Since its inception in 2002, the DRCR Retina Network has given us many insights into the evaluation and management of diabetic retinopathy (DR) and its sequelae. Protocol T compared anti-VEGF molecules for diabetic macular edema (DME) in a way that industry likely would not have. The recent results of 5-year data from Protocol S and 6-month results in Protocol U have yielded additional information regarding proliferative DR (PDR) and DME.

Now, with a recent expansion of its mission, the DRCR Retina Network has begun to initiate protocols for other retinal diseases. This article provides a brief synopsis of recent results and looks ahead at some upcoming trials.

**Protocol S**
In Protocol S at 2 years, patients with PDR receiving ranibizumab (Lucentis, Genentech) had a 0.5-line improvement in VA compared with patients who underwent panretinal photocoagulation (PRP). In addition, visual fields were better maintained in the ranibizumab group compared with the laser group.

At 5 years, however, the visual field loss in the ranibizumab group approached that in the PRP group. And mean change in VA in the two groups was similar at 5 years. In the ranibizumab group, fewer patients developed center-involved DME and retinal detachments. The PRP group had fewer visits and injections. Both groups had an incidence of vitreous hemorrhage of almost 50% throughout the 5 years. Fortunately, substantial vision loss (3 lines or more) was rare in both groups (6%). These results suggest that both PRP and ranibizumab injection are good options for the treatment of PDR, with similar results at 5 years.

**Protocol U**
Protocol U evaluated short-term visual improvement at 6 months after the addition of corticosteroid therapy in patients with persistent DME despite anti-VEGF treatment. Patients who had persistent edema and had received at least three anti-VEGF injections were randomly assigned to receive ranibizumab plus the dexamethasone intravitreal implant 0.7 mg (Ozurdex, Allergan) or ranibizumab alone.

At 6 months, there was no difference in mean VA improvement between the two groups. Of note, this was not a head-to-head comparison of the two medications but instead evaluated whether adding the dexamethasone intravitreal implant for patients who continue to receive anti-VEGF therapy was of any benefit.

**ongoing and enrolling trials**
Ongoing and currently enrolling trials by the DRCR Retina Network for DR include Protocols W, AA, AB, TX, AC, and AE. In addition, there is a sustained effort to create a repository of genetic information from patients enrolled in all DRCR Retina Network trials for future evaluation and as a resource for the research community.

**AT A GLANCE**
- The DRCR Retina Network has completed a number of trials that have yielded important clinical information regarding DR and DME. Multiple protocols are ongoing.
- The results of Protocol V, which compares treatment strategies for patients with DME and good vision, were presented at ARVO 2019.
- The DRCR Retina Network is expanding its mission to include evaluation of all retinal pathology. New members are welcome.
"At the beginning of 2018, the DCRRetina Network’s scope was expanded to include evaluation of all retinal pathology in a collaborative clinical research setting."

Protocol W
Protocol W is evaluating intravitreous anti-VEGF for the prevention of vision-threatening outcomes (DME or PDR) in patients who present with severe nonproliferative DR. This outcome will be important to determine whether preventive anti-VEGF therapy in DR is beneficial. The study is anticipated to be completed in April 2022.

Protocol AA
Protocol AA is comparing ultra-widefield fundus imaging to ETDRS seven-standard-fields imaging for the assessment of DR and prediction rates for worsening of DR.

Protocol AB
Protocol AB is a surgical study evaluating prompt vitrectomy versus anti-VEGF therapy for vitreous hemorrhage due to PDR.

Protocols TX and AC
Currently enrolling trials include Protocols TX and AC. Protocol TX is a single-visit 5-year follow-up study of patients who were enrolled in Protocol T. This study will provide information on long-term VA, changes in treatment, and remission or recurrence of DME after protocol-specified treatment was stopped.

Protocol AC is an evolution of Protocol T that is examining the real-world cost burden for patients and insurance systems and considering the potential results of a step-therapy approach to anti-VEGF therapy. Patients with DME will be randomly assigned to bevacizumab (Avastin, Genentech) with deferred aflibercept (Eylea, Regeneron) as needed compared with monotherapy aflibercept from the outset. The study will evaluate whether switching patients to aflibercept only if needed can be a cost-effective option with similar visual results to aflibercept for DME.

Protocol AE
The DCR Retina Network will soon begin a pilot study investigating photobiomodulation. Protocol AE will investigate the role of daily photobiomodulation therapy for patients with center-involved DME. Recent preclinical and small phase 1 trials have shown photobiomodulation to affect the pathogenesis of DR and to improve DME. This would potentially be the first at-home therapy to treat DR and DME.

Protocol V Results to Be Discussed in Future Retina Today Issues
Protocol V has been completed, and the results were presented at the Association for Research in Vision and Ophthalmology meeting in April.

In the anti-VEGF era, all large randomized controlled trials evaluating DME treatments have been conducted in patients with decreased vision. However, there are many patients with very good vision and center-involved diabetic macular edema. There are no current guidelines with respect to which therapy to initiate, and when, for such patients.

Protocol V evaluated three treatment strategies for these patients. Patients were randomly assigned to observation with deferred aflibercept as needed, focal laser with deferred aflibercept as needed, or initiation of prompt aflibercept. The September issue of Retina Today, which will focus on diabetic eye disease, will feature coverage of Protocol V’s findings.

Evaluating Other Retinal Pathology
At the beginning of 2018, the DCR Retina Network’s scope was expanded to include evaluation of all retinal pathology in a collaborative clinical research setting. Many excellent protocol ideas have been submitted by members of the network and by the whole retina community. The first two protocols not involving DR are now enrolling patients.

Protocols AG and AH are sister trials. Protocol AG is evaluating pneumatic vitreolysis for vitreomacular traction (VMT). Investigators will compare clinic-based injection of C3F8 gas with sham injection for VMT. Protocol AH will evaluate full thickness macular holes associated with VMT. Protocol AH does not have a sham group, but it will evaluate the effectiveness of pneumatic vitreolysis in closure rates for macular holes associated with VMT.

Conclusion
The DCR Retina Network has greatly influenced how retina physicians manage DR. With the expansion of its mission, the DCR Retina Network will continue to help shape the management of DR and other retinal pathologies. I highly recommend that all retina subspecialists become involved in the DCR Retina Network. Protocol ideas can be submitted by anyone online at DCRR.net.