decision to switch or initiate treatment with biosimilars. This finding mirrors other surveys such as the European Crohn's and Colitis Organization (ECCO) performed in 2013 when the first biosimilar of the monoclonal antibody infliximab was approved by EMA. Sixty-one percent of responding clinicians reported little or no confidence in using biosimilars in everyday clinical practice [21]. Similarly, a survey of the Canadian Rheumatology Association (CRA) revealed that 72% of the clinicians would be unlikely, or very unlikely, to select a biosimilar as the initial therapy [22]. In the Bio-USER survey, some physicians were ready to switch from off-label bevacizumab to biosimilar ranibizumab. However, most preferred to wait for more significant scientific and real-world data. The price of ranibizumab-nuna was not known at the time of the survey, which could certainly impact physician decision-making. As per the experience of ophthalmic biosimilars from India and with regard to other systemic biosimilars globally, biosimilars are generally priced 20–30% less than the innovator molecule, which would still be much higher than off-label bevacizumab making the price benefit of the biosimilars limited.

The Bio-USER survey has clearly indicated that most of the physicians surveyed have some degree of reservation about the quality, safety, efficacy, and immunogenicity of biosimilar molecules. Moreover, many physicians expressed major concerns regarding safety and immunogenicity. Physicians are likely questioning differences in the manufacturing process or other components of the drug. However, it is well established that even originator molecules may undergo changes in their manufacturing process. One example is the originator molecule for infliximab, which has undergone more than 3 dozen manufacturing changes since its approval [23]. The FDA has an established evaluation process to review manufacturing changes and their potential impact on the performance of a product [24]. Prior studies did not identify any immunogenicity signals during the switch from originator ranibizumab (Lucentis) to biosimilar ranibizumab (Razumab) approved in India, which is in agreement with other major studies related to biosimilars for systemic diseases [11,25]. Furthermore, FDA approval of ranibizumab-eqrn (CIMERLI, Coherus Biosciences, USA) as interchangeable drug without any additional data also indicates that switching might not be the concern [26]. Another reason for physicians to have concern about the efficacy and safety of a biosimilar is due to the clinical trial design for the approval process of biosimilars. The phase 3 clinical registration trials for biosimilars require fewer patients and shorter primary end points compared to the innovator molecule. It is important therefore for manufacturers of biosimilars to develop appropriate communication channels so that physicians are educated about the regulatory requirements for the approval of such drugs and the rationale behind the short trials with early end points [9].

Off-label bevacizumab will be the major differentiating factor when comparing success of biosimilars in ophthalmology to biosimilars in other areas of medicine. In this survey, we tried to assess awareness regarding on-label bevacizumab currently under investigation by Outlook Therapeutics. Most respondents felt that on-label bevacizumab would be a biosimilar of bevacizumab which is not true. To refer to a drug as biosimilar, it is mandatory to have an on-label originator drug for the same indication. This has never been the case with bevacizumab for retinal diseases. Hence, on-label bevacizumab is considered an innovator molecule, and if it gets approval, it might be granted 12 years of market exclusivity [27].

The advent of biosimilars, molecules highly similar to their originator biologics, has offered the promise of ameliorating cost and access challenges. However, limitations with biosimilar adoption by prescribing physicians remain. Generics have remarkably improved availability and affordability of small-molecule drugs; biosimilars could do the same for biologics in the future. Historically, there has been a slow adoption of biosimilars by clinicians in other specialties. Most of the clinicians in the Bio-USER survey wanted more information before prescribing. This could probably be mitigated over time with education and real-world data. This has influenced prescribers in the past, with prescription of biosimilar infliximab growing from 13% in 2013 to 47% in 2015 following a strong educational initiative. A similar survey on ranibizumab biosimilar uptake in India showed the same trend [28].

Our Bio-USER survey did identify some knowledge gaps as pertaining to biosimilars. For example, some of the clinicians suggested that they would switch patients to a biosimilar if the patient showed a poor clinical response with the originator. It is unlikely that switching to a biosimilar from the originator would change the clinical outcome as they would be expected to produce a similar clinical effect. Furthermore, some physicians still do not differentiate between biologics and generics. Many physicians reported a belief that biosimilars have similar efficacy and purity but have less safety. In addition, some physicians in our survey expressed the belief that aflibercept (Eylea) is not an originator molecule. These knowledge gaps can be addressed with further education.

Education of physicians is a key component to promoting adoption of biosimilars, as recognized by the US-FDA in its Biosimilars Action Plan [29]. Another major factor for biosimilar administration is patient education. To achieve that, healthcare providers first need to be confidant with prescribing these molecules. Only then can they convey confidence to their patients that they are being treated with a product of similar efficacy and safety. The Bio-USER survey might be of value in highlighting the areas to focus on to achieve

improved biosimilar education. A second survey will be conducted in 1–2 years in order to monitor trends in the awareness, knowledge, and perceptions of biosimilars.

This study has several limitations. First, the sample size is inadequate to represent the view of all the retina specialists in the United States and Europe. Furthermore, since the healthcare systems are organized and financed in different ways across Europe, the results of the study may not necessarily be generalized to the whole of Europe. However, being an index manuscript about this new entity called biosimilars, the results of this survey holds value to understand the dynamics and might be of help to the FDA and EMA in their ongoing educational efforts toward biosimilars. We would be initiating a survey with a larger sample size in the future across various regions worldwide. Second, there was unequal representation between practitioners from private and academic institutes. Furthermore, years of practice of respondents and subspecialty such as medical retina, surgical retina, or both were not taken into account. As the main focus of the survey was to understand the awareness about these new molecules, practice pattern, years of practice and subspecialty might not have affected the overall results and the outcome. Third, pricing of biosimilar ranibizumab had not been disclosed at the time of this survey, which might affect some responses.

5. Conclusion

The Bio-USER survey revealed that retinal communities in the United States and Europe are generally aware of biosimilars. Lower pricing is not the only factor for clinicians to consider in order to make a decision to switch to or use biosimilar as an initial therapy. Biosimilar ranibizumab and on-label bevacizumab could partially replace off-label bevacizumab as a treatment of choice for macular disease if approved and priced relatively low, but these alternative therapies still need robust real-world clinical data to bolster confidence in the safety and efficacy of these newer products. Off-label bevacizumab is valued much more in the United States compared to Europe. With the availability of two FDA and EMA ranibizumab biosimilars and a strong pipeline of biosimilars (ranibizumab and aflibercept) for the management of retinal diseases, this survey highlights the need for better and more comprehensive sources of information on these therapeutic alternatives specifically to mitigate the concerns on safety and efficacy of biosimilars among retina physicians in the United States and Europe.

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Declaration of interest

A Sharma is a consultant for Intas, Novartis, Bayer, Allergan and Lupin.

FG Holz reports research grants and personal fees from Acucel, Allergan, Apellis, Bayer, Bioeq/Formycon, Roche/Genentech, Geuder, Heidelberg Engineering, ivericBio, Pixium Vision, Novartis and Zeiss; and personal fees from Alexion, Grayburg Vision, LinBioscience, Stealth BioTherapeutics, Aerie and Oxurion.

CD Regillo is a consultant for Adverum, Allergan, Annexon, Bausch and Lomb, Clearside, Eyepoint, Genentech/Roche, Iveric, Novartis, Kodiak, Notal, Merck, Ocular therapeutics, Regenxbio, Stealth, Takeda, Zeiss and receives research support from Adverum, Allergan, Annexon, Eyepoint, Genentech/Roche, Novartis, Kodiak, Iveric, Regenxbio, Regeneron.

KB Freund is a consultant for Heidelberg Engineering, Zeiss, Genentech, Bayer, Novartis, and Allergan. He receives research support from Genentech/Roche.

David Sarraf is a consultant for Amgen, Bayer, Endogena Therapeutics, Genentech, Iveric Bio, Novartis, and Optovue/Visionix and receives research grants from Amgen, Boehringer, Genentech, Heidelberg, Optovue/Visionix, Regeneron, and Topcon.

AM Khanani is a consultant for Adverum, Aerpio, Alimera, Allergan, Apellis, Asclepix, Aviceda, Bausch, and Lomb, Broadwing Bio, Chengdu Kanghong, Cholgene, 4DMT, Dutch Ophthalmic Research Center, Gemini, Genentech, Glaukos, Graybug, Gyroscope, Iveric Bio, Janssen, Kato Pharma, Kodiak, Oculis, Opthea, Oxurion, Novartis, Pollphotonix, Recens Medical, Regeneron, Retrotope, Regenxbio, Roche, Surrozen, Thea, and Unity Bio. He has received research support from Adverum, Apellis, Asclepix, Chengdu Kanghong, 4DMT, Gemini, Genentech, Graybug Vision, Gyroscope, Iveric Bio, Kodiak, Neurotech, NGM Bio, Ocular Therapeutix, Oculis, Opthea, Oxurion, Novartis, Recens Medical, Regerxbio, Roche, and Unity Bio. He has received equity from Aviceda, Gyroscope, Recens Medical, Retrotope, and Pollphotonix and has acted as a speaker for Allergan, Genentech and Novartis.

C Baumal is a consultant for Genentech, Novartis, Ora, and Apellis and has been a speaker for Regeneron.

N Holekamp has received consulting fees from 4DMT. AGTC, Abbvie/Allergan, Annexon, Apellis, Bayer, Biogen, Boehringer, Cardinal, Clearside Biosciences, EyePoint Pharmaceuticals, Genentech, Gyroscope, Medpace, Medscape, Nacuity, NGM, Notal Vision, Novartis, Ocuphire, Outlook Therapeutics, Regeneron, Roche, Thea Laboratoires, Stealth Biosciences, Vial Speakers Bureau: Abbvie, Apellis, Genentech, Regeneron, Bausch and Lomb Contracted Research: Genentech, Gemini, Gyroscope, Notal Vision Data Monitoring and Safety Committee: Editas, Ocuphire, Roche Stock or Stock options: Apellis, Notal Vision Employee: Roche "Visiting Professor".

R Tadayoni is a consultant for AbbVie, Allergan, Alcon, Apellis, Bayer, Boehringer Ingelheim, Genentech, Iveric Bio, KHB, Novartis, Oculis, Roche, Thea, and Zeiss.

BD Kuppermann has conducted clinical research for Alcon, Alimera, Allegro, Allergan, Apellis, Clearside, Genentech, GSK, Ionis, jCyte, Novartis, Regeneron, and ThromboGenics. He is a consultant for Alimera, Allegro, Allergan, Cell Care, Dose, Eyedaptic, Galimedix, Genentech, Glaukos, Interface Biologics, jCyte, Novartis, Ophthotech, Regeneron, Revana, and Theravance Biopharma. He also acknowledges an unrestricted grant from Research to Prevent Blindness to the Gavin Herbert Eye Institute at the University of California, Irvine.

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Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Ethics

The survey did not require any medical record review or patient interaction therefore institutional review board approval was not required. Consent was obtained from participants after informing them about the purpose of the survey and how their responses would be used with the protection of confidential information.

Author contributions

A Sharma: conception, analysis, drafting, integrity check, final approval. FG Holz, CD Regillo, KB Freund, D Sarraf, AM Khanani, C Baumal, N Holekamp, R Tadayoni, N Kumar, N Parachuri, BD Kupperman: review, drafting, editing, revision, integrity check. Other Inter BIOS Group members: review.

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