Hot Topics: Tools for Improving Glaucoma Management

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Double-masked, randomized, dose-response study of AR-13324 Ophthalmic Solution compared to latanoprost in patients with elevated intraocular pressure

AR-13324 is a new class of ocular hypotensive that inhibits both Rho kinase and norepinephrine transporter increasing trabecular outflow and decreasing aqueous production. Study objectives were to evaluate the hypotensive efficacy, ocular and systemic safety, of AR-13324 compared to latanoprost.

Methods: Patients with open-angle glaucoma or ocular hypertension were randomized to receive either AR-13324 0.01% or 0.02% q.d. (PM) or latanoprost q.d. (PM) for 28 days.

224 patients were randomized (baseline IOP’s 22-36 mm Hg). Mean unmedicated diurnal baseline was 25 to 26 mm Hg across groups. On Day 28 mean diurnal IOP decrease from baseline was 5.5, 5.7 and 6.8 mm Hg in AR-13324 0.01%, 0.02% and latanoprost respectively (p < 0.0001). The difference between AR-13324 0.02% and latanoprost was 1.2 mm Hg (p=0.009). In a pre-specified analysis of patients <26mmHg (n=106) the difference was 0.2 mm Hg (p=0.754) demonstrating equivalence to latanoprost at baselines < 26mmHg, due to AR-13324 maintaining efficacy regardless of baseline, while latanoprost lost efficacy at lower baselines. The only drug-related safety finding of note for AR-13324 was mild to moderate conjunctival hyperemia. AR-13324 0.02% produced clinically and statistically significant reductions in IOP and was approximately 1mmHg less effective than latanoprost in patients with baseline IOPs in the range of 22 – 36 mm Hg. However AR-13324 0.02% was equivalent to latanoprost in patients with baseline IOPs in the range of 22 – 26 mm Hg. In this 28-day study, AR-13324 was effective and well tolerated in patients with glaucoma and ocular hypertension.

Rate of Retinal Nerve Fiber Layer thickness loss in eyes with and without glaucoma

To investigate rates of global and regional retinal nerve fiber layer (RNFL) loss in normal (NML) and primary open angle glaucoma (POAG) eyes.

From an ongoing prospective, longitudinal study, we identified 83 POAG and 63 NML subjects who had 3 or more RNFL scans over a 2-year period. We used SD-OCT to measure circumpapillary RNFL thickness and recorded global, inferior, nasal, superior and temporal thickness values for each eye. We calculated rates of change for each parameter in each group, and investigated time-related trends with analysis of variance. To investigate structure/function relationships, we also recorded visual field index (VFI) slope and mean defect (MD) values from 24-2 visual field tests that were obtained during the same timeframe as the RNFL measures.

POAG eyes had a mean of 5.9 scans over an interval of 2.6 ± 0.4 years and NML eyes had a mean of 3.3 scans over an interval of 2.1 ± 0.8 years. Mean rate of global RNFL thinning was significantly greater in POAG (slope = -0.96 µm/year [95% CI: 1.76, -3.68]) compared to NML (slope = -0.05 µm/year [95% CI: 3.72, -3.82]). When examined by sector, the superior, inferior, and temporal RNFL in POAG eyes all significantly decreased over time while only inferior RNFL significantly decreased over time in NML eyes. When rate of visual field loss was evenly split into fast and slow rates of progression, the rate of global, superior, inferior, and nasal RNFL loss was greater in eyes with faster rate of visual field loss compared to eyes with slower rate of VF loss. Despite the short timeframe of this study, reduction of RNFL thickness was faster in POAG than NML eyes. Rate of RNFL loss was correlated, though weakly, with rate of visual field loss. While these findings support the use of using serial measures of RNFL for monitoring glaucoma, further investigation is needed to determine optimal strategies for clinical use of these parameters.
Influence of Optic Disc Size and Neuro-retinal Rim Configuration on Accurate Identification of Glaucomatous Optic Neuropathy

To determine the influence of optic disc size on practitioners ability to accurately identify glaucomatous optic neuropathy in optic nerve photographs and to determine the correlation of the ISNT rule with normal and glaucomatous optic nerves.

After consent, 261 attendees in the exhibit hall at an optometric meeting volunteered to participate in this study. Each subject evaluated stereoscopic photographs of 6 optic nerves and answered the following 3 yes/no questions for each photo. Each participant viewed both normal and glaucomatous optic nerves in three sizes (small, medium and large).

1) Does this optic nerve follow the ISNT rule?
2) Is this optic nerve glaucomatous?
3) Based on this optic nerve appearance, is this a patient you would typically order an OCT for further glaucoma evaluation?

Logistic regression analyses using SAS Version 9.2 were completed to investigate the impact of nerve type and size on each of the three outcomes.

Optic disc size had a statistically significant influence on the accuracy of glaucoma identification (p<0.0001). The effect was most evident in large, normal nerves and in small, glaucomatous nerves that were correctly identified only 34.2% and 8.8% of the time respectively. While there was a statistically significant difference in the likelihood of the ISNT rule not being followed in medium and large glaucomatous nerves as it was in medium and large normal nerves (p<0.0001), the same was not true for small nerves. In fact, small glaucomatous nerves were more likely than small normal nerves to be perceived as following the ISNT rule (p<0.0001).

Optic disc size is an important component to accurately diagnose glaucoma. Whether done subjectively or with the aid of an objective imaging device, all optic nerve assessments for glaucoma should include optic disc size evaluation. To avoid the risk of underdetection, a thorough evaluation is warranted to determine glaucomatous risk when small optic nerves are noted.