
PURPOSE: To evaluate the pharmacokinetics of ciliary neurotrophic factor (CNTF) delivered over a period of up to 2 years by an intraocular encapsulated cell technology (ECT) implant in patients with retinitis pigmentosa (RP) and geographic atrophy (GA). METHODS: Patients from phase 1 RP (CNTF1); phase 2 GA (CNTF2); and phase 2 late and early stage RP (CNTF3, and CNTF4) studies received an ECT-CNTF implant, designated as "NT-501," in one eye. Per protocol, all implants (n = 10) were removed at 6 months from the CNTF1 study patients. Explant for the phase 2 studies was optional, but several patients were explanted at 12, 18, and 24 months post implant. A small amount of vitreous sample was collected at the time of explant. The rate of CNTF secretion from the explants and the corresponding vitreous CNTF levels were evaluated for each time point. Serum samples from these patients were evaluated for CNTF, anti-CNTF antibodies, and antibodies to the encapsulated cells. RESULTS: NT-501 implants produced CNTF consistently over a 2-year period. The calculated half-life of CNTF in the vitreous continuously delivered by ECT implants was 51 months, with CNTF levels statistically equivalent between the 6- and 24-month implant period. CNTF, anti-CNTF antibodies, and antibodies to the encapsulated cells were not detected in the serum of patients. CONCLUSIONS: This retrospective study demonstrated that the intraocular ECT implant has a favorable pharmacokinetic profile for the treatment of chronic retinal degenerative diseases without systemic exposure.


Lutein and zeaxanthin are lipid-soluble antioxidants found within the macula region of the retina. Links have been suggested between increased levels of these carotenoids and reduced risk for age-related macular disease (ARMD). Therefore, the effect of lutein-based supplementation on retinal and visual function in people with early stages of ARMD (age-related maculopathy, ARM) was assessed using multi-focal electroretinography (mERG), contrast sensitivity and distance visual acuity. A total of fourteen participants were randomly allocated to either receive a lutein-based oral supplement (treated group) or no supplement (non-treated group). There were eight participants aged between 56 and 81 years (65·50 (sd 9·27) years) in the treated group and six participants aged between 61 and 83 years (69·67 (sd 7·52) years) in the non-treated group. Sample sizes provided 80 % power at the 5 % significance level. Participants attended for three visits (0, 20 and 40 weeks). At 60 weeks, the treated group attended a fourth visit following 20 weeks of supplement withdrawal. No changes were seen between the treated and non-treated groups during supplementation. Although not clinically significant, mERG ring 3 N2 latency (P = 0·041) and ring 4 P1 latency (P = 0·016) increased, and a trend for reduction of mERG amplitudes was observed in rings 1, 3 and 4 on supplement withdrawal. The statistically significant increase in mERG latencies and the trend for reduced mERG amplitudes on withdrawal are encouraging and may suggest a potentially beneficial effect of lutein-based supplementation in ARM-affected eyes.

PURPOSE: To evaluate methods which account for both eyes as a single, independent variable in glaucoma clinical trials. METHODS: A review of clinical trial articles published between January 1995 and April 2011 evaluating currently used topical glaucoma medications. RESULTS: This analysis included 17 articles with 36 treatment arms of which 14 were prostaglandins, 13 β-blockers, 6 topical carbonic anhydrase inhibitors and 3 α-agonists. Twenty-four articles used average intraocular pressure (IOP) analysis, 12 used the highest IOP analysis and none utilized the randomized eye method. At untreated baseline, there was a difference in the IOP between average IOP and highest baseline IOP analyses at 8 a.m. (p = 0.001) and for the diurnal curve (p = 0.02) as well as specifically for β-blockers (p = 0.002) at 8 a.m. and β-blockers for the diurnal curve (p = 0.01). CONCLUSIONS: This study suggests that the highest IOP analysis method generally provides slightly higher IOPs at baseline than the average IOP analysis method.


OBJECTIVE: To review the pharmacology, pharmacokinetics, clinical trial data, efficacy data, and adverse effect incidence of tafluprost. DATA SOURCES: A literature search was completed using PubMed, Web of Science, and Google Scholar. Tafluprost was the primary search term. Articles published between January 2008 and April 2012 were included in this review. Additional limits placed on the searches were “human” and “English.” Citations in which tafluprost appeared in the title were 36, 29, and more than 300 in PubMed, Web of Science, and Google Scholar, respectively. STUDY SELECTION AND DATA EXTRACTION: Three clinical trials were included in this review. One trial enrolled more than 500 subjects in a randomized fashion. Another also enrolled more than 500 subjects, although the study design was not randomized. The third trial evaluated the effects of tafluprost on subjects who had recently discontinued use of latanoprost, another prostaglandin that is approved to treat glaucoma and ocular hypertension. The duration of all 3 trials was 12 weeks. DATA SYNTHESIS: Tafluprost 0.0015% is the first topical prostaglandin approved by the Food and Drug Administration for treatment of open-angle glaucoma and ocular hypertension that does not contain the widely used preservative, benzalkonium chloride (BAK). Although some controversy surrounds the long-term safety of exposure to BAK, clinical trial data are inconclusive. Tafluprost, like other prostaglandin analogues, exerts its effects on prostaglandin F receptors to reduce intraocular pressure (IOP). Results from 1 trial demonstrated significant reductions in IOP when monotherapy was switched to tafluprost monotherapy. Reductions in IOP with tafluprost use were compared with those seen with use of timolol and latanoprost in 2 trials, and noninferiority was observed. Significant reductions in tear osmolality were noted in subjects who changed from latanoprost, another prostaglandin analogue, to tafluprost therapy. Conjunctival hyperemia is the most common adverse effect seen in patients receiving drugs from this class. Many have also reported stinging, ocular pruritus, increased darkening or growth of eyelashes, and darkening of eyelids, as well as irreversible brown pigmentation of the iris. CONCLUSIONS: Clinical trial data suggest that tafluprost is as efficacious as other agents used in the management of ocular hypertension and glaucoma. Its use may be especially advantageous in people with allergies, sensitivities to preservatives, or dry or sensitive eyes.


PURPOSE: To study the effect of patient education and the TravAlert®-Eyot® drop guider on intraocular pressure (IOP) and adherence in patients with primary open angle glaucoma (POAG) or ocular hypertension (OHT) monitored with the TravAlert® dosing aid. METHODS: Multicentre, randomized, controlled clinical trial among 18 Dutch hospitals. Patients were randomized to one of the four study arms: (1) use of the dosing aid, (2) use of the dosing aid with the drop guider, (3) use of the dosing aid together with patient education or (4) use of the dosing aid and drop guider together with patient education. IOP was recorded at baseline and after 3 and 6 months. Data on adherence generated by the dosing aid were collected and studied at the end of the study. RESULTS: Mean IOP dropped from 20.3 ± 5.7 mmHg at baseline to 16.3 ± 4.0 mmHg (right eye) after 6 months and from 20.2 ± 5.9 mmHg to 16.4 ± 4.1 mmHg (left eye). The mean adherence rate was 0.91 ± 0.1. IOP and adherence rate were not statistically different between the study arms. Patients with ‘drug holidays’ had a significantly higher mean IOP after 6 months. Patients who used the drop guider were less adherent. A lower adherence level was also associated.
with new patients with glaucoma and patients with a lower level of knowledge on glaucoma. CONCLUSION: Patient education is especially useful for new patients with glaucoma. The use of a drop guider does not improve adherence. Especially patients with 'drug holidays' are at risk for developing uncontrolled IOP levels.


PURPOSE: To compare the 2-year efficacy of phacoemulsification and intraocular lens implant (phaco/IOL) with laser peripheral iridotomy (LPI) in the early management of acute primary angle closure (APAC) and coexisting cataract. DESIGN: Randomized, controlled trial. PARTICIPANTS: We included 37 subjects presenting with APAC who had responded to medical treatment such that intraocular pressure (IOP) was ≤30 mmHg within 24 hours, and had cataract with visual acuity of ≤6/15. MAIN OUTCOME MEASURES: The primary outcome measure was failure of IOP control defined as IOP between 22 to 24 mmHg on 2 occasions (readings taken within 1 month of each other) or IOP ≥25 mmHg on 1 occasion, either occurring after week 3. Secondary outcome measures were complications, degree of angle opening, amount of peripheral anterior synechiae, visual acuity, and corneal endothelial cell count (CECC). METHODS: Subjects were randomized to receive either LPI or phaco/IOL in the affected eye within 1 week of presentation and were examined at fixed intervals over 24 months. Patients underwent a standardized examination that included Goldmann applanation tonometry, gonioscopy, and CECC measurements. Logistic regression was used to estimate the effect of treatment on failure of IOP control. Time to failure was evaluated using the Kaplan-Meier technique and Cox regression was used to estimate the relative risk of failure. RESULTS: There were 18 patients randomized to LPI and 19 to phaco/IOL. The average age of subjects was 66.0±9.0 years and mean IOP after medical treatment was 14.5±6.9 mmHg. The 2-year cumulative survival was 61.1% and 89.5% for the LPI and phaco/IOL groups, respectively (P = 0.034). There was no change in CECC for either group from baseline to month 6. There was 1 postoperative complication in the phaco/IOL group compared with 4 in the LPI group (P = 0.180). CONCLUSIONS: Performed within 1 week in patients with APAC and coexisting cataract, LPI resulted in lower rate of IOP failure at 2 years compared with LPI.

DRY EYE


SARcode Bioscience, Inc., announced topline results from OPUS-1, a pivotal Phase 3 study of lifitegrast ophthalmic solution, 5.0%, versus placebo for the treatment of dry eye disease. In the study, which included 588 subjects, lifitegrast demonstrated superior over placebo in the improvement of inferior and total corneal staining scores from baseline to week 12 (P=0.0007 and P=0.0148, respectively). Ocular surface damage, which is a hallmark of chronic inflammation from dry eye disease, is often detected using these staining parameters. Lifitegrast also significantly improved the most commonly reported symptoms of dry eye disease in the study, which were ocular discomfort and eye dryness. The mean ocular discomfort score and mean eye dryness score were lower in the lifitegrast group than in the placebo group at week 12 (P=0.0273 and P=0.0291, respectively). Lifitegrast was well tolerated and there were no unexpected or serious ocular adverse events. The most commonly reported ocular adverse events were irritation and pain upon initial instillation of lifitegrast, and were generally mild and transient in nature. “We are pleased that lifitegrast demonstrated impressive results in corneal staining parameters, since this has been historically challenging in the development of new therapies for patients with dry eye disease” commented Charles Semba, MD, Chief Medical Officer of SARcode Bioscience. “It is especially encouraging that common symptoms of dry eye disease were also reduced, providing evidence that improvement of the ocular surface may ameliorate symptoms of the disease.” SARcode Bioscience recently commenced a year-long safety study (SONATA) and will soon begin a second pivotal Phase 3 confirmatory study (OPUS-2). Both studies will support a planned New Drug Application filing. “Dry eye is a debilitating disease affecting 25 million patients in the US, and contributes to significant social and economic costs,” said Quinton Oswald, Chief Executive Officer of SARcode Bioscience. “Our team has spent several years developing this novel molecule specifically for dry eye disease. We are very pleased to continue advancing the program so patients suffering from this disease may have additional therapeutic options in the future.” Data from the OPUS-1 study will be presented during the Late Breaker Session at the upcoming American Academy of Ophthalmology meeting.

OBJECTIVE: To assess the effect of the use of containers with an adapted sterilizing filter on the contamination of autologous serum eyedrops. DESIGN: Prospective, consecutive, comparative, and randomized study. PARTICIPANTS: Thirty patients with Sjögren’s syndrome. METHODS: One hundred seventy-six autologous serum containers used in home therapy were studied; 48 of them included an adapted filter (Hyabak; Thea, Clermont-Ferrand, France), and the other 128 were conventional containers. Containers equipped with a filter were tested at 7, 14, 21, and 28 days of use, whereas conventional containers were studied after 7 days of use. In addition, testing for contamination was carried out in 14 conventional containers used during in-patient therapy every week for 4 weeks. In all cases, the preparation of the autologous serum was similar. Blood agar and chocolate agar were used as regular culture media for the microbiologic studies, whereas Sabouraud agar with chloramphenicol was the medium for fungal studies. MAIN OUTCOMES MEASURES: Microbiologic contamination of containers with autologous serum eyedrops. RESULTS: Only one of the containers with an adapted sterilizing filter (2.1%) became contaminated with Staphylococcus epidermidis after 1 month of treatment, whereas the contamination rate among conventional containers reached 28.9% after 7 days of treatment. The most frequent germs found in the samples were coagulase-negative Staphylococcus (48.6%). With regard the containers used in the in-patient setting, 2 (14.3%) became contaminated after 2 weeks, 5 (35.7%) became contaminated after 3 weeks, and 5 (50%) became contaminated after 4 weeks, leaving 7 (50%) that did not become contaminated after 1 month of treatment. CONCLUSIONS: Using containers with an adapted filter significantly reduces the contamination rates in autologous serum eyedrops, thus extending the use of such container by the patients for up to 4 weeks with virtually no contamination risks.


PURPOSE: To compare changes in reading performance parameters after implantation of 4 multifocal intraocular lens (IOL) models and a monofocal IOL. SETTING: Department of Ophthalmology, Paracelsus Medical University, Salzburg, Austria. DESIGN: Prospective randomized controlled clinical trial. METHODS: Patients with bilateral cataract without additional ocular pathology were scheduled for bilateral implantation of AcriSmart 48S monofocal, Acrysof Restor SN6AD3 apodized multifocal, AT LISA 366D diffractive multifocal, Tecnis ZMA00 diffractive multifocal, or Rezoom refractive multifocal IOLs. Bilateral corrected and uncorrected reading acuity, reading distance, mean and maximum reading speeds, and smallest log-scaled print size of a Radner reading chart were evaluated under bright lighting conditions (500 lux) using the Salzburg Reading Desk. Pupil size was not measured throughout the trial. The minimum follow-up was 12 months. RESULTS: The diffractive multifocal groups had
significantly better uncorrected reading acuity and uncorrected smallest print size than the monofocal and refractive multifocal groups 1, 6, and 12 months postoperatively. The diffractive IOL groups had comparable uncorrected reading distance of approximately 32 cm, which was larger in the monofocal group (38.9 ± 8.4 cm) and refractive multifocal group (37.1 ± 7.3 cm) at the last visit. Patients with diffractive IOLs could read print sizes of approximately 0.74 to 0.87 mm, which was much better than in the monofocal and refractive multifocal groups. The diffractive AT LISA IOL provided the best reading speed values (mean and maximum, corrected and uncorrected). CONCLUSION: Multifocal IOLs with a diffractive component provided good reading performance that was significantly better than that obtained with a refractive multifocal or monofocal IOL. 

REFRACTIVE SURGERY


PURPOSE: To investigate the effect of omega-3 oral nutritional supplementation on corneal reepithelialization, visual acuity, and tear stability after photorefractive keratectomy (PRK). METHODS: This is a prospective, randomized, single-blinded controlled therapeutic trial using omega-3 oral nutritional supplements (TheraTears Nutrition for Dry Eyes; Advanced Vision Research-Akorn, Ann Arbor, MI) conducted at our center. Eighteen healthy patients with refractive error between -1 and -8 diopters were recruited and had bilateral PRK. The treatment group (n = 9 subjects) received omega-3 2 weeks before surgery through 1 month after PRK. The control group (n = 9 subjects) was not given omega-3. Epithelial defects were photographed on postoperative days 0 to 5. Reepithelialization (area in square millimeters) was assessed by fluorescein staining until healing. Tear breakup time (TBUT) and uncorrected distance visual acuity were measured at 1 week, and 1 and 3 months postoperatively. RESULTS: Epithelial defect in the treatment group eyes healed faster compared with that of the controls (P = 0.04). The treatment group eyes healed at an average rate of 1.19% [SD = 0.002; 95% confidence interval (CI), 1.04%-1.34%] per hour, versus 0.83% (SD = 0.0008; 95% CI, 0.77%-0.89%) for controls (Mann-Whitney rank-sum test, P < 0.001). The treatment group eyes maintained a significantly longer TBUT from week 1 through 3 months (mean = 9.52 seconds, SD = 0.81; 95% CI, 8.93-10.10), compared with the controls (mean = 5.52 seconds, SD = 0.81; 95% CI, 4.93-6.10; P < 0.001), and all reached 20/20 vision versus only 4 in the control group 1 month after surgery (P = 0.03). CONCLUSIONS: Omega-3 oral nutritional supplements decreased the average time for epithelial healing, and improved TBUT and visual acuity recovery in PRK. These findings suggested that omega-3 oral nutritional supplementation may be a beneficial adjunct therapy for PRK patients.