and retinal vascular occlusion associated with brolucizumab and was concerned enough to perform a post hoc review of the data from the HAWK and HARRIER trials regarding these relevant adverse events. Novartis is to be commended for providing all the data to review. The SRC report is only available to ASRS members, but the results were emailed to members of our specialty societies, so we will take this opportunity to discuss these recent findings (Table 1).

The SRC found that the observed incidences of both retinal vasculitis and retinal vascular occlusion in these trials were higher than reported previously in the HAWK and HARRIER trials. These data, and the discrepancy from the previously released results, in addition to the cases arising from the community use of brolucizumab, raise red flags.

In response to our call for a moratorium, Kayath and Sauer[1] recommend that physicians carefully monitor each patient for evidence of inflammation and respond according to the current recommendations set forth by the revised package insert and the ASRS. But once inflammation develops, it is too late. While they state that "brolucizumab represents an important treatment option for patients with neovascular age-related macular degeneration," we believe that the benefits of brolucizumab are not worth the risks compared with similarly effective therapies that do not have the same risk of an occlusive vasculitis. Novartis suggests that physicians follow the advice from the ASRS, but the most recent SRC report from June 4th made no recommendations other than to monitor patients.

While brolucizumab had a greater rate of inflammation, vasculitis, and occlusion, Novartis argues that the overall rates of vision loss (≥15 Early Treatment of Diabetic Retinopathy Study letters) in the studies were comparable between brolucizumab (81/1088; 7.4%) and aflibercept (56/729; 7.7%). However, this comparison is flawed. Patients with neovascular age-related macular degeneration lose vision even when managed properly, so the most meaningful comparison is not based on the total study population but based on the risk of vision loss from the drug and not from the natural history of disease progression after anti–vascular endothelial growth factor injections. The denominators for these comparisons should not include all of the patients in the study but instead should include only those patients who develop inflammation and related complications because of our choice of drugs. Of the 23 patients who developed inflammation, vasculitis, and vascular occlusion from brolucizumab, 7 eyes (30.4%) lost ≥15 Early Treatment of Diabetic Retinopathy Study letters compared with the 1 eye treated with aflibercept that had probable, not definite, inflammation, vasculitis, and occlusion resulting in lost vision.

While we encourage continued vigilance on the part of Novartis and the retinal community in reporting and investigating the causes of inflammation, vasculitis, and occlusion caused by brolucizumab, we reiterate our recommendation that a moratorium be imposed on the use of brolucizumab until the cause is discovered for these inflammatory side effects and until remedies are devised. It comes down to a simple question for Novartis and the vitreoretinal community: how many more patients need to lose vision before this moratorium is implemented?

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TABLE 1. Risk of Intraocular Inflammation, Retinal Vasculitis, Vascular Occlusion, and Vision Loss in the HAWK and HARRIER Trials

Condition	Brolucizumab	Aflibercept
Sample size, N	1088	729
IOI ± vasculitis ± vascular occlusion, n (%)	50 (4.6)	8 (1.1)
IOI + retinal vasculitis, n (%)	36 (3.3)	0
IOI + retinal vasculitis + vascular occlusion, n (%)	23 (2.1)	1 (0.1)
ETDRS letters lost, n (%)		
≥15	8 (0.7)	1 (0.1)
≥30	5 (0.5)	Not given

ETDRS = Early Treatment of Diabetic Retinopathy Study; IOI = intraocular inflammation.

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Comment on: Posterior Capsule Opacification With Two Hydrophobic Acrylic Intraocular Lenses: 3-Year Results of a Randomized Trial

EDITOR:

WE READ WITH GREAT INTEREST THE ARTICLE BY LEYDOLT and associates, which set out to compare the incidence

TABLE. Summary of Evidence on Nd:YAG Capsulotomy Rates

No.	Evidence Source	Type of Evidence	Key Results
1	Ursell et al. 5 year incidence of YAG capsulotomy and PCO after cataract surgery with single-piece monofocal intraocular lenses: a real-world evidence study of 20,763 eyes. *Eye* 2020; 34:960-968.	Real-world evidence study, UK	The 3-year incidence of Nd:YAG capsulotomy was: Alcon AcrySof (2.4%), J&J Tecnis (5.1%), B&L Akreos (9.2%), Lenstec Softec (12.3%), and Rayner Flex (12.6%) The 5-year incidence of Nd:YAG capsulotomy was: Alcon AcrySof (5.8%, J&J Tecnis (8.5%), B&L Akreos (15.2%), and Lenstec Softec (19.3%).
2	Horn et al. Incidence of YAG Due to PCO Following IOL Implantation: An Analysis of AAO IRIS Registry. Poster presented at 2019 American Academy of Ophthalmology (AAO) Conference, San Francisco, California, USA.	Real-world evidence study, USA	At 12 months, monofocal YAG rates, AcrySof 3.7% vs Tecnis 7.8% ($P < .0001$).
3	Lindholm et al. Five-year cumulative incidence and risk factors of Nd:YAG capsulotomy in 10,044 hydrophobic acrylic 1-piece and 3-piece IOLs. *Am J Ophthalmol* 2019; 200:218-223.	Real-world evidence study, Finland	5-year cumulative incidence of Nd:YAG capsulotomy was 11.5% (95% CI 10.5%–12.6%) for SN60WF and 18.1% (16.5%–20.0%) for ZCB00. AcrySof SN60WF were associated with a 38% reduction in Nd:YAG compared to Tecnis ZCB00 after accounting for other predictors ($P < .001$).
4	Thom et al. Effect of AcrySof versus other intraocular lens properties on the risk of Nd:YAG capsulotomy after cataract surgery: A systematic literature review and network meta-analysis. *PLoS One* 2019; 14:e0220498.	Systematic review and meta-analyses of published RCTs	Risk of Nd:YAG capsulotomy is lower in eyes implanted with AcrySof IOLs compared to non-AcrySof hydrophobic or hydrophilic acrylic IOLs.
5	Belda et al. Incidence of Nd:YAG capsulotomy after cataract surgery with AcrySof vs. non-AcrySof acrylic monofocal IOLs: real-world evidence from Spain. Abstract submitted to ESCRS.	Real-world evidence study, Spain	3 years post surgery, Nd:YAG incidence was significantly lower for AcrySof IOLs compared to the other models.

IOL = intraocular lens; RCTs = randomized clinical trials.

and intensity of posterior capsule opacification (PCO) and Nd:YAG capsulotomy rates between Vivinex XY1 and AcrySof SN60WF intraocular lens (IOL).[1] To our understanding, this is a first long-term evidence on the new Vivinex IOL. While reduction of PCO is a worthwhile endeavor that will improve the quality of visual function in the long term and reduce costs, we want to express our concerns in relation to the data representation and its interpretation.

The first aspect of concern is the assessment of PCO, which was measured on a scale of 0-10, where 0 stands for a "clear" capsule and 10 for exceptionally severe PCO. The AQUA scores that emerged and, as the authors concluded, were "generally low," were 0.9 for Vivinex and 1.4 for AcrySof. We contend that these scores not only were "generally low" but were of no real clinical significance, as such low scores are not viewed as being associated with decreased visual function.[2] We feel this did not receive due consideration or explanation in the article. We are concerned by the presentation of differences in Nd:YAG capsulotomy rates between 2 IOL groups as a major finding, when these results were clearly nonsignificant ($P = .73$ before and $P = .23$ after the 3-year follow-up). Of note, neither differences in BCVA nor with respect to any of the subjective optical symptoms were found. Furthermore, it would have been justified to assess the eyes that underwent Nd:YAG capsulotomy for intensity of PCO, as not doing so may have resulted in a misrepresentation of the true AQUA score and thus the overall picture.[2]

The very high PCO levels in the study may not be reflective of the real world. The literature for AcrySof demonstrates consistently low Nd:YAG rates both in randomized controlled trials and in large registry-based studies, which offer an insight into real-world clinical practice.[3] For example, Ursell and associates[4] (n = 52,162) showed that 3-year incidence of Nd:YAG capsulotomy was lowest for the AcrySof lens at 2.4% (Table), While similar conclusions on the AcrySof platform were drawn in a further large cohort study in Finland[5] (n =10,044) (Table).

In Leydolt and associates' description of PCO in the introduction of their paper, PCO is characterized as being associated with decreased visual function. However, the resulting PCO scores and analysis that follow, the reasons for which are aforementioned, should not be viewed in this context. We believe that these considerations should have received further treatment in this article, which, in our view, would lead to furnishing the reader with a better understanding of the results presented.

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Reply to Comment on: Posterior Capsule Opacification With Two Hydrophobic Acrylic Intraocular Lenses: 3-Year Results of a Randomized Trial

WE READ WITH GREAT INTEREST THE COMMENT ON OUR study "Posterior capsule opacification with two hydrophobic acrylic intraocular lenses: 3-Year results of a randomized trial." Although puzzled about some inconsistencies of the authors' statements (generally low posterior capsule opacification [PCO] rates with no real clinical significance, but then stated very high PCO levels), we can hereby dispel the authors' concerns.

This is a randomized controlled trial (RCT) study that assessed not a "real-world clinical significance" but a scientific statistical significance of the main outcome of the study—that is, posterior capsule opacification. Although the intensity of PCO indeed correlates well with visual acuity and contrast sensitivity,[1] this study aimed at evaluating morphologic-anatomic differences between the 2 intraocular lens (IOL) implants compared—which is PCO, with functional tests like visual acuity included only as a subordinate secondary outcome.

RCTs are the "gold standard" of evidence-based medicine and are superior to retrospective data evaluation of, for example, electronic medical record data, minimizing selection bias and confounding. It is also very interesting that the authors stated that they were concerned about the presentation of differences in Nd:YAG capsulotomy rates between 2 IOL groups as a major finding, considering that these were clearly nonsignificant. First, Nd:YAG capsulotomy rates were not the main outcome of this study (unlike the objective PCO rate); and second, this would implicate that nonsignificant data are not worth being published. In fact, this would support what has been proven in the past: that studies showing statistically significant differences in the results are more likely to be published than those not arriving at such differences between study groups—a fact that is well known in the scientific world and termed "publication bias."[2]

The assessment of PCO is a well-validated method described in many studies in the literature.[3] The Acrysof IOL has shown very consistent and comparable AQUA scores assessing long-term PCO and Nd:YAG capsulotomy rates in the past: PCO 1.4 ± 1.1, YAG 18.6% in this study, compared to 0.9 ± 1.3, 21.7%[4]; 1.9 ± 1.4, 13.7%[5]; and 1.7 ± 1.7, 16%.[6]

As mentioned above, Nd:YAG capsulotomy rates were a secondary outcome in this study and data were provided as