

News in Review

COMMENTARY AND PERSPECTIVE

RETINA

Five Years of Anti-VEGF for RVO Offers VA Gains

LONG-TERM MONITORING AND

treatment with anti-VEGF therapy improves vision in patients with retinal vein occlusion (RVO), researchers have confirmed.¹ The results, from the SCORE2 study, indicate that anti-VEGF therapy was associated with a significant improvement in visual acuity (VA) for up to five years in patients with macular edema due to central retinal or hemiretinal vein occlusion (CRVO; HRVO).

“Prior to this study, retinal vein occlusion was considered to be an acute illness. However, our findings suggest that macular edema associated with RVO is a chronic disease that warrants continued monitoring and individualized treatment to optimize visual outcomes of anti-VEGF therapy,” said Ingrid Scott, MD, MPH, at Penn State College of Medicine in Hershey, Pennsylvania. Dr. Scott is the principal investigator and chair of SCORE2 (Study of Comparative Treatments for Retinal Vein Occlusion 2).

Study overview. In 2017, the SCORE2 investigators published results indicating that bevacizumab (Avastin) and aflibercept (Eylea) provide similar benefits in terms of VA at six months in patients with macular edema associated with CRVO or HRVO.²

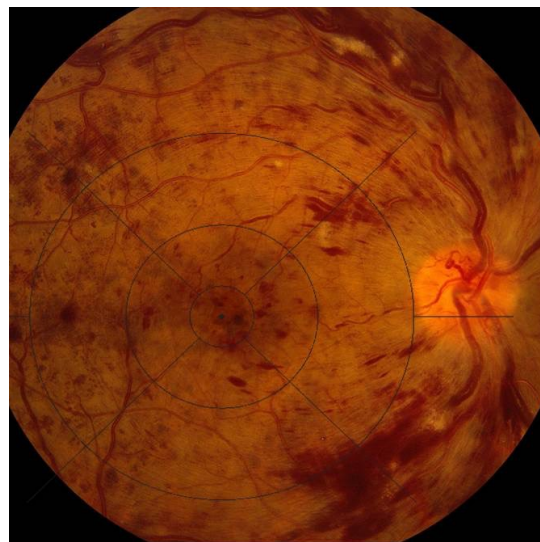
Initially, 362 eyes were enrolled,

with 180 study eyes receiving aflibercept and 182 receiving bevacizumab. Of these, 330 eyes were followed through month 12 and eligible to be enrolled in the long-term analysis.¹ At this point, participants were treated per investigator discretion, using any commercially available drug (including nonstudy anti-VEGF or no drug). In addition, after the initial year, participants were evaluated annually for VA letter score and central subfield thickness (CST) for four years.

Five-year outcomes. Overall mean improvement in VA letter score from baseline among patients completing the month 60 visit was 13.5 (95% confidence interval [CI], 9.6-17.5), with no significant differences between patients initially treated with bevacizumab and those initially treated with aflibercept. The five-year improvement in letter score was lower than the mean improvement observed at month 12 (20.6; 95% CI, 18.7-22.4). CST also improved, from a mean of 671 μm at baseline to 261 μm at month 60.

However, as Dr. Scott noted, only 45% of eligible participants completed the month 60 visit. “One of the biggest challenges in conducting long-term studies is participant retention.”

An unexpected finding. “Interestingly, only 24% of patients had complete resolution of macular edema at month 60,” Dr. Scott said. More than 65% of completers received at least one anti-



CRVO. This image of a SCORE2 participant with CRVO shows extensive retinal hemorrhage and dilated retinal veins.

VEGF injection between months 48 and 60, with a mean of 3.41 treatments received during this 12-month period, she added. “These findings suggest that monitoring and individualized treatment with anti-VEGF therapy are warranted to optimize visual outcomes in patients with macular edema associated with CRVO or HRVO.”

Dr. Scott also noted that the fact that treatment was per investigator discretion after month 12 resulted in considerable heterogeneity with respect to treatment regimens. “This limited our ability to make comparisons between originally assigned treatment arms but provides useful information about real-world clinical practice and outcomes.”

Next steps. Future plans include detailed imaging studies to investigate for imaging biomarkers associated with visual and anatomic outcomes in patients treated with anti-VEGF therapy, Dr. Scott said. The investigators also are planning genetic analyses to identify genetic markers of response to treatment.

—Christos Evangelou, PhD

1 Scott IU et al., for the SCORE2 Investigator Group. *Am J Ophthalmol.* 2022;240:330-341.

2 Scott IU et al., for the SCORE2 Investigator Group. *JAMA.* 2017;317(20):2072-2087.

Relevant financial disclosures: Dr Scott—NEI: S.

COMPREHENSIVE

Vitamin D and Ocular Diseases

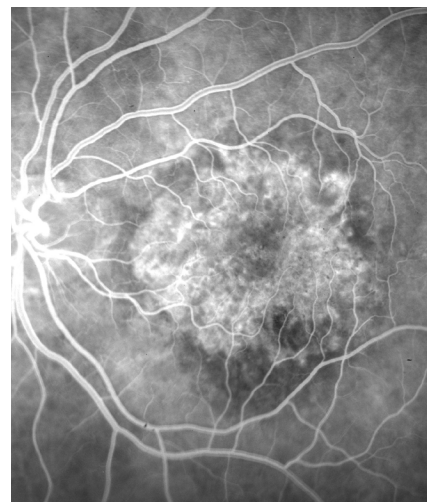
IN AN EFFORT TO PROVIDE A COMPREHENSIVE analysis of the effect of vitamin D on eye health, researchers in Hong Kong set out to conduct a systematic review of the topic. Although some studies were hampered by significant limitations, they found evidence of an association between vitamin D and age-related macular degeneration (AMD), diabetic retinopathy (DR), and dry eye syndrome (DES).¹

Study rationale. “Because vitamin D participates in a wide variety of actions [in the body], it is important for main-

taining our [overall] health,” said Jason C. Yam, MD, at the Chinese University of Hong Kong. “We hypothesized that vitamin D is important for ocular health.” Indeed, a number of recently published studies have investigated the relationship between serum vitamin D levels and ocular disease.

Findings and limitations. Dr. Yam and his coauthors searched two databases and found 162 published studies eligible for their review. Of 27 studies on AMD, 17 reported an association with vitamin D. In addition, 48 of 54 studies reported a link with DR, and 25 of 27 studies reported an association with DES. The available evidence for an association with other ocular disease is limited.

However, as Dr. Yam noted, “Currently, there is not any standardized protocol for conducting vitamin D research” in ophthalmology. For instance, different studies had different cut-off levels for vitamin D deficiency and



IMPACT ON AMD. Although evidence from cross-sectional studies suggests that vitamin D may protect against AMD development, this effect is small or may only apply to specific populations.

insufficiency. Given the varying analysis methods used, as well as the inconsistent findings for some ocular diseases,

TELEMEDICINE

At-Home VA Testing Comparable to In-Office Version

RESEARCHERS AT THE CASEY EYE INSTITUTE AT OREGON Health and Science University (OHSU) in Portland have validated three at-home visual acuity (VA) tests. Their findings suggest that these home VA tests are comparable within 1 line to a standard in-office version.¹

Prompted by the pandemic. “Our collective experiences with telehealth during the COVID-19 pandemic highlighted the benefits and challenges of providing ophthalmology care through virtual visits,” said coauthors Kellyn N. Bellsmith, MD, and Merina Thomas, MD.

The unprecedented surge in demand for telehealth services heightened the need for reliable at-home VA tests. Hence, the OHSU team set out to evaluate the validity of three no-cost, at-home tests: a printed chart (University of Arizona/Banner Eye Health Chart), a mobile app (Verana Vision Test), and a website (www.Farsight.care).

Study design. Eligible participants with VA of 20/200 or better were recruited from July 2020 to April 2021. Participants with internet or mobile device access were randomized to receive two of the three at-home tests to form the randomized cohort, while those without access were assigned to a mail-only cohort.

At-home VA tests were completed within three

days before a clinic visit, at which the best-corrected distance VA was measured as the reference standard.

Results. A total of 121 participants (mean age, 63.8 years) completed the study. The mean in-office VA was 0.11 logMAR (Snellen equivalent 20/25). Mean difference (logMAR) between the at-home test and in-office acuity was -0.07 (95% confidence interval [CI], -0.10 to -0.04) for the printed chart, -0.12 (95% CI, -0.15 to -0.09) for the mobile app, and -0.13 (95% CI, -0.16 to -0.10) for the website.

Key finding. The analysis of the comparison data found all three at-home VA tests valid within 1 line of in-office results. “It was interesting that the printed chart had the smallest mean difference and greatest correlation compared with the in-office acuity measurement, although there was no statistically significant difference among the three tests,” Dr. Bellsmith said.

A new normal? At-home VA testing provides important data that can help providers with clinical decision making between in-person clinic visits, Dr. Bellsmith noted. And in looking to the future, Dr. Thomas said that ophthalmology “is very reliant on the physical exam, but the ability to have different care options will allow clinicians to provide care to a larger and more diverse population.”

—Patricia Weiser, PharmD

1 Bellsmith KN et al. *JAMA Ophthalmol.* 2022;140(5):465-471.

Relevant financial disclosures—Drs. Bellsmith and Thomas: NIH: S; Research to Prevent Blindness: S.

“it is difficult for us to draw a conclusion on whether vitamin D has a role in some ocular diseases,” Dr. Yam said.

Need for standardization. In the future, researchers will need to carefully consider different potential confounders such as sunlight intensity and duration of exposure, Dr. Yam noted. Thus, “before conducting more studies, we may need a standard protocol and questionnaire for collecting the data and accounting for confounding factors.”

—Jean Shaw

1 Chan H-N et al. *Int J Mol Sci.* 2022;23:4226.
Relevant financial disclosures: Dr. Yam—None.

OCULAR ONCOLOGY

Differentiating Neoplasia from Metaplasia in OSSN

OCULAR SURFACE SQUAMOUS NEOPLASIA (OSSN) is a common ocular malignancy with variable clinical features and a challenging diagnosis. High-resolution OCT (HR-OCT) can overcome many of the limitations of traditional biopsy for OSSN diagnosis. However, accumulating evidence suggests that HR-OCT has low specificity for differentiating dysplasia (e.g., OSSN) from metaplasia, which may lead to unnecessary treatment of patients with non-neoplastic lesions.

Researchers from Bascom Palmer in Miami recently compared the HR-OCT findings between OSSN and corneal squamous metaplasia. They found significant overlap in HR-OCT findings and clinical characteristics between OSSN and metaplasia.¹

“Many clinicians use HR-OCT to diagnose ocular cancer and make clinical decisions. Our findings, however, show that the inability of HR-OCT to provide information at the cellular level makes this technology incapable of distinguishing OSSN from corneal squamous metaplasia,” said coauthor Anat Galor, MD, MSPH.

Moreover, she said, the study’s results suggest that “in patients with lesions

showing some HR-OCT findings suggestive of OSSN, clinicians should also consider squamous metaplasia, especially when patients do not respond to the treatment.”

She warned that, in some cases, biopsy may be needed to confirm or rule out a diagnosis.

Addressing a clinical gap. “We see many patients with ocular surface abnormalities, only some of which are malignant,” said Dr. Galor. HR-OCT findings in OSSN include thickened epithelium, hyperreflectivity, and abrupt transition between normal and abnormal epithelium.¹ “Anterior segment HR-OCT allows us to observe corneal lesions cross-sectionally and determine whether the lesion is malignant. However, we had instances where a biopsy of lesions with HR-OCT findings suggestive of OSSN showed that the lesions were, in fact, metaplasia,” Dr. Galor said.

Overlapping HR-OCT findings. For this study, the Bascom Palmer team compared HR-OCT findings between patients with histologically proven corneal OSSN and metaplasia (n = 4 per group), and they found that HR-OCT could not differentiate OSSN from metaplasia.

Dr. Galor suggested that the similarities in the histological characteristics of OSSN and metaplasia may contribute to the overlap in HR-OCT findings. “The histological features of both lesion types include epithelial thickening, keratinization, and loss of goblet cells.

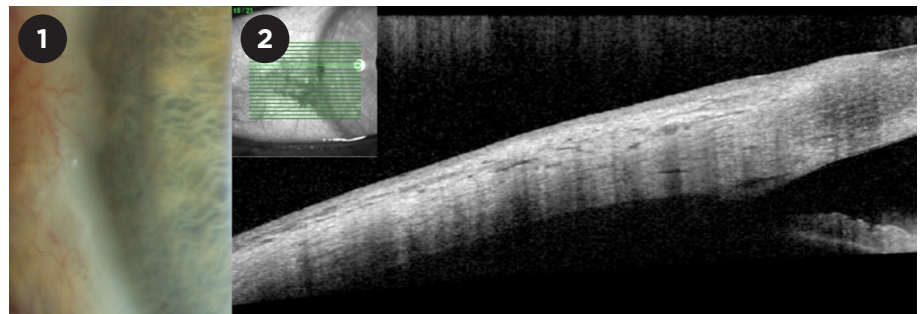
Because of its resolution, HR-OCT cannot detect mitotic figures and other histological features unique to OSSN.”

How clinical clues may help. Although all lesions were opalescent and localized at the limbus, metaplastic lesions had smoother and more rounded borders than did OSSN. Additionally, OSSN was more common in fair-skinned individuals, while metaplasia was seen in pigmented individuals. “Combining imaging findings with clinical and demographic clues may better differentiate between the two conditions than imaging alone,” Dr. Galor noted.

Outlook. “We’re always looking for ways to improve the diagnosis of ocular surface lesions. We are trying to optimize the use of HR-OCT to diagnose different types of ocular surface lesions, such as nevi and melanoma, as each of these conditions prompts a different therapeutic algorithm,” Dr. Galor concluded.

Overall, she said, patients with OSSN should be treated to prevent tumor progression. In contrast, those with nonneoplastic lesions can receive monitoring alone. Incisional biopsy, the gold standard for OSSN diagnosis, is invasive and may have long turnaround times, leading to potential treatment delays. —Christos Evangelou, PhD

1 Stevens SM et al. *Cornea.* 2022. Published online April 9, 2022.
Relevant financial disclosures: Dr Galor—None.



COLLECTING CLUES. Representative (1) slit-lamp photograph and (2) HR-OCT image of an eye with an ocular surface lesion. As neoplastic ocular surface lesions may exhibit characteristics similar to those seen with their nonneoplastic counterparts, combining imaging findings with clinicopathological clues may help clinicians differentiate between different types of lesions.

See the financial disclosure key, page 8. For full disclosures, including category descriptions, view this News in Review at aao.org/eyenet.