AAO RECAP

As a service to our readers, we are providing a recap of the major presentations at the American Academy of Ophthalmology (AAO) Annual Meeting in Chicago, held October 17 to 22, 2014. This feature is not intended to be all-inclusive, but rather reflects our editor's picks as some of the top presentations at the meeting.

VIBRANT, NEWTON Trials Showed Aflibercept Effective in Treating RVO

Monthly intravitreal aflibercept (Eylea, Regeneron) injections provided significantly greater visual benefit and reduction in central retinal thickness (CRT) at 24 weeks compared with grid laser photocoagulation in eyes with branch retinal vein occlusion (BRVO) in the VIBRANT trial, Robert E. Leonard II, MD, reported.1

The VIBRANT trial was a phase 3, multicenter, randomized, double-masked, 52-week trial in treatment-naive patients with unilateral macular edema secondary to BRVO diagnosed within 12 months and BCVA between 73 and 24 letters (20/40 to 20/320 Snellen equivalent) at enrollment. Patients received 2.0 mg intravitreal aflibercept injections every 4 weeks (n = 91) or laser (n = 92) from baseline to week 24. At week 24, receiving aflibercept were switched to 2.0 mg aflibercept every 8 weeks. Patients in the aflibercept arm who required rescue received laser at week 36; patients in the laser group who required rescue received 2.0 mg aflibercept monthly for 3 months, then every 8 weeks.

Of the patients in the aflibercept group, 53% gained at least 15 letters from baseline at week 24 compared with 27% in the laser group (P < .001). Mean improvement in BCVA was 17.0 letters for the aflibercept group and 6.9 letters for the laser group (P < .001). The mean reduction in CRT from baseline to week 24 was 280.5 µm in the aflibercept group and 128.8 µm in the laser group (P < .0001).

One eye in the aflibercept group had a traumatic cath-oact; it was the only serious ocular adverse event that occurred from baseline to week 24. The most common ocular adverse events were conjunctival hemorrhage (19.8%) and eye pain (4.4%).

Rahul Khurana, MD, presented on data from the NEWTON study. NEWTON is a phase 4, prospective, single-arm, single-center, interventional study testing whether the interval between injections in eyes with macular edema secondary to central retinal vein occlusion (CRVO) previously treated with bevacizumab (Avastin, Genentech) or ranibizumab (Lucentis, Genentech) increased when switched to aflibercept. Researchers enrolled patients who were previously treated with ranibizumab or bevacizumab for 6 months and had an occurrence of macular edema when extended beyond 4-week dosing intervals. Patients received 2.0 mg aflibercept on a treat-and-extend regimen.

Data from an interim analysis of 14 patients who switched to aflibercept showed that the macular edema-free period increased from an average of 39 days to 62 days, which was statistically significant. The increase in the numbers of days without edema ranged from 7 days to 49 days; 13 of 14 patients had an increase in interval.

BRIGHTER/CRYSTAL Studies: PRN a Viable Strategy for BRVO, CRVO

Ongoing long-term trials support the safety and efficacy of intravitreal ranibizumab for treatment of BRVO and CRVO with dosing on an as-needed basis after stabilization of disease, said Jordi M. Mones, MD.1

The BRIGHTER study is an ongoing 24-month trial with patients randomized 2:2:1 to receive 0.5 mg ranibizumab (group 1), 0.5 ranibizumab plus laser (group 2), or laser alone (group 3) for treatment of BRVO. The open-label CRYSTAL study enrolled patients with CRVO for treatment with 0.5 mg ranibizumab. Patients in both studies received monthly injections until visual acuity was stable for 3 consecutive months, and were followed out to 12 months thereafter with treatment on an as-needed, or PRN, basis.

The BRIGHTER study confirmed the efficacy of ranibizumab for BRVO with no additional benefit of laser. There were mean gains of BCVA from baseline of 14.4 letters in group 1, 14.8 letters in group 2, and 6.0 letters in group 3 (P < .0001). Patients received a mean 4.8 injections in group 1 and 4.5 in group 2. There was no difference in visual acuity outcomes among patients who had ischemic versus nonischemic BRVO, Dr. Mones said. These likely represent patients who would not have been studied in pivotal clinical trials, Dr. Mones said.

The CRYSTAL study also enrolled patients with more advanced disease than studied in previous clinical trials for CRVO involving ranibizumab. Still, Dr. Mones said, mean change in BCVA at month 12 was 12.3 letters after a mean 8.1 injections. There were no new safety signals identified in either study, Dr. Mones said.

MEAD: Dexamethasone Implant Superior to Sham

A higher percentage of patients with diabetic macular edema (DME) randomized to receive a dexamethasone intravitreal implant (Ozurdex, Allergan) had gains of at least 15 letters in BCVA compared with sham in the MEAD study, according to Anat Lowenstein, MD.1

The MEAD study was a 3-year, randomized, multi-center, masked, sham-controlled phase 3 study in which patients (n = 1048) were randomized to receive treatment via 0.7 mg dexamethasone intravitreal implant, 0.35 mg dexamethasone intravitreal implant, or sham. At 3 years, the mean number of treatments was 4.1 for the 0.7-mg group, 4.4 for the 0.35-mg group, and 3.3 for the sham group. The number of patients who met the primary efficacy endpoint of an improvement of at least 15 letters was 22.2% for the 0.7-mg group, 18.4% in the 0.35-mg group, and 12.0% in the sham group (P < .018).

The effects of the implant on BCVA compared with sham were similar to those in the total population for a number of patient subgroups, including men versus women, white versus nonwhite, those with diabetes duration less than 15 years versus more than 15 years, and DME duration less than 3 years versus more than 3 years.

Improvements in BCVA for patients in the treatment groups who were phakic were complicated by cataract development in year 2; improvements in BCVA were seen upon removal of cataract. Improvements in BCVA were consistent each year of the study in patients in the treatment groups who were pseudophakic.

Two Trials Showed Visual Gains at 52 Weeks with Conbercept

Patients with wet age-related macular degeneration (AMD) treated with conbercept had visual gains at 52 weeks in the AURORA and PHOENIX trials, according to Peter Kaiser, MD. Conbercept, an anti-VEGF agent, is approved in China for the treatment of wet AMD.1

The AURORA study was a phase 2 trial in which researchers treated patients (n = 111) with either 0.5 mg conbercept or 2.0 mg conbercept for 3 months before randomizing patients to 1 of 4 treatment groups: 0.5 mg conbercept PRN, 0.5 mg conbercept monthly, 2.0 mg conbercept PRN, and 2.0 mg conbercept monthly. At 52 weeks, the 0.5-mg PRN group gained 14.3 letters, the 0.5-mg monthly group gained 9.3 letters, the 2.0-mg PRN group gained 12.4 letters, and the 2.0-mg monthly group gained 15.4 letters. Mean CRT improved in all groups over the same time period.

Dr. Kaiser also reported on the PHOENIX study, a phase 3 study in which treatment-naïve patients (n = 124) with wet AMD received 0.5 mg conbercept monthly for 3 months or sham monthly for 3 months. After 3 months, each group received 0.5 mg conbercept every 3 months. At 52 weeks, the continuous treatment group had a 9.9-letter gain in vision and the delayed treatment group had an 8.8-letter gain in vision; both gains were statistically significant from baseline. Each group also had significant reduction in CRT.

LUCAS: Similar VA Gains With Ranibizumab, Bevacizumab

Patients in the LUCAS study with active choroidal neovascular membrane and foveal-involving edema had similar improvements in visual acuity following treatment with bevacizumab or ranibizumab using a treat-and-extend protocol, according to Karina Berg, MD.1

The mean change in visual acuity from baseline was not significantly different between the treatment groups. Patients in the ranibizumab group had a 6.6-letter change from baseline; patients in the bevacizumab group had a 7.4-letter change. The mean number of treatments in the ranibizumab group was 69; it was 82 in the bevacizumab group.

Retinal thickness decreased significantly for both treatment groups from baseline over 2 years, but no significant difference was noted between the groups. Patients in the ranibizumab group had a 122-µm reduction in retinal thickness from baseline; patients in the bevacizumab group had a reduction of 130 µm.

DE-109 Effective in Treating Uveitis in SAKURA

DE-109 was effective in treating uveitis in SAKURA, according to Sunil K. Srivastava, MD.1

Dr. Srivastava presented data on SAKURA, a stage 3, multinational, multicenter, randomized, double-masked clinical trial testing the safety and efficacy of intravitreal injections of DE-109 for the treatment of active, noninfectious uveitis of the posterior segment. Researchers randomized patients (n = 347) to regiments of 44 µg, 440 µg, or 880 µg every 2 months. The primary endpoint of the study was the percentage of eyes with a vitreous haze (VH) score of 0 at month 5.

At month 5, 22.8% of eyes randomized to the 440-µg regimen had a VH score of 0, compared with 10.3% in the 44-µg arm and 16.6% in the 880-µg arm (P = .025). At month 5, 52.6% of subjects in the 440-µg arm achieved a


VH score of 0 or 0.5+, compared with 43.1% in the 880-µg arm and 35% in the 44-µg arm (P = .008). Some improvements in VH score from baseline were seen as early as 2 weeks from start of treatment.

There were no cases of culture-positive endophthalmitis among the 3 study arms and 1 case of culture-negative endophthalmitis in the 880-µg arm. No patient in the 44-µg arm had noninfectious endophthalmitis, but 0.9% of patients in the 440-µg arm and 3.4% of patients in the 880-µg arm developed noninfectious endophthalmitis.

**Phase 1b/2a Study of Tie2 Activator in DME**

Therapeutic activation of the Tie2 pathway may provide a novel target for treatment of diabetic macular edema, said Daniel Matthew Miller, MD, PhD.¹

Tie2 is known to maintain normal vessel function, and its deactivation by dephosphorylation leads to pericyte loss, endothelial cell degeneration, capillary occlusion, and blood vessel barrier break down, Dr. Miller said.

“Therapeutic activation of the Tie2 pathway may provide a novel target for treatment of diabetic macular edema,” Dr. Miller said.

Protocol M was a randomized trial which examined the effect personalized intervention had on A1C levels in patients with type 1 or type 2 diabetes. Researchers randomized patients to receive a personalized education plan or normal in-office advice. Researchers determined that no significant difference in A1C levels existed between the groups at 1 year.

Dr. Jampol reported that in a randomized clinical trial, use of topical nonsteroid drops did not improve vision in patients with noncenter-involving macular edema and good vision. Patients were randomized to receive nepafenac ophthalmic suspension drops (Nevanac, Alcon) or placebo 3 times per day for 1 year. At the end of 1 year, researchers found no difference in volume of macular edema and no difference in central subfield thickness.

Analysis of Protocol I data showed that over 3 years, 9.4% of eyes that received repeated injections of ranibizumab had persistently elevated intraocular pressure (IOP), which was significant compared with the 3.3% of eyes in the sham group. The difference at 1 year (2.3% in the sham group vs 5.5% in the ranibizumab group) was not statistically significant.

“Repeated injections may be associated with increased risk of persistently elevated IOP as defined in our study,” Dr. Jampol said. Eyes which measured 22 mg Hg on 2 visits, eyes in which IOP increased by 6 mm Hg from baseline, or eyes that needed medical therapy or surgery to great elevated IOP were considered eyes with persistently elevated IOP.

Dr. Jampol reported that Protocol S, a 2-year study comparing panretinal photocoagulation versus anti-VEGF treatment for proliferative diabetic retinopathy, should be completed in December 2014.

**PACORES: Bevacizumab Less Effective for AMD at 5 years**

Bevacizumab was less effective at treating patients with AMD at 60 months compared with 36 months in PACORES, according to J. Fernando Arevalo, MD.¹

Eyes with choroidal neovascularization secondary to AMD (n = 292) treated with at least 1 intravitreal injection of 1.25 mg bevacizumab were followed for 60 months. Dr. Arevalo reported that compared with 36 months of follow up, eyes had a decrease in visual acuity, from 20/150 to 20/250, at 60 months. The difference was statistically significant. There was also an increase in central macular thickness from 36 months to 60 months.
