

ASRS RECAP

We know that the busy readers of Retina Today may not be able to attend every ophthalmology meeting. We also know that the full schedules of those present at meetings rarely allow attendees to attend every paper, roundtable, and symposium. For this reason, Retina Today offers a brief recap of some of the major topics covered at the American Society of Retina Specialists (ASRS) 2014 Annual Meeting in San Diego, California, held August 8-13, 2014. This feature is not intended to be all-inclusive; rather, it reflects our editors' picks of some of the top presentations at the meeting.

Monthly and As-Needed Treatment in the SHORE Study Resulted in Similar Visual Acuity Gains in RVO

Monthly and as-needed dosing of ranibizumab (Lucentis, Genentech) for macular edema due to central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO) resulted in similar visual acuity gains in the SHORE study, John Kitchens, MD, reported.¹

Patients with macular edema secondary to CRVO or BRVO who were stable after receiving ranibizumab treatment were enrolled in the SHORE study, a phase 4 clinical trial designed to investigate the effects continued treatment with 0.5 mg ranibizumab on patients. Patients were randomized to monthly (n = 85) or as-needed (n = 86) regimens of ranibizumab.

No significant difference was found between the slopes of BCVA mean change from baseline for the monthly and as-needed arms during months 7 to 15. Patients in the monthly treatment group had an 18.7-letter increase in BCVA from baseline; patients in the as-needed treatment group had a 21.0-letter gain from baseline.

Patients without intraretinal edema had a significantly larger mean gain in BCVA at month 7 (+9.6 letters) and month 15 (+9.3 letters; $P < .001$ at both time points).

Patients without intraretinal edema had an approximately 18% to 20% higher likelihood of gaining 15 or more letters from baseline at month 7 and month 15. They also had an approximately 29% to 33% higher likelihood of achieving 20/40 or better vision at month 7 and month 15. Both increases in likelihood of positive response were significant.

Patients in both groups had the same likelihood of achieving a dry retina at month 7 or 15. Patients with a dry retina at months 7 and 15 had a higher chance of achieving 20/40 or better visual acuity at those same time points.

1. Kitchens J. Effect of intraretinal edema on BCVA gains in patients with retinal vein occlusion receiving alternate ranibizumab dosing regimens in the SHORE study. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

Intraocular Pressure Increases Controlled with Medication in the MEAD Study

Increases in intraocular pressure (IOP) due to response to the dexamethasone intravitreal implant (Ozurdex, Allergan) were controlled medically in the MEAD study, Michael Singer, MD, reported.¹

The MEAD study was a pair of 3-year, randomized, multicenter, masked, sham-controlled, phase 3 clinical trials with identical protocols that included 1048 patients with diabetic macular edema (DME). Patients (n = 1048) were randomized 1:1:1 to receive the dexamethasone intravitreal implant in doses of 0.7 mg or 0.35 mg, or sham.

"Increased IOP was a common side effect of using the dexamethasone intravitreal implant," Dr. Singer said.

During the trial, 36.0% of patients randomized to the 0.7 mg treatment group had an IOP adverse event, and 41.5% of patients in the 0.7-mg dexamethasone arm used medication to control IOP. Similarly, 34.1% of patients randomized to the 0.35 mg treatment group had an IOP adverse event, and 37.6% of patients in the 0.35-mg arm used medication to control IOP. The decision to use medication to treat IOP increases was at the discretion of the investigator.

According to Dr. Singer, initial IOP increases mostly occurred following the first or second injection of the dexamethasone intravitreal implant, but up to 25% of events were spikes after the third, fourth, fifth, sixth, or seventh injections.

There was approximately a 75% chance of a spike occurring during the first 2 injection cycles and an approximately 85% chance of seeing a spike during the first 3 injection cycles. "If you do not get [an IOP spike]

in the first 3 cycles, there is a very small chance that you are going to see 1 going forward,” Dr. Singer said.

A higher number of doses was not related to a higher likelihood of developing an IOP spike. Patients with IOP spikes of at least 10 mm Hg in the 07-mg treatment group had similar mean visual acuity outcomes to those without IOP spikes.

1. Singer M. Intraocular pressure in patients with diabetic macular edema treated with dexamethasone intravitreal implant: MEAD study findings. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

At-Home Monitoring of Choroidal Neovascularization Led To Higher Detection Rate, Less Vision Loss Than Office Visits

Daily use of a home monitoring device (ForeseeHome device, Notal Vision) resulted in better detection of choroidal neovascularization (CNV) and showed that routine office visits did not detect CNV at a high rate when compared with device use, according to David S. Boyer, MD.¹

In the HOME study, 1520 patients were randomized to standard care or device use. Patients in the standard care arm were required to attend routine office visits to detect CNV. Patients in the device arm performed at-home testing in addition to attending routine office visits. Both groups were self-monitored and were examined following the report of symptoms. Patients in the device arm were also examined following an alert from the device.

Mean follow up was 1.4 years. Over that time period, 51 patients in the device arm and 31 patients in the standard care arm developed CNV. Patients with CNV in the device arm lost a median of 4 letters from baseline to detection of CNV (interquartile range [IQR], -11.0 to -1.0 letters); patients with CNV in the standard care arm lost a median 9 letters from baseline to detection of CNV (IQR, -14.0 to -4.0 letters; $P = .021$).

The rate of detecting incidence of CNV in the device arm (as reported by symptoms or by device alerts) was 11.6% (95% CI, 8.1%–15.2%). The detection rate for incidence of CNV in the standard care arm (as reported by symptoms) was 26% (95% CI; 15.5%–36.8%). Eyes with new incidence of CNV in the device arm when the device was used as instructed (ie, twice per week) lost a median 3 letters upon presentation due to symptoms or device alerts, and eyes with new incidence of CNV in the standard care arm lost 11.5 letters upon presentation due to symptoms ($P = .03$).

Speaking about the standard care arm, Dr. Boyer said that the “detection rate was very high. If patients come in with symptoms, there is a high chance that they have

CNV.” Still, these patients presented late in the disease course. “So you get very few visits [in the standard of care arm], but you get very poor vision results.”

Judy E. Kim, MD, reported on lesion size in eyes with incidence of CNV confirmed by fluorescein angiography or optical coherence tomography.² Eyes with CNV detected in the standard care arm ($n = 23$) had a 1.46 disc area mean lesion area. Eyes with CNV detected in the device arm ($n = 39$) had a 0.64 disc area mean lesion size ($P = .05$).

“Like many diseases, early detection of a disease increases the likelihood of better patient outcomes,” Dr. Kim said. Dr. Kim noted the importance of this data when considered alongside data from the CATT study, which, she said, found that “eyes that had small lesion size at the time of diagnosis were more likely to have better visual acuity at 1 year of treatment.”

1. Boyer DS. The Home Monitoring of the Eye (HOME) study: potential implication of findings on management of intermediate-AMD patients. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

2. Kim JE. The HOME Study: lesion characteristics of early choroidal neovascularization. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

Phase 2 Study: ESBA 1008 Noninferior to Ranibizumab

In a phase 2 study, 4.5-mg and 6.0-mg doses of ESBA 1008 were noninferior to 0.5-mg doses of ranibizumab in treatment of neovascular AMD, according to Pravin Dugel, MD.¹

“ESBA 1008 is a humanized single-chain antibody fragment that inhibits VEGF,” Dr. Dugel explained. “It is a first-of-its-kind molecule in retina. It binds with high affinity to all isoforms of VEGF-A and is a significantly smaller molecule than other treatment options.”

In a prospective, active-controlled, randomized, double-masked, single-dose ascending, multicenter, phase 2 study, patients were randomized to ESBA 1008 at doses of 0.5 mg, 3.0 mg, 4.5 mg, or 6.0 mg, or to ranibizumab 0.5 mg. The primary endpoint of the study was change in central subfield thickness from baseline at month 1.

ESBA 1008 in doses of 4.5 mg and 6.0 mg was shown to be noninferior to ranibizumab 0.5 mg for reduction of central subfield thickness. After 1 month, there was a tendency toward increased thickness in the ranibizumab group, while thickness in the ESBA 1008 4.5 mg and 6.0 mg groups stayed consistent.

At week 6, patients who received ESBA 1008 6.0 mg gained a mean 10.4 (± 9.2) letters of BCVA; patients who received 0.5 mg ranibizumab gained 6.5 (± 9.5) letters.

Rates of adverse events were low, and similar rates were seen across all treatment groups.

1. Dugel P. Results of ESBA 1008, a single-chain antibody fragment for the treatment of neovascular AMD. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

Use of Multiple Dexamethasone Intravitreal Implants for Retinal Vein Occlusion was Safe and Effective in SHASTA Study

Treatment with 2 or more dexamethasone intravitreal implants, used as monotherapy or combination therapy, for treating macular edema associated with CRVO or BRVO was safe and effective, according to Antonio Capone, MD.¹

The results of a multicenter retrospective chart review of a subgroup of patients (n = 289) in the SHASTA study showed that mean duration of macular edema was 18.4 months for patients who received 2 or more dexamethasone intravitreal implants. Most patients (86.5%) had received treatment prior to receiving dexamethasone therapy. The chart analysis found that 29.1% of patients (n = 84) were given dexamethasone intravitreal implants as monotherapy and 70.9% of patients (n = 205) were given dexamethasone intravitreal implants with adjunctive therapy. A statistically significant difference between the 2 groups was seen in mean duration of the disease at baseline: Patients in the monotherapy group had a mean duration of approximately 26 months, and those on combination therapy had a mean duration of approximately 16 months.

There was no significant difference in the mean number of dexamethasone implant injections (3.1 in monotherapy vs 3.3 in combination therapy). Mean change in BCVA was similar in the 2 groups.

The number of days between injections was greater in the combination therapy group (177 days) than in the monotherapy group (151 days; $P < .001$). Patients undergoing combination therapy had a higher incidence of increased IOP: 25.0% of patients in the monotherapy group, and 37.1% of patients receiving combination therapy had IOP of at least 25 mm Hg ($P = .048$).

"Prior steroid response to intravitreal triamcinolone was not a predictor of steroid response to [the dexamethasone intravitreal implant], speaking to the differential impact of the various steroid drugs on IOP," Dr. Capone said.

1. Capone A. Two or more dexamethasone intravitreal implants used alone vs. with adjunctive therapy in patients with RVO-associated macular edema. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

Better Baseline Characteristics Resulted in Fewer Treatments in RISE/RIDE Extension Trial

Patients at the start of the core RIDE/RISE trials with better baseline characteristics—including shorter duration of diabetes, better vision, and less edema—were more likely than those with poor characteristics to

require no additional ranibizumab injections during the trials, according to Michael Elman, MD.¹

RISE/RIE investigated the safety and efficacy of 0.5 mg ranibizumab for treatment of DME over a 36-month period. Patients with DME were randomized to 0.5 mg ranibizumab monthly or sham injection for 24 months. After 24 months, patients in the sham arm were eligible for crossover into the treatment arm.

An open-label extension study enrolled 500 patients who finished the 36-month RIDE/RISE core trials. The extension investigated the efficacy of criteria-based ranibizumab 0.5-mg as-needed treatments to maintain disease stability established in the core trials and recorded the number of treatments required to maintain vision.

During the follow-up year, 121 (24.2%) patients required no further treatment, 132 (26.4%) required 1 to 3 treatments, 159 (31.8%) required 3 to 7 treatments, and 88 (17.6%) required more than 7 treatments.

Patients in the extension trial who received no injections, compared with those who received more than 7 injections, had at baseline of the core studies a shorter duration of diabetes (by approximately 2 years), shorter time from DME diagnosis to the start of the study (by approximately 10 months), better baseline visual acuity (58.4 vs 54.3 letters), less edema (440.5 vs 525.5 μ m), and lower diabetic retinopathy severity scores.

1. Elman M. Open-label extension of the phase 3 RIDE and RISE trials—characteristics of DME patients associated with treatment frequency. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

No Difference Seen in Results Between Vitrectomized and Nonvitrectomized Eyes Receiving Ranibizumab for Diabetic Macular Edema

At 3 years, patients who underwent vitrectomy prior to receiving ranibizumab injections for DME in a DRCR.net study had similar anatomic and visual results compared with patients in the study who had not undergone vitrectomy, according to Andrew Antoszyk, MD.¹

Researchers analyzed data from the study, which enrolled patients with DME (n = 360) and randomized them to receive ranibizumab with prompt laser or ranibizumab with deferred laser. All eyes in the study had baseline visual acuity of between 20/32 and 20/320 and had center-involved DME with central subfield thickness of at least 250 μ m.

No significant visual acuity differences were noted between vitrectomized (n = 25) and nonvitrectomized (n = 335) eyes at any point during the 3-year treatment protocol. Minor anatomic differences favoring the nonvitrectomized group appeared on OCT at the

16-week and 32-week follow-up visits, but no differences in thickness between the groups was observed after 1 year. Similarly, vitrectomized eyes required a greater number of injections than did nonvitrectomized eyes during the first year of the study, but no difference in the total number of injections was noted at 3 years.

1. Antoszyk AN. Effect of ranibizumab for DME in eyes with vitrectomy prior to anti-vascular endothelial growth factor treatment. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

Ranibizumab Appeared Safe and Well-Tolerated in Patients with Choroidal Melanoma, Helped Preserve Vision

Patients with choroidal melanoma who received ranibizumab in combination with proton beam irradiation had high rates of visual acuity at 2 years, according to Ivana Kim, MD.¹ The anti-VEGF agent appeared to be safe and well-tolerated in these patients.

In a phase 1, investigator-sponsored pilot study of 40 patients with choroidal melanoma who were scheduled for proton beam irradiation, patients were divided into 2 groups: those with large tumors (>15 mm in diameter or >5 mm in height; n = 15) and those with small tumors (<15 mm in diameter and <5 mm in height; n = 20). Those with large tumors received 0.5 mg ranibizumab starting approximately 2 weeks before proton beam irradiation and then bimonthly for 2 years. Those with small tumors received 0.5 mg or 1.0 mg ranibizumab on a similar schedule.

Of the 40 patients enrolled in the study, 30 have completed 12 months of follow up and 20 have completed 24 months of follow up. In the large tumor group, 7 patients discontinued the study; 1 patient in the small tumor group discontinued the study.

At 12 months and 24 months, 100% of patients in the small tumor group had visual acuity of 20/200 or better. Of the patients in the large tumor group, 67% of patients at 12 months had visual acuity of 20/200 or better; at 24 months, 86% of patients had visual acuity of 20/200 or better.

Researchers compared results from this study to results from historical controls, which were selected to match age, sex, and tumor characteristics of the patients in this study. In the study population, a significantly greater proportion of patients treated with ranibizumab had visual acuity of 20/200 or better at month 12 when compared with historical controls. Similarly, a significantly greater proportion of ranibizumab-treated patients in the study population had visual acuity of 20/40 or better at month 12 compared with historical controls.

At 24 months, the significantly significant difference persisted for both the large and small tumor subgroups.

A significantly greater proportion of ranibizumab-treated patients in the study population had visual acuity of 20/40 or better at month 24 when compared with historical controls; this significance existed for both the large and small tumor subgroups.

No serious ocular or systemic adverse events related to ranibizumab were observed. One death occurred due to metastasis during the study. None of the patients in the large tumor group developed neovascular glaucoma. Median tumor regression was not different between the study cohort and historical controls, Dr. Kim said.

1. Kim I. Ranibizumab in combination with proton beam irradiation for choroidal melanoma. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

Cost of Aflibercept and Ranibizumab for Age-Related Macular Degeneration Similar, Claims Data Showed

The cost of using aflibercept (Eylea, Regeneron) or ranibizumab to treat AMD over 6 months or 12 months was similar in a review of US claims data from November 18, 2011, to July 31, 2013, according to Szilárd Kiss, MD.¹ Additionally, the injection frequency over the study's time period did not differ.

Researchers reviewed claims data from patients who were older than 18 years at the time of injection, had no evidence of bilateral disease, had AMD at the time of injection, and continued use of the same anti-VEGF agent during a 6-month or 12-month follow up period.

Mean injection frequency for treatment with aflibercept or ranibizumab for AMD was similar over 6-month and 12-month periods: Over 6 months, patients averaged 3.7 injections of aflibercept or ranibizumab, and over 12 months they averaged 5.0 injections of aflibercept or ranibizumab.

Mean costs of treatment over 6 months were \$6757 for aflibercept and \$7277 for ranibizumab; over 12 months, the costs were \$10 288 for aflibercept and \$9894 for ranibizumab. The differences in cost were not statistically significant. ■

1. Kiss S. The pattern of anti-VEGF use in neovascular age-related macular degeneration and diabetic macular edema: a US claims analysis. Paper presented at: American Society of Retina Specialists 2014 Annual Meeting; August 9-13, 2014; San Diego, CA.

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