

Overview and Update: Diabetic Clinical Research Network

The network currently has seven protocols underway that directly apply to diabetic eye disease.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

Diabetic retinopathy is an active area of clinical research, according to Lloyd P. Aiello, MD, PhD. He spoke during the American Academy of Ophthalmology 2005 Annual Meeting's Retina Subspecialty Day in Chicago. Dr. Aiello is head of Joslin's Section on Eye Research, director of Joslin Clinic's Beetham Eye Institute and associate professor of ophthalmology at Harvard Medical School.

There are numerous novel therapeutic modalities under investigation for the treatment of diabetic retinopathy. A group of steroid modalities include intravitreal, implant/bio-erodable and peribulbar systems such as Macugen (EyeTech/Pfizer), Lucentis (Genentech), Avastin (Genentech) and vascular endothelial growth factor (VEGF)-trap (Regeneron Pharmaceuticals).

Other treatments under investigation include pigment epithelium derived factor (PEDF), endostatin, kininogen, protein kinase-C (PKC)-beta inhibitors, GH/IGF-1 inhibitors, anti-advanced glycation end products (anti-AGE), antioxidants, aldose reductase inhibitors, neuro-protectants and vitreolysis.

Numerous other agents are under investigation for disorders that directly apply to diabetic eye disease. Combination therapy has been largely unexplored in this area.

CLINICAL TRIAL DEVELOPMENT

Multiple clinical trials are simultaneously ongoing. Most of these address primarily the same patient cohorts. Within this study area, it is important for investigators to identify and prioritize numerous trial opportunities, Dr. Aiello said. Trial development must be promoted in specific study areas, and trials must be quickly implemented in order to benefit patients. Researchers should be looking at ways to optimize recruitment for trial efficiency and involve large

numbers of broadly distributed centers. Other important points regarding clinical trials are for investigators to interact with industry when appropriate and to maintain scientific rigor.

The Diabetic Retinopathy Clinical Research Network (DRCR.net) is a National Eye Institute-funded cooperative initiated in September 2002. We reported on this network in our November/December 2004 issue. The program's objective is to develop a collaborative network to facilitate multicenter clinical research on diabetic retinopathy, diabetic macular edema and associated conditions.

The DRCR.net's function, Dr. Aiello said, is to identify trial needs, design protocols, standardize key procedures, implement trials and leverage information technology.

PRIORITY INITIATIVES

One priority initiative of the DRCR.net is an open-network policy. This means that the involvement of community-based as well as academically oriented partnerships is encouraged. Another priority initiative is collaboration with industry to facilitate investigations and pursue opportunities otherwise not possible. These partnerships must be conducted in a manner consistent with the network's dedication to academic integrity and optimal clinical trial performance.

The final priority initiative of the DRCR.net, according to Dr. Aiello, is to institute novel approaches to data standardization, information acquisition and site communication in order to optimize trial and site efficiency.

As of June, the DRCR.net participation included 155 sites overall, with 61 institutional, 94 community based and 143 that are certified for one or more trials. The sites are located in 34 states, with 450 certified investigators and more than 1,000 personnel.

In the DRCR.net, community based sites are involved in a

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collaborative manner with academic sites, Dr. Aiello said. Senior investigators work closely with junior investigators in order to train them as potential future leaders. Participation is distributed throughout the network, with 57 investigators having served on at least one committee and seven different investigators having served as a protocol chair (Table 1).

Since the DRCR.net's inception, seven protocols have been developed, one has been completed, four are being conducted, two are pending Institutional Review Board (IRB) approval and two are under active development. The current protocols are:

- **Pilot Study of Laser Photocoagulation for Diabetic Macular Edema.** The protocol chair for this trial is Donald S. Fong, MD, MPH; photographic evaluation head is Ronald P. Danis MD. Enrollment is complete with 319 patients, the results are still masked and results will be presented.

- **Randomized Trial Comparing Intravitreal Triamcinolone Acetonide and Laser Photocoagulation for Diabetic Macular Edema.** The protocol chair is Michael S. Ip, MD, and the enrollment is continuing with 490 patients in the trial to date.

- **Temporal Variation in OCT Measurements of Retinal Thickening in Diabetic Macular Edema.** The protocol chair is Ronald P. Danis, MD. The status of this trial enrollment is complete with 107 patients. The results will be presented at an upcoming meeting.

- **Evaluation of Vitrectomy for Diabetic Macular Edema.** The protocol chair is Julia Haller, MD. Enrollment has begun, with two patients so far.

- **Pilot Study of Peribulbar Triamcinolone Acetonide for Diabetic Macular Edema.** The protocol chair is Emily Chew, MD. Enrollment in this trial is continuing, with 103 entered to date.

- **Observational Study of the Development of DME Following Scatter Laser Photocoagulation.** Protocol chair is Alexander Brucker, MD. Enrollment will be initiating shortly.

- **Preclinical Thickening and OCT.** The protocol chair is Neil M. Bressler, MD, and enrollment will be initiating shortly.

The DRCR.net Web site is extensive, multifunctional and integrated into the daily activities of the investigation sites and the infrastructure of the network. On the Web site, researchers will find protocol templates and data collection modules used across protocols, facilitating rapid establishment of a database and electronic case report forms, Dr. Aiello said. There are many interactive applications on the DRCR.net Web site, including:

- electronic case report form completion;
- real-time validity checks;
- patient randomization;
- investigator assistance with protocol options based on patient data;
- real-time reports;
- repository for all protocol-specific and general network documents;
- patient scheduling;
- viewing, editing, electronic sign-off/on forms, review and sign-off of protocol deviations;
- customized IRB submission materials;
- printing customized patient instruction sheets;
- ordering supplies;
- interactive protocol certification;
- refractive and visual acuity testing training tutorial;
- human subjects/ethics training tutorial and test; and
- closed-loop drug distribution and accountability systems.

The DRCR.net has electronic case report forms on the Web site that are used for data capture. Dr. Aiello noted that these are the primary documentation source. The protocols also use real-time data checking, which has resulted in large reductions in data errors and queries. There is a protocol option feedback that allows more complex protocol to still be handled efficiently by the site. All sites have wireless networks and touch-sensitive tablet computers.

Standardization is an integral part of the DRCR.net program. An electronic visual acuity tester is used at all sites. There are standardized protocols for key procedures including photography, OCT, photocoagulation, refraction, visual acuity measurement, data acquisition and interpretation, Dr. Aiello said.

To enhance patient retention in DRCR.net, patient appointment schedules are maintained on the Web site, Dr. Aiello said. An automated weekly e-mail system notifies the site of upcoming and past due visits. The coordinating center maintains an IRB-approved and patient consented registry with patient contact information. Direct contact from the Coordinating Center helps maintain patient rapport and facilitates the completion of follow-up visits and recapture of lost patients, he explained. For more information, visit www.DRCR.net. ■

Aiello LP. DRCR.net Laser Study. Presented at the American Academy of Ophthalmology 2005 Annual Meeting. Retina Subspecialty Day, October 14-18, 2005.