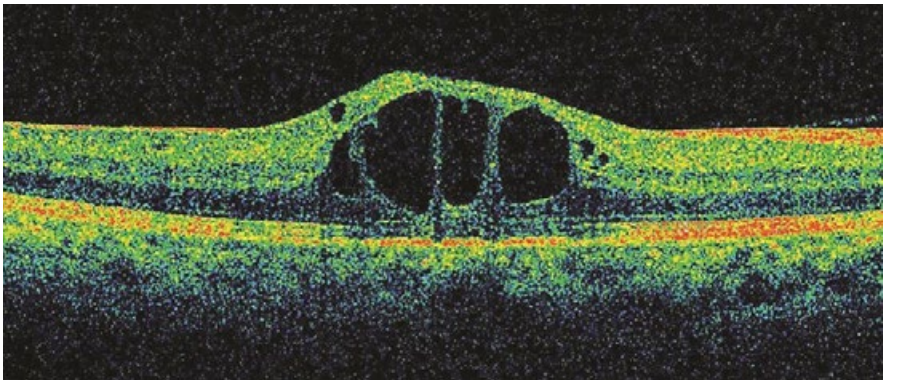
News in Review

COMMENTARY AND PERSPECTIVE



NEW OPTION. *In January, the FDA approved faricimab for treatment of DME (shown here) and neovascular age-related macular degeneration.*

RETINA

Faricimab Effective for DME

IN TWO PHASE 3 CLINICAL TRIALS OF patients with diabetic macular edema (DME), faricimab (Vabysmo, Genentech) achieved robust vision gains, anatomical improvements, and sustained effect with variable dosing periods ranging up to 16 weeks at the one-year mark.[1]

The durability of treatment effect, not previously reported in a phase 3 DME trial, demonstrates faricimab's potential to reduce the treatment burden that accompanies intravitreal anti-VEGF treatment.

A novel approach. Faricimab is a bispecific monoclonal antibody. It targets two disease pathways, angiopoietin-2 (Ang-2) and VEGF-A, that synergistically drive vascular leakage and inflammation in DME. The FDA approved faricimab for DME earlier this year based on the one-year phase 3 results, which support the hypothesis that inhibiting Ang-2–mediated leakage and inflammation promotes vascular stability beyond anti-VEGF monotherapy.[1] (Faricimab also was approved for wet age-related macular degeneration based on results of two other trials.)

The drug's approval for DME is significant because it offers patients "a new class of medicine that inhibits two disease pathways linked to vision loss and can improve their vision as well as the current standards of care, with potentially fewer injections over time," said Charles C. Wykoff, MD, PhD, at Retina Consultants of Texas in Houston.

Dr. Wykoff added, "patients with faricimab given at intervals of up to four months achieved noninferior vision gains versus aflibercept given every two months in the first year." These results held through the second year, with increasing proportions of patients treated via extended dosing, he said.

A tale of two trials. To demonstrate consistency and reproducibility in outcomes, researchers simultaneously conducted two trials at 353 sites worldwide. The studies—YOSEMITE (n = 940) and RHINE (n = 951)—had identical protocols and patient characteristics, with a screening period of up to 28 days, a 96-week treatment period, and a final visit at 100 weeks. Monitoring occurred every four weeks from day 1 to study end.

Patients' mean age was 61.6 years, and their mean best-corrected visual acuity was 61.9-62.5 ETDRS letters. In YOSEMITE, their mean central subfield thickness was 485-492 µm, versus 466-477 µm in RHINE. Most were treatment-naive, as only 20% to 24% previously received anti-VEGF.

Fixed or adjustable dosing? Patients were randomly assigned to one of three dosing groups:

- faricimab 6 mg every eight weeks, following initial treatment with six monthly loading doses;
- faricimab 6 mg, determined by a personalized treatment interval (PTI) algorithm, following initial treatment with four monthly loading doses; or
- aflibercept 2 mg at fixed eight-week intervals, following five monthly loading doses.

Of note, patients in the PTI cohort were managed via a treat-and-extend approach. After the initial loading doses, they received faricimab every four, eight, 12, or 16 weeks based on treatment response. In addition, all participants attended study visits every four weeks and received sham injections during nonactive dosing visits.

Durability of treatment effect. Primary one-year data from both trials demonstrated that faricimab every eight weeks and faricimab PTI offered noninferior vision gains when compared to aflibercept every eight weeks. In addition, faricimab led to improved anatomical outcomes.

With regard to central subfield thickness (CST), in YOSEMITE, the adjusted mean CST change from baseline was –206.6 µm in those who received faricimab every eight weeks and –196.5 µm in the faricimab PTI

group, versus –170.3 µm in those who received aflibercept. In RHINE, these CST outcomes were –195.8 µm for faricimab eight weeks, –187.6 µm for faricimab PTI, and –170.1 µm for aflibercept. Moreover, a higher proportion of faricimab-treated patients achieved absence of retinal fluid, and a large proportion of patients treated with faricimab PTI advanced to dosing every 12 or 16 weeks at one year (71% to 74%). This proportion increased to 78% at the end of year 2.

Faricimab was generally well tolerated, and ocular inflammation events were low across both trials.

—Miriam Karmel

1 Wykoff CC et al. *The Lancet.* 2022;399(10326):741-755.

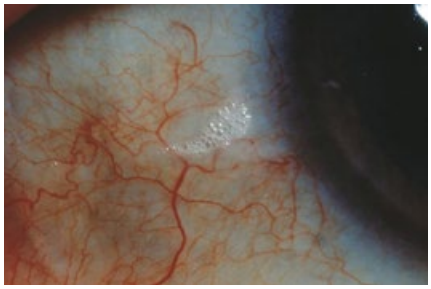
Relevant financial disclosures—Dr. Wykoff: Genentech: C,S; Regeneron: C,S; Roche: C,S.

COMPREHENSIVE

Beware Vitamin A Deficiency

IN A CASE OF A BLINDING CONDITION masquerading as glaucoma,[1] a 35-year-old Haitian woman with rapidly failing vision on four glaucoma medications traveled to the United States for consultation and surgery. Although the OR was already booked, the consulting ophthalmologist quickly suspected a different diagnosis. "I was certain that it was not glaucoma," said Richard D. Ten Hulzen, MD, at Mayo Clinic Florida in Jacksonville.

Dr. Ten Hulzen ruled out cancer, retinitis pigmentosa, retinal dystrophies, and inherited retinal disease. After consulting with a retina specialist, he settled on vitamin A deficiency



CLASSIC SIGN. *Foamy Bitot spots are tell-tale signs of vitamin A deficiency.*

(VAD) as the likely cause of the patient's visual loss, even though he had never seen an actual case. VAD occurs most frequently in developing countries. In the United States, its prevalence is under 1%.

Clinical diagnosis. The patient's serum vitamin A levels were within normal limits, as is often the case with VAD, thus requiring clinical diagno-

CATARACT

Novel Simulator Enables Multifocal IOL Testing Before Surgery

IN AN EFFORT TO IMPROVE SATISFACTION RATES IN patients who receive multifocal IOLs, researchers in Korea have developed an IOL simulator to assess the performance of the IOLs before surgery actually occurs.[1]

"Our device successfully simulated how the world appears to patients with multifocal IOLs," said Ho Sik Hwang, MD, PhD, at the Catholic University of Korea in Seoul. "By allowing patients to try different lenses before surgery, the simulator may help ophthalmologists select the appropriate multifocal IOL for their patients and improve patient satisfaction after cataract surgery."

A wearable mobile option. The IOL simulator consists of a bi-concave lens, a commercially available IOL, a lens tube, a spacer, and a wet cell. The device is mounted on a trial lens frame through an adapter. Dr. Hwang explained that this setup allows the trial lens frame containing the IOL simulator to be worn like glasses. "Because the device is mobile and a concave lens was used instead of a convex lens, the field view vertically and horizontally remained unaltered. Consequently, patients wearing the trial lens frame can walk around and experience their surroundings in real time through the IOL simulator," he said.

Study specifics. To evaluate the performance of the simulator, the researchers assessed patient satisfaction with near and distance vision, halos, defocus curve, and near point accommodation in 20 participants between 50 and 70 years of age (median, 61 years). Two IOLs were used: a Tecnis monofocal and a Tecnis bifocal (Johnson & Johnson); neither the examiner nor the patient was informed about which IOL was used during the testing.

Study results. The defocus curve, halo around the light, and satisfaction with near and distance vision in patients wearing the IOL simulator were similar to those in patients who underwent multifocal IOL implantation in published studies, Dr. Hwang said.

However, in this study, patients who tested the multifocal IOLs were less satisfied than those who tried the monofocal IOLs with distance vision (5.0 vs. 10.0; $p < .001$) and experienced more halos around the light (9.0 vs. 1.3; $p < .001$). In contrast, multifocal IOLs provided significantly shorter near point accommodation (24.0 vs. 44.5; $p < .001$) and higher satisfaction with near vision (7.6 vs. 2.4; $p < .001$) than did the monofocal IOLs.

Looking ahead. Dr. Hwang noted that further testing of the IOL simulator will be necessary. "We also plan to further improve the device to make it easier to wear and to better seal the wet cell," he added. With regard to the last point, he explained that because the sealing of the wet cell is imperfect, the saline in the wet cell evaporates and needs to be replaced every three to four hours.

—Christos Evangelou, PhD

1 Na K-S et al. *Transl Vis Sci Technol.* 2022;11(3):14.

Relevant financial disclosures—Dr. Hwang: Catholic University of Korea: P; Ministry of Education, Republic of Korea: S.

sis, Dr. Ten Hulzen explained. Here, the findings suggesting VAD included progressive visual field loss over an 18-month period, dry eye, nyctalopia, and ocular surface keratinization. OCT imaging and slit-lamp examination revealed an absence of optic neuropathy and features of secondary glaucoma in both eyes. Her angles were open, and her IOP was normal after 24 hours off glaucoma medications.

Rx: a fast-acting, affordable treatment. As vitamin A supplementation is known to reverse dry eye symptoms and rapidly restore severe peripheral vision loss, the patient received a loading dose of 200,000 IU per day for two days, followed by a maintenance dosage of 8,000 IU per day. The treatment plan also included stopping all glaucoma medications and use of artificial tears.

The patient's symptoms significantly improved within 11 days, and she returned to Haiti. By 5½ months, her visual fields had returned to normal, her visual acuity was 20/20 in both eyes, and her IOP was 15 mm Hg in her right eye and 16 mm Hg in her left. Color vision also was preserved.

"We were surprised at how rapidly her dry eye symptoms and visual fields improved following a course of vitamin A supplementation," said Dr. Ten Hulzen. He noted the irony that the patient, a nurse, had spent 80% of her income on glaucoma medications, when the remedy was a supplement that costs under $10 for a 100-day supply. *—Miriam Karmel*

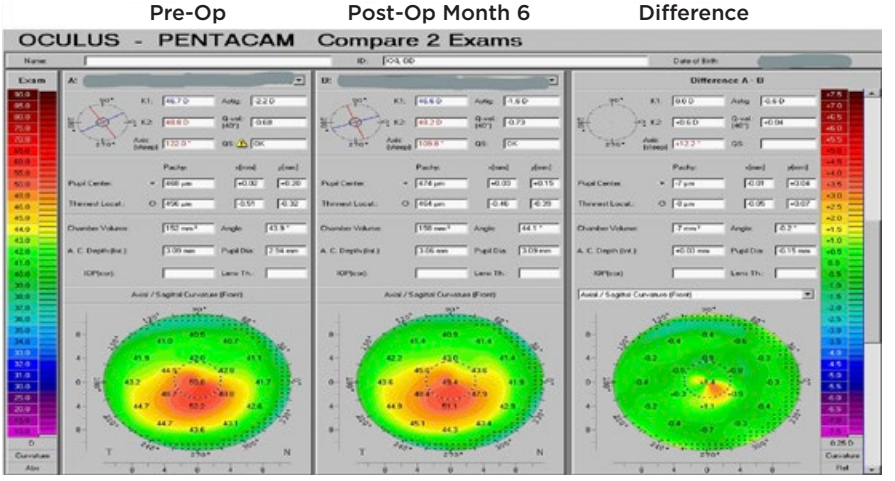
1 Ten Hulzen RD et al. *Am J Ophthalmol.* 2022; 26:101471.

Relevant financial disclosures—Dr. Ten Hulzen: None.

CORNEA

More Support for CXL in Young Keratoconus Patients

RESEARCH FROM STANFORD UNIVER- sity confirms that corneal cross-linking (CXL) stabilizes and may improve visual and corneal parameters in children and young adults with keratoconus. This new evidence adds to that from previous studies supporting CXL as a safe, well-tolerated intervention in these younger patients with keratoconus.[1]



CXL RESULTS. *In this Pentacam set, the pre-op, post-op, and difference map images show the flattening that occurs following CXL.*

Reassuring outcomes in kids. Keratoconus typically starts at puberty but may also occur in younger children. "We were curious to see how well CXL worked in a cohort of young patients with keratoconus," said study coauthor Edward E. Manche, MD. He added, "We were expecting to have similar results to previously published studies. Our results confirmed that the technique is safe and effective in this group of patients."

Study details. The researchers retrospectively reviewed the medical records of 49 keratoconus patients (57 eyes) between the ages of 12 and 22 years who underwent CXL between January 2013 and November 2019 at Byers Eye Institute at Stanford University in Palo Alto, California. Eight of these patients underwent bilateral CXL.

Outcome measures included various visual and corneal parameters taken at baseline and at 12 and 24 months postoperatively. The researchers' analysis revealed post-CXL improvement in corrected distance visual acuity (CDVA), with a mean CDVA of 0.38 ± 0.32 at baseline, a mean CDVA of 0.29 ± 0.31 at 12 months post-op, and a mean CDVA of 0.31 ± 0.31 at 24 months post-op. A significant improvement in maximum keratometry was seen at 12 and 24 months post-CXL.

Corneal thinning (as measured by minimum central corneal thickness) initially occurred but stabilized by 24 months post-CXL. The procedure was well-tolerated by all patients, with no lasting side effects reported. There were no cases of microbial keratitis or delayed epithelial healing beyond one month. Two eyes continued to have mild haze at the 24-month examination, but this was not visually significant.

A call for early intervention. CXL has become a first-line treatment for keratoconus in adults. Although the condition typically progresses more rapidly in children, standardization of its management in pediatric patients is lacking.

"I believe that we should implement topographic screening protocols for children and young adolescents in order to identify patients with keratoconus at an early stage," said Dr. Manche. He added that earlier diagnosis and treatment of keratoconus "can prevent the long-term morbidity of the disease, including need for specialty contact lenses and corneal transplantation." *—Patricia Weiser, PharmD*

1 Saleh S et al. *Cornea.* 2022;41(4):408-416.

Relevant financial disclosures—Dr. Manche: NIH: S; Research to Prevent Blindness: S.

Edward S. Manche, MD

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