QUALITY IN RESEARCH

EVICR.NET clinical studies tackle some of the biggest problems in retina.

Leigh Spielberg MD reports

Clinical studies now being conducted under the auspices of the European Vision Institute Clinical Research Network (EVICR.NET) are addressing some of the most urgent questions concerning the treatment of retinal vascular disease.

Researchers updated delegates on three of these studies during a symposium at the 17th Annual EURETINA Congress in Barcelona, Spain, in September 2017. The studies are known as: MACUSTAR, which is developing novel clinical endpoints for clinical trials in patients with intermediate age-related macular degeneration (AMD); EUROCONDOR, a clinical trial for neuroprotection in non-proliferative diabetic retinopathy (DR); and PROTEUS, which will study the effects of anti-VEGF injections for proliferative DR (PDR).

Robert Finger MD, professor of ophthalmology, University Eye Clinic, Bonn, Germany, shared the details of MACUSTAR. Described by Chairman Professor José Cunha-Vaz, University of Coimbra, Portugal, as a landmark study that will become a point of reference, MACUSTAR seeks to characterise the functional deficit in intermediate AMD.

"The goal is to evaluate and validate candidate clinical endpoints for intermediate AMD and for progression from intermediate AMD to late-stage AMD," said Dr Finger.

Outcome measures can be categorised as functional outcomes, structural outcomes and patient-reported outcomes. The challenge will be developing testing protocols for functional tests under low luminance, including scotopic microperimetry, dark adaptation and contrast sensitivity. MACUSTAR will also implement a specifically developed, patient-reported outcome measure, the Vision Impairment in Low Luminance (VILL) questionnaire. The ultimate goal is to find composite endpoints representing both structure and function.

The study seeks to enrol 750 patients across seven countries for a three-year follow-up period, and the first results are expected in early 2019.

Cristina Hernández Pascual MD, presenting for Rafael Simó, both of Vall d'Hebron Research Institute, Barcelona, Spain, informed delegates about the European Consortium for the Early Treatment of Diabetic Retinopathy (EUROCONDOR). This consortium carried out the first clinical trial for retinal neuroprotection for non-proliferative DR. The study showed that topical administration of neuroprotective agents, especially somatostatin, can ameliorate neurodysfunction in DR.

There is a growing body of evidence that retinal neurodegeneration precedes retinal microvascular impairment in patients with diabetes mellitus. This has been demonstrated with multifocal ERG (mfERG) and OCT studies.

Somatostatin has been shown to be neuroprotective and anti-angiogenic. However, its production in the RPE is down-regulated in the diabetic retina, and its concentration has been shown to be significantly lower in the vitreous fluid as compared to controls. Previous studies had shown that topical administration offered retinal neuroprotection in rat models of diabetes.

The EUROCONDOR study included patients with either no DR or only mild disease, and aimed to prevent its development via a non-invasive method without systemic adverse events. It used mfERG to quantify retinal neurodysfunction. Dr Cunha-Vaz pointed out that this study also showed that topically administered drops can have therapeutic effects at the back of the eye.

Joao Figueira MD, professor of ophthalmology, Universidade de Coimbra, Portugal, shared the results of the PROTEUS trial. This study compared the efficacy and safety of intravitreal ranibizumab plus panretinal photocoagulation (PRP) versus PRP alone in 87 patients with high-risk PDR over a 12-month treatment period. The main endpoint was regression of the total area of neovascularisation.

The results were clear: PRP associated with ranibizumab was more effective than PRP alone in the regression of neovascularisation in high-risk PDR. Significantly fewer eyes needed rescue treatment, such as vitrectomy or treatment for diabetic macular oedema.

Another session chair, Professor Francesco Bandello, University Vita-Salute, San Raffaele Scientific Institute, Milan, Italy, brought up a good point.

"This study was conceived when PRP was still the standard of care. What we need to know now is whether PRP + anti-VEGF is better than anti-VEGF alone. I think that anti-VEGF is better in the short term, but what happens in the long term is not yet known, whereas we know what happens in the long term after PRP."

The EVICR.NET network, founded in 2010, comprises 102 clinical sites in 18 European countries. The network, headed by Cecília Martinho, Coimbra, Portugal, helps promote multinational collaboration for large-scale trials in ophthalmology within the European Union.

The Coordinating Centre in Coimbra serves as a single contact point, and thus as a resource for both academia and industry. By certifying clinical sites and coordinating training activities for its member sites, EVICR.NET helps guarantee a high level of quality in the clinical research performed. It also serves as a liaison: EVICR.NET is contacted by industry and clinical research organisations (the sponsors) to identify certified clinical sites to participate in clinical studies. After a feasibility assessment, the sponsor selects the clinical sites with which it would like to work.

Because the European Union is comprised of different countries, each with their own laws, entities and languages, an organisation such as the EVICR.NET serves to assist with the overall management and logistical activities necessary to carry out multinational studies. More information can be found at *www.evicr.net.*

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