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REPLY

WE WOULD LIKE TO REPLY TO THE ISSUES ADDRESSED BY Dan Călugăru and Mihai Călugăru.

In our study, 3 types of choroidal neovascularization (CNV) of neovascular age-related macular degeneration (AMD) were revealed: the occult, the predominantly classic, and the minimally classic. The classification was based on the results of Fundus Fluorescein Angiography (FFA). This classification has been adopted not only in the PHOENIX study, but also in the previous VIEW study (aflibercept vs ranibizumab),[1] MARINA study (ranibizumab vs sham),[2] and ANCHOR study (ranibizumab vs verteporfin).[3] Though there are now different ways to classify CNV according to optical coherence tomography, optical coherence tomography angiography, or indocyanine green (ICG) angiography, the way we used in the study was still the classic method as used in the previous anti-VEGF studies.

Considering the prevalence of polypoidal choroidal vasculopathy (PCV) in Chinese people, the PHOENIX study initially planned to exclude PCV patients by using ICG angiography examination, which was regarded as the gold standard for diagnosing PCV. However, the supply of ICG agents ran out in the year 2012 in China, which made it impossible to give patients ICG examinations. Without ICG, PCV could not be accurately diagnosed. In the end, pooling PCV may influence interpretation of the data, which we have already stated in the paper and analyzed in the discussion.

Best-corrected visual acuity (BCVA) was our main outcome measure. There is no statistical difference of BCVA between the 2 groups of patients at baseline, so it is for sure that the 2 groups are comparable.

We find several suggestions from the correspondence letter quite constructive and we really appreciate that. It should be noted that the main purpose of the present paper was to demonstrate the main results of the PHOENIX study. In the future, we would consider further analyzing the data, including the changes in the choroid and different layers of the retina.

Till now, other anti-VEGF agents cannot support this dosing regimen. Treatment using conbercept has the potential to be a more patient-friendly treatment than are existing treatments.

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CONFLICT OF INTEREST DISCLOSURES: SEE THE ORIGINAL article for any disclosures of the authors.

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Boston Type I Keratoprosthesis: Antibacterial Resistance and Microbiota Evaluation of Soft Contact Lenses

EDITOR:

WE READ WITH GREAT INTEREST THE ARTICLE BY TORRES-Netto and associates titled "Boston Type I Keratoprosthesis: Antibacterial Resistance and Microbiota Evaluation of Soft Contact Lenses."[1] Infections after Boston keratoprosthesis are devastating, and any evidence of an antibacterial resistance pattern in this field will be an essential addition to the existing literature.

However, we have some concerns. The authors concluded that "prophylaxis with topical 5% povidone-

iodine (PI) and low fluoroquinolone (FQ) dose might increase resistance to antibiotics," but we believe that it may not be appropriate to attribute the development of resistance against fourth-generation FQ to PI. PI was used just once every 4 weeks just before changing the contact lens. We wonder if this frequency could play any role in the development of resistance against a completely different class of drug that is fourth-generation FQ. Moreover, the authors themselves have mentioned in their discussion part that "Furthermore, so far there is no report of resistance induced by PI in ophthalmologic use.[2] Hence, this reinforces that the resistance induction in our series is most likely attributed to the daily use of antibiotic." The conclusion in the abstract looks contradictory to what has been discussed in the text.

The study included 31 samples from 19 eyes of 18 patients with Boston keratoprosthesis. This suggests that few of the samples were taken from the same patient's eye, although at different points of time. Local microorganism flora could play an essential role in the development of infection as well as colonization of the contact lenses used. Taking multiple samples from the same eye or patient, even at different points in time, could affect the study results. It would be interesting to know the microorganism and resistance pattern without the inclusion of multiple samples from a single patient.

Finally, in addition to the relatively smaller sample size for making any conclusive statement, the study included 3 different groups of patients: multiple graft failure in 9 patients (50%), chemical burn in 8 patients (44.4%), and Stevens–Johnson syndrome in 1 patient (5.6%). The 3 groups differ significantly in their pathogenesis as well the chronic changes produced in the eye, which again could have an impact on colonization of contact lenses and the development of antibiotic resistance. It would be interesting to see if there were any differences in the antibacterial resistance and microbiota patterns between these 3 groups.

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REPLY

WE READ WITH INTEREST THE COMMENTS ABOUT OUR article by Sahay and associates.[1] We agree with the authors that it is not appropriate to attribute the development of antibiotic resistance to povidone-iodine (PI). While we understand the authors' concern, their interpretation must be analyzed with discretion. Even though in the discussion of our article it is clear that resistance was probably attributed to fourth-generation fluoroquinolone, it is necessary to disclose that all patients used a prophylactic regimen that not only included antibiotic therapy, but also PI. As the authors have noted, we have already said that there is no report of resistance induced by PI in ophthalmologic use.[2]

The ocular flora undoubtedly could have had a role in corneal infection. However, our study did not aim to analyze the flora of a specific patient in a single time point, but to investigate the antibacterial resistance under a given chronic prophylactic scheme.[3] Moreover, sampling the same patient at different time points may potentially confirm resistance in a given eye and also allow genotypic investigation to characterize microbial resistance development.

We are aware that the natural flora could differ depending on the preoperative diagnosis. Nonetheless, because contact lenses were only used during the postoperative period, microbiologic investigations on contact lenses were not possible before Boston type I Keratoprosthesis implantation. In addition, soon after the surgery all eyes were placed on the same prophylactic regimen, and therefore one could assume that the flora was no longer virgin and that this would not interfere in the proposed analysis. Antibacterial resistance and microbiota pattern in patients with different preoperative diagnoses can be checked in the table in our article. Although resistance to fourth-generation fluoroquinolone was identified in 6 different eyes, we do not believe that an analysis between groups would add relevant information given our sample size. Ideally, multicenter studies with larger samples may bring about more conclusive knowledge. We reinforce that recognizing the pattern of resistance to antibiotics is critical to outline future changes of prophylactic guidelines and therapeutic strategies.

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