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Phase 3 Trials for Uveal Melanoma Therapy, Behçet Disease Uveitis Fail to Reach Primary Endpoints

Phase 3 clinical trials investigating potential therapies for uveal melanoma and for Behçet disease uveitis failed to reach their primary endpoints, according to information from the two drugs' developers.

A randomized, double-masked, placebo-controlled phase 3 trial investigating selumetinib (AstraZeneca) in combination with dacarbazine (DTIC-Dome, Bayer Pharmaceutical) for treatment of uveal melanoma did not reach its primary endpoint of progression-free survival. The adverse event profile for patients in combination therapy in the trial was consistent with the individual safety profiles of dacarbazine and selumetinib.

Selumetinib inhibits the MEK enzyme in the RAS/RAF/MEK/ERK pathway, and the trial investigated its potential to prevent uveal melanoma tumors from growing. The drug received orphan drug designation from the US Food and Drug Administration (FDA) in April 2015. Clinical trials investigating selumetinib as treatment for thyroid cancer and for neurofibromatosis type 1 are ongoing, according to the manufacturer.

Another monoclonal antibody, gevokizumab (Xoma) failed to meet the primary endpoint of time to first acute ocular exacerbation in the phase 3 EYEGUARD-B study, which examined the safety and efficacy of gevokizumab in patients with Behçet disease uveitis, according to a press release from Xoma.

In the EYEGUARD-B trial, patients (n = 83) with Beçhet disease uveitis were randomly assigned to treatment with 60 mg gevokizumab (n = 40) or placebo (n = 43). Patients continued previously administered immunosuppressive and corticosteroid therapies during the trial.

Although the study did not achieve its primary endpoint, signals of drug activity such as preserved visual acuity, less severe ocular exacerbations, and reduced incidence of reported macular edema were seen in patients treated with gevokizumab, according to the company.

The EYEGUARD-A and EYEGUARD-C studies, exploring the broader range of noninfectious uveitis, are still recruiting.

UK Regulators: Dexamethasone Intravitreal Implant Recommended for Some Pseudophakic Patients With DME

The UK National Institute for Health and Care Excellence has recommended the use of the dexamethasone intravitreal implant (Ozurdex, Allergan) for pseudophakic patients with diabetic macular edema (DME) who are unresponsive to or unsuitable for noncorticosteroid therapy.

The drug will be available within 3 months, according to the company.

Dry AMD Patient Receives Argus II Implant

A patient with late-stage dry age-related macular degeneration (AMD) has received the Argus II retinal prosthesis (Second Sight Medical Products). This is the first patient with dry AMD to receive the device, according to the company.

The patient, whose device was activated 2 weeks after implantation, has thus far demonstrated some useful vision.

A study enrolling five patients will assess the safety and efficacy of the retinal prosthesis in patients with late-stage dry AMD. Eligibility criteria for the study require patients to be 25 to 85 years of age with advanced dry AMD, some residual light perception, and a history of useful vision. The study will follow patients for 3 years.

The retinal prosthesis is approved in the United States for use in patients with retinitis pigmentosa and in the European Union for patients with outer retinal degeneration. It is not approved for use in dry AMD in either location.

Top-Line Results Positive for AKB-9778 in DME

Top-line results from the TIME-2 study examining the safety and efficacy of AKB-9778 (Aerpio Therapeutics) for treatment of DME showed that AKB-9778 and

ranibizumab (Lucentis, Genentech) combination therapy produced significantly greater central subfield thickness (CST) reduction compared with ranibizumab monotherapy ($P = .008$).

In the secondary endpoint of gain of 3 lines or greater in visual acuity, there was a trend favoring the combination therapy arm compared with the ranibizumab arm. Patients receiving AKB-9778 monotherapy had no reduction in CST.

In the phase 2A proof-of-concept study, patients with DME (n = 144) were randomly assigned to AKB-9778 monotherapy, ranibizumab monotherapy, or combination therapy. The study's primary endpoint was mean CST change from baseline.

The safety profile showed no clinically significant differences in the percentage of patients who experienced ocular or nonocular adverse events. Full study results will be presented at an upcoming scientific meeting.

Study: OCTA Detected CNV Comparably With FA

Optical coherence tomography angiography (OCTA) demonstrated sensitivity and specificity comparable with fluorescein angiography (FA) for detection of choroidal neovascularization (CNV) in eyes with chronic central serous chorioretinopathy (CSCR), according to a study published in *JAMA Ophthalmology*.[1]

Researchers at the New England Eye Center imaged 27 eyes of 23 patients with suspected CNV complicating chronic CSCR. Patients underwent standard assessment for CNV diagnosis, which included FA imaging. Patients also underwent OCTA imaging. Two independent readers analyzed OCTA depictions of vascular flow representing CNV and the morphologic appearance of CNV. FA was used as the standard examination reference.

FA imaging identified eight of 27 eyes (30%) as having CNV. OCTA and corresponding OCT b-scans detected 100% (eight of eight) of the CNV lesions and excluded 100% (19 of 19) of eyes with CSCR without CNV: that is, sensitivity was 100% (95% CI, 0.62-1.00) and specificity was 100% (95% CI, 0.82-1.00).

1. Filho MAB, de Carlo TE, Ferrana D, et al. Association of choroidal neovascularization and central serous chorioretinopathy with optical coherence tomography angiography [published online ahead of print May 21, 2015]. *JAMA Ophthalmol*. doi:10.1001/jamaophthalmol.2015.1320.

Visual Function Improved 6 Months After Ocriplasmin Use

Patients who received ocriplasmin (Jetrea, ThromboGenics) therapy for vitreomacular traction (VMT) or vitreomacular adhesion (VMA) reported better visual function compared with patients who received placebo injection, according to a study published in *JAMA Ophthalmology*.[1]

Researchers analyzed survey responses from patients (n = 652) with VMT or VMA enrolled in the TG-MV-006 or TG-MV-007 studies. Patients reported visual function using the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) at baseline and at 6 months.

At 6 months, patients who received ocriplasmin (n = 464) reported greater mean improvement from baseline in the NEI VFQ-25 composite score compared with patients who received placebo (n = 188; mean change 3.4 vs. 0.7, respectively; $P = .005$). Of patients in the ocriplasmin group, 36.0% had a composite score improvement of at least five points, which was considered clinically meaningful; 27.2% of patients in the placebo group had a clinically meaningful improvement ($P = .03$). Fewer patients in the treatment group had clinically meaningful worsening of visual function at 6 months compared with patients in the placebo group (15.0% vs. 24.3%, respectively; $P = .005$).

1. Varma R, Haller JA, Kaiser PK. Improvement in patient-reported visual function after ocriplasmin for vitreomacular adhesion: results of the microplasmin for intravitreous injection–traction release without surgical treatment (MIVI-TRUST) trials [published online ahead of print June 11, 2015]. *JAMA Ophthalmol*. doi:10.1001/jamaophthalmol.2015.1746.

Study: Most Patients Had VMT or VMA Release After ALG-1001 Use

Among patients with VMT or VMA who received 3.2 mg of ALG-1001 (Luminate, Allegro) in a study, 65% of eyes achieved release by day 90 compared with 9.7% of eyes receiving placebo ($P = .0129$), according to a company press release.

In a phase 2, double-masked, placebo-controlled trial evaluating the safety and efficacy of intravitreal ALG-1001, patients (n = 106) were randomly assigned to one of three ALG-1001 treatment arms (2.0 mg, 2.5 mg, or 3.2 mg) or to balanced salt solution placebo. Patients were followed for 90 days. Researchers observed no rod or cone photoreceptor dysfunction, drug toxicity, or intraocular inflammation.

Phase 2 Trial of Gene Therapy for Choroideremia Commences

A phase 2 open-label clinical trial investigating the use of gene therapy for treatment of choroideremia has started enrolling and treating patients, according to a press release from NightstaRx. In the treatment, the adeno-associated virus (AAV) will be used to deliver a wild-type copy of the Rab-escort protein 1 (REP-1) gene (AAV2-REP1) to eye cells.

The trial at the University of Alberta will enroll six

men. Each will receive a single dose of AAV2-REP1 via subretinal injection.

Choroideremia is an inherited X-linked disease in which mutations affect the CHM gene, which encodes REP-1. It affects approximately 1 in 50 000 people.

Vision Improvements Maintained at 60 Months in Patients With IMT

In patients who received the Implantable Miniature Telescope (VisionCare Ophthalmics) for untreatable geographic atrophy (GA), disciform scars, or both, improvements in distance BCVA were maintained at 60 months, according to a study published in *Clinical Ophthalmology*.[1]

Patients (n = 217) were divided into two groups: those 65 to 74 years old (n = 70) and those 75 years and older (n = 127). In the younger group, data were available for 31 patients at 60 months; in the older group, data were available for 32 patients.

At 60 months, patients in the younger group had distance BCVA improvement of 2.64 ± 2.55 lines from baseline; in the older group, improvement was 2.09 ± 2.88 lines.

Persistent corneal edema occurred in 4.3% (three of 70) of patients in the younger group and in 4.7% (six of 127) of patients in the older group. In the younger group, 2.9% (two of 70) of patients received a corneal transplant; 1.6% (two of 127) of the older patients received a corneal transplant. Overall, younger patients had fewer adverse events.

In an interview with *Retina Today*, David Boyer, MD, the first author of the study, commented on the finding of decreased distance BCVA in older versus younger patients. "That decline is probably secondary to progression of AMD," he said. "These are GA patients, and we're not treating their GA at this moment."

1. Boyer D, Freund KB, Regillo C, et al. Long-term (60-month) results from the implantable miniature telescope: efficacy and safety outcomes stratified by age in patients with end-stage age-related macular degeneration. *Clin Ophthalmol*. 2015;9:1099-1107.

Doheny Eye Institute Names New President, Chief Scientific Officer.

The Doheny Eye Institute named SriniVas Sadda, MD, as the institution's new president and chief scientific officer, according to a press release.

Dr. Sadda joined the Doheny Eye Institute in 2002 and worked closely with the organization's previous president, Stephen J. Ryan, MD. Dr. Ryan, who was president of the Doheny Eye Institute for 27 years, died in 2014. ■