An Update on Innovative Retina Technologies

The first Ophthalmology Innovation Summit was held at the 2009 American Academy of Ophthalmology (AAO) meeting. At the event, 25 companies presented innovative ophthalmic technologies in various stages of development. This article provides an update on the development of up-and-coming retina devices and therapies.

DEVICES

Argus II

The Argus II (Second Sight Medical Products, Inc., Sylmar, CA) is the second generation of an electronic retinal implant designed for the treatment of blindness due to retinitis pigmentosa (RP). The implant consists of an array of electrodes that is attached to the retina and used in conjunction with an external camera and video processing system to provide a rudimentary form of sight to implanted patients. The implant is reportedly designed to last a lifetime but can be safely removed if necessary. A clinical trial of the Argus II is under way. Thirty-two patients have been enrolled at 11 sites in five countries, including 14 patients in the United States. According to the company, interim results presented at the AAO showed significant improvements in orientation and mobility measures for the trial participants, including their ability to walk in outdoor environments. Preliminary data presented also indicated that many of the trial participants are able to read large letters.

VIDION ANV

The Vidion Anti-Neovascular (ANV) therapy system, manufactured by NeoVista, Inc. (Fremont, CA), is an ophthalmic surgical device for the treatment of age-related macular degeneration (AMD). The Vidion ANV is designed to deliver targeted beta radiation to leaking blood vessels that affect central vision without causing damage to surrounding tissues. According to NeoVista, the targeted delivery of radiation, or epimacular brachytherapy, has been shown to be safe and effective in preliminary clinical trials and may offer a cost-effective solution to the current treatment burden posed by continuous injections of anti-vascular endothelial growth factor (VEGF) therapy. In 2009, the device received the Conformité Européene (CE) Mark, which allows NeoVista to distribute Vidion throughout the European Union and other parts of the world where a CE Mark is accepted. According to the company, US Food and Drug Administration (FDA) approval is targeted for 2011.

IMPLANTABLE TELESCOPE FOR AMD

VisionCare Ophthalmic Technologies, Inc. (Saratoga, CA), completed a phase 2/3 multicenter trial in the United States that evaluated the safety and efficacy of the Implantable Miniature Telescope in patients with moderate to profound central vision impairment due to stable AMD. According to the company, the device received a recommendation for approval from the FDA Ophthalmic Devices Advisory Panel last year, and approval is anticipated this year.

IRay

The IRay system (Oraya Therapeutics, Newark, CA) is an investigational stereotactic radiosurgical device designed to deliver low-energy X-rays to treat wet AMD. The company announced in January 2010 that enrollment is under way for what it called the first masked and sham-controlled study to demonstrate the efficacy and safety of radiation therapy for wet AMD. The clinical trial is being conducted at seven European sites and will include a minimum of 150 patients, with approximately one-third of those receiving a sham exposure and the remainder receiving radiation dosing with the IRay system. More than 60 patients have reportedly been treated in a phase 1 study of the

device, and results from that trial led to the design and initiation of this newly announced trial.

PASCAL

The PASCAL Photocoagulator (Pattern Scan Laser; OptiMedica, Santa Clara, CA) uses a 532-nm wavelength laser and is designed to deliver energy rapidly to provide better patient comfort. According to the company, numerous studies show that in addition to reducing treatment duration for typical patients with proliferative diabetic retinopathy, the number of sessions may also be reduced. Since its worldwide market introduction in 2006, PASCAL photocoagulator technology has been used to treat more than 500,000 patients, representing more than 25 million patterns delivered, OptiMedica said. US and International patents are pending.

THERAPEUTICS

ARC1905

Ophthotech's ARC1905 is a potent and selective inhibitor of factor C5 of the complement cascade. ARC1905 spares the formation of upstream complement components such as C3b, which are important in host defense mechanisms. By inhibiting C5-mediated inflammatory and membrane attack complex activities, therapeutic benefit may be achieved in both dry and wet AMD while sparing the immunoprotective functions of the complement system, according to Ophthotech. A phase 1, open-label, multicenter study of ARC1905 in combination with ranibizumab (Lucentis; Genentech, Inc.) in patients with wet AMD is ongoing. Additionally, a study investigating ARC1905 in patients with dry AMD was initiated in 2009, the company said.

E10030

E10030 (Ophthotech) is a novel anti-platelet derived growth factor (anti-PDGF) that is being investigated for use in combination with an anti-VEGF agent. E10030 strips pericytes, which have been shown to be protective and play a major role in resistance to anti-VEGF treatment, from neovascular tissue, rendering it highly sensitive to anti-VEGF therapy, the company said. Without pericytes present, VEGF blockage may result not only in reduced leakage, but also in neovascular regression.

Ophthotech recently completed a phase 1 open-label, multicenter study of E10030 in combination with ranibizumab (Lucentis; Genentech, Inc.) in patients with wet AMD. The study showed that when used in combination with ranibizumab, E10030 was well tolerated with no evidence of drug-related adverse events. Assessment of visual acuity revealed that 59% of patients gained three or more lines of visual acuity (≥15 ETDRS letters)

at week 12, and there was a mean decrease of 86% in choroidal neovascularization (CNV) at week 12.

iCo 007

iCo-007 (iCo Therapeutics, Inc.) is a second-generation antisense molecule targeting c-raf (raf-1) kinase that results in the down-regulation of the pathway of multiple growth factors (including vascular endothial growth factor [VEGF], erythropoietin, and hepatocyte growth factor) that seem to play critical roles in the process of ocular angiogenesis and vascular leakage, according to iCo. To date, a phase 1 dose-escalation study using a single intravitreal injection of iCo-007 in patients with diffuse diabetic macular edema (DME) demonstrated a positive safety profile. iCo said that it expects to present final data in the second quarter of 2010 and has entered the planning stage for phase 2 clinical studies.

FENRETINIDE

Fenretinide (Sirion Therapeutics, Inc.) is an oral vitamin A binding protein antagonist being studied in patients with geographic atrophy (GA). Fenretinide is believed to halt the accumulation of retinol (vitamin A) toxins through affinity for retinol-binding protein. It is also believed to slow the formation and accumulation of toxic byproducts thought to be responsible for vision loss in GA. Interim analysis of a phase 2 trial found that fenretinide slows GA lesion growth in a dose-dependent manner, according to Sirion. After 12 months, fenretinide 300 mg slowed growth more effectively than placebo regardless of lesion size at entry, but was more effective in small lesions. Fenretinide 100 mg promoted slower growth in smaller lesions. Based on these results, Sirion said it plans to continue the current study and meet with its scientific advisors and the FDA to design an appropriate phase 3 program for fenretinide.

MACUGEN

Macugen (pegaptanib sodium injection) is a novel selective anti-VEGF inhibitor indicated for the treatment of wet AMD. Macugen specifically binds to VEGF-165, a protein that plays a crucial role in angiogenesis and increased vascular permeability, two of the primary pathological processes responsible for the vision loss associated with neovascular AMD. Macugen received FDA approval in 2004 as the first anti-VEGF therapy in ophthalmology and is the only FDA-approved pre-filled syringe for intravitreal injection.

Eyetech Inc. markets and sells Macugen in the United States. Pfizer, Inc., has exclusive rights to commercialize Macugen in countries outside the United States. Pfizer is conducting a phase 3 trial of Macugen for the treatment of DME in the European Union.

NT-501

NT-501 (Neurotech) is currently in late-stage clinical development for GA and RP. NT-501 is an intraocular implant containing encapsulated cells genetically modified to secrete ciliary neurotrophic factor (CNTF) and deliver it to the posterior segment. In March 2009, Neurotech announced positive results and the achievement of proof of concept in a phase 2 clinical study of NT-501 for the treatment GA.

PERCEIVA

Perceiva (MacuSight, Inc.) is a proprietary clear, liquid formulation of sirolimus. As mammalian target of rapamycin (mTOR) inhibitor, sirolimus possesses a broad spectrum of therapeutic action potentially relevant to the treatment of retinal diseases, including the inhibition of inflammation, angiogenesis, vascular permeability, proliferation and fibrosis. The product is administered through a subconjunctival injection using a standard 30-gauge needle. Following injection, this highly lipophilic drug preferentially migrates into the sclera, which subsequently acts as a reservoir, allowing the slow, sustained release of sirolimus into the intraocular tissues.

MacuSight said that it is advancing Perceiva in a broad phase 2 clinical program across several indications including DME, wet AMD, and uveitis. Additionally, the company is evaluating sirolimus as a potential therapy for dry eye syndrome. MacuSight plans to announce data from its phase 2 studies in the first half of 2010.

VOLOCIXIMAB

Volociximab (Ophthotech), a high-affinity monoclonal antibody, binds to $\alpha 5\beta 1$ integrin and blocks the binding of $\alpha 5\beta 1$ integrin to fibronectin, thereby inhibiting a pivotal interaction required for angiogenesis. Volociximab administration has resulted in strong inhibition of rabbit and primate retinal neovascularization, according to Ophthotech. In cynomolgus monkeys with laser-induced CNV, volociximab significantly inhibited CNV proliferation and reduced the degree of lesion formation. In a rabbit model, volociximab administered either intravenously or intravitreally prior to the onset of neovascularization significantly reduced angiogenesis as compared to control. Similar antiangiogenic efficacy with volociximab has also been shown in multiple preclinical models of tumor angiogenesis. A phase 1, open-label, multicenter study of volociximab in combination with ranibizumab in patients with wet AMD is ongoing. ■