

DME and Good Vision: Do We Need to Treat Early?



The DRCR Retina Network Protocol V trial recruited patients with DME and VA of 20/25 to evaluate their responses to treatment.

BY CHIRAG JHAVERI, MD

Before the anti-VEGF era, focal laser was the mainstay for the treatment of diabetic macular edema (DME). The ETDRS showed that application of focal or grid macular laser resulted in better visual outcomes than observation in patients with clinically significant macular edema (CSME).¹ CSME was identified during clinical examination and did not include any vision criteria. At the time, diagnosis of CSME did not rely on results from imaging modalities such as fluorescein angiography and OCT. The latter was unavailable in that era.

OCT is more effective than a clinical exam for detecting DME, leading to earlier diagnosis.² An increase in OCT utilization coincided with the beginning of the anti-VEGF era, forever revolutionizing the way our field manages patients with DME. The landmark trials that evaluated ranibizumab (Lucentis, Genentech)³ and aflibercept (Eylea, Regeneron)⁴ for treatment of DME typically had entry criteria of 20/40 VA or worse and a specified minimum retinal thickness as documented on OCT. In other words, only patients with bad vision were evaluated in our field's landmark anti-VEGF clinical trials in DME. This has led to a gap in our knowledge regarding anti-VEGF therapy for patients with very good vision (ie, VA better than 20/40).

Before the OCT age, focal laser treatments did not have vision requirements and depended on a less sensitive assessment of CSME. Today, OCT allows detection of minimal amounts of fluid. Until recently, no randomized trial had evaluated anti-VEGF therapy in patients with DME and VA 20/25 or better, and the treatment strategy for anti-VEGF therapy for this patient population was unknown.

Should patients with DME be started on anti-VEGF therapy as soon as macular edema is detected on OCT, regardless of VA? Or can anti-VEGF therapy be delayed until patients' VA worsens without affecting long-term visual outcomes?

PROTOCOL V

The DRCR Retina Network Protocol V trial aimed to evaluate

treatment strategies for patients with very good VA and center-involved DME in the era of anti-VEGF therapy and OCT.⁵ Patients had DME as determined on OCT and VA of 79 letters or better on ETDRS testing (Snellen equivalent 20/25).

Study Design

Researchers randomly assigned patients to one of three groups: initiation of monthly aflibercept, focal laser therapy with deferred aflibercept, or initial observation with deferred aflibercept. Patients in the initial observation group and focal laser group would receive aflibercept if vision declined by 10 letters compared with baseline at any visit or by 5 to 9 letters on two consecutive visits; OCT worsening was not used to determine initiation of aflibercept in the laser or observation groups. Patients in the

AT A GLANCE

- ▶ Until recently, no clinical trial had examined whether anti-VEGF therapy in patients with good vision and DME leads to better long-term visual outcomes compared with focal laser or initial observation.
- ▶ Researchers in the DRCR Retina Network Protocol V trial randomly assigned patients with VA 20/25 or better to receive anti-VEGF injections, focal laser treatment, or initial observation followed by anti-VEGF therapy if needed and followed them for 2 years.

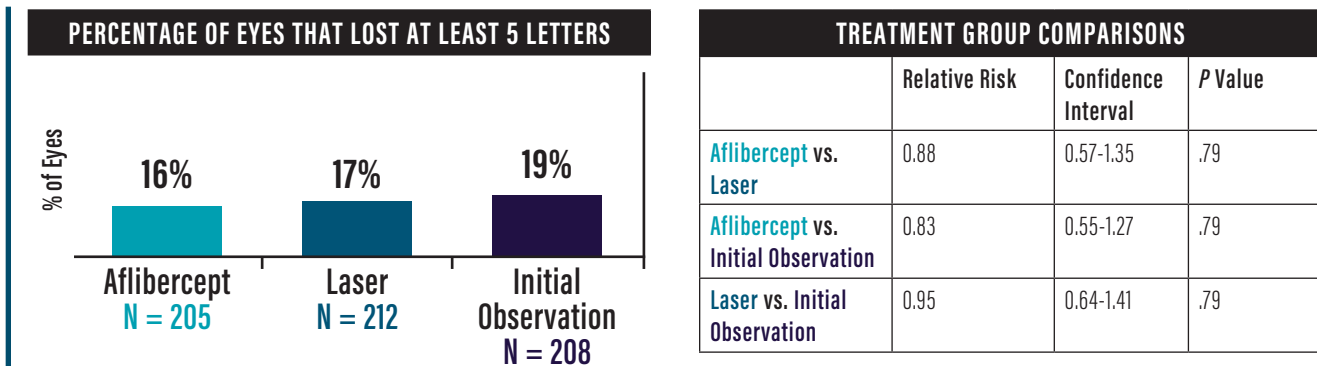


Figure 1. No statistically significant difference was observed in the percentages of patients who had a loss of 5 letters or more at 2 years. Graph courtesy of: DRCR Retina Network.

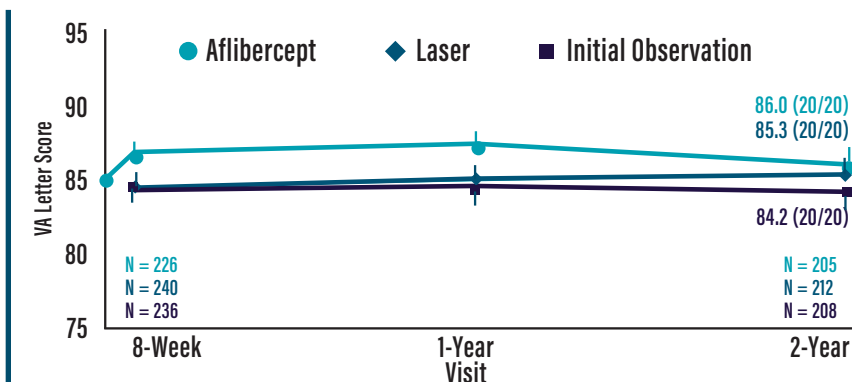


Figure 2. At 2 years, mean VA was identical across all three groups. Graph courtesy of: DRCR Retina Network.

laser and initial observation groups were seen at 8-week intervals at the start of the study and then at 16-week intervals unless VA worsened.

Patients in the aflibercept group were treated monthly. After a patient was given aflibercept, if a patient showed improvement on two consecutive visits with VA of at least 20/20 and OCT thickness better than screening visit threshold, then treatment could be deferred and the patient monitored.

Results

The study's primary outcome was the proportion of eyes that lost at least 5 letters of vision at 2 years (Figure 1).

At 2 years, patients in each treatment group had similar visual outcomes with no statistically significant difference of vision loss. Mean VA at 2 years was not statistically

significantly different among the three groups, and mean VA in all three groups at 2 years was 20/20 (Figure 2).

In the laser and initial observation groups, 25% and 34%, respectively, of patients needed to have initiated aflibercept therapy during the 2-year trial period. Therefore, about two-thirds of patients who had DME with good vision maintained good vision without any treatment.

WHAT DOES THIS MEAN IN THE CLINIC?

The findings from Protocol V are important because clinicians may now initially observe patients with DME who have good VA with confidence that this will not harm long-term visual outcomes. Anti-VEGF treatment can be initiated when the patient's vision begins to decline. This approach will significantly reduce treatment burden

and costs for both patients and the health care system in general. ■

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CHIRAG JHAVERI, MD

- Retina Specialist, Retina Consultants of Austin, Austin, Texas
- Retina Specialist, Retina Research Center, Austin, Texas
- Clinical Assistant Professor, Dell Medical School, The University of Texas at Austin, Austin, Texas
- Executive Committee Member, DRCR Retina Network
- Protocol Chair for DRCR Retina Network Protocol AC
- cjhaveri@e-retina.net
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