Effect of Latanoprost on Aqueous Humor Dynamics with an Objective Method of Episcleral Venous Pressure Measurement in Normal Eyes


Purpose: Mechanisms of action of latanoprost have not been completely understood. Its primary action appears to be on the uveoscleral outflow pathway, but some studies have also suggested increased outflow facility. As well, the effect of latanoprost on episcleral venous pressure (EVP) remains poorly understood. In this study we evaluated the effect of latanoprost on all aqueous humor dynamic (AHD) parameters in normal subjects.

Methods: Forty-eight eyes from 24 normal subjects (6 males, 18 females; 52±8 years, mean±SD) were included as part of a larger study (NCT01677507, ClinicalTrials.gov) to examine the variation of IOP response. The following AHD parameters were assessed: IOP by pneumatonometry; EVP by using a computer-controlled episcleral venomanometer with video recording and processing to determine the pressure required to initiate collapse of the vein; aqueous humor flow by fluorophotometry; outflow facility by 2-minute pneumatonography and uveoscleral outflow calculated by using the modified Goldmann equation. After 7 days treatment with latanoprost 0.005% OU daily, AHD parameters were remeasured. Changes in IOP, EVP, outflow facility and aqueous flow in response to latanoprost were analyzed by using generalized estimating equation models to account for possible correlation between fellow eyes of the same subject.

Results: IOP decreased from 13.2±2.2 mmHg to 11.4±1.6 (mean ± SD, P<0.001), and EVP decreased from 6.6±1.5 mmHg to 6.1±1.6 (P=0.047). Topographic outflow facility increased from 0.21±0.07 μl/min/mmHg to 0.26±0.08 (P<0.001). There was no significant change in either aqueous humor flow rate (2.6±0.52 μl/min at baseline and 2.6±0.65 after treatment, P=0.9) or uveoscleral outflow rate (1.31±0.9 μl/min at baseline and 1.24±1.0 after treatment, P=0.7).

Conclusions: Our complete assessment of AHD parameters indicates that latanoprost increases tonographic outflow facility but not the pressure-insensitive uveoscleral outflow rate. This suggests that any changes in the uveoscleral pathway with latanoprost treatment may be related to the development of IOP-dependent (not pressure-insensitive) flow. The small decrease in EVP is possibly due to vasodilatation of episcleral veins. Future AHD studies in ocular hypertensive and glaucoma patients are required to better understand if the mechanisms of action are similar in other patient populations.

Commercial Relationships: Arash Kazemi, None; Jay W. McLaren, None; Shuai-Chun Lin, None; Carol B. Toris, None; Vikas Gulati, None; David M. Reed, None; Sayoko E. Moroi, None; Arthur J. Sit, None

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Clinical Trial: NCT01677507

Efficacy and safety of fixed-dose combination brinzolamide 1%/brimonidine 0.2% as adjunctive therapy to prostanlgandin analogs in patients with elevated intraocular pressure: Results from pooled analysis of two multicenter, randomized studies

Doug Hubatsch, Tony Realiini.

Purpose: Brinzolamide 1%/brimonidine 0.2% fixed combination (BBFC) is an effective intraocular pressure (IOP)-lowering therapy in adult patients with open-angle glaucoma or ocular hypertension. Here, we discuss the pooled analysis of two studies that evaluated the IOP lowering efficacy and safety of BBFC when added to prostanlgandin analog (PGA) therapy in patients with open-angle glaucoma or ocular hypertension.

Methods: Both were multicenter, randomized, double-masked, parallel-group studies conducted in the United States (study 1, NCT01937299; study 2, NCT01937312). Patients discontinued prior glaucoma medications and received once-daily PGA (study 1: travoprost 0.004%; study 2: latanoprost 0.005%, bimatoprost 0.01%, or travoprost 0.004%) for a four-week run-in period. Eligible patients were randomized to BBFC or a vehicle thrice-daily along with PGA once-daily for six weeks. Key efficacy endpoints were (1) mean diurnal IOP and between-group difference in mean diurnal IOP at week 6 and (2) mean diurnal IOP change, and mean between-group difference in diurnal IOP change from baseline to week 6. Adverse events (AEs) were monitored in both studies.

Results: In all, 411 patients were included in the intent-to-treat population (BBFC+PGA, n=201; vehicle+PGA; n=210). Mean patient age was 66.0 years, 61.3% patients were female and 74.9% were diagnosed with open-angle glaucoma. Mean diurnal IOP at baseline was 22.6±2.3 mmHg with BBFC+PGA and 22.5±2.6 mmHg with vehicle+PGA. Least squares (LS) mean ± standard error (SE) diurnal IOP at week 6 was 17.3±0.3 mmHg with BBFC+PGA and 20.5±0.3 mmHg with vehicle+PGA. Between-group difference was −3.3±0.4 mmHg (P<0.0001). LS mean ± SE diurnal IOP reduction from baseline to week 6 was −5.4±0.3 mmHg vs. −2.1±0.2 mmHg (difference, −3.3±0.3 mmHg; P<0.0001) with BBFC+PGA vs. vehicle+PGA, respectively. The most common treatment-emergent AE was blurred vision (BBFC+PGA, 7.6%; vehicle+PGA, 5.2%). AE-related study discontinuations were reported for 11% and 0.5% patients receiving BBFC+PGA and vehicle+PGA, respectively.

Conclusions: Treatment with BBFC in combination with PGA is effective and shows an additive effect in lowering IOP. AEs were similar to the known BBFC and PGA safety profiles.

Commercial Relationships: Doug Hubatsch, Novartis Pharmaceutical Corporation (E); Tony Realini, Inotek (C), Smith and Nephew (C), Bausch and Lomb (C), Alcon (C)

Support: The study was sponsored by Alcon Research, Ltd., Fort Worth, Texas

Clinical Trial: 1. NCT01937299 and 2. NCT01937312

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**Difference in intraocular pressure following involuntary switch from bimatoprost 0.03% to bimatoprost 0.01% in glaucoma patients**

Kristy Nguyen1, Kareem Moussa2, Jason Chien1, Robert L. Stamper2.
1Chicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, IL; 2Department of Ophthalmology, University of California, San Francisco, San Francisco, CA; 3School of Medicine and Health Sciences, George Washington University, Washington, DC.

**Purpose:** To determine the difference in IOP in patients with glaucoma following an involuntary switch from bimatoprost 0.03% to bimatoprost 0.01%

**Methods:** This retrospective chart audit was performed at an academic institution in San Francisco, California. Patients who were switched from bimatoprost 0.03% to 0.01% between June 2012 to June 2014 and had at least two recorded intraocular pressures before and after the January 2013 switch date were included. Patients with an insufficient number of records of IOP’s, other medication switches, glaucoma or cataract surgery, laser trabeculoplasty, or intravitreal injections during the study period were excluded. A linear mixed effects regression model was used to estimate the difference of IOP.

**Results:** A total of 53 eyes met the criteria for inclusion and their results are presented here. The mean patient age was 70.54 ± 13.16 (mean ± SD). Mean IOP’s in glaucoma patients with use of Bimatoprost 0.03% and 0.01% were 15.1 mmHg (CI=14.3-15.8) and 16.0 mmHg (CI=15.2-16.7), respectively (p=0.0027). Mean difference (adjusted for time) was 1.01 mm Hg. The range of difference was from -5.75 mmHg to 6.00 mmHg. 8 of 53 eyes (15.1%) had a pressure rise of ≥ 3 mm Hg. No IOP differences were found in subgroups by age, race, gender and glaucoma type.

**Conclusions:** Switching from bimatoprost 0.03% to bimatoprost 0.01% led to a small but statistically significant increase in intraocular IOP. The range of differences suggest that, in some patients, the difference could, in fact, be clinically significant. A prospective study would be helpful in determining if the differences noted in retrospective are real.

**Commercial Relationships:** Kristy Nguyen, None; Kareem Moussa, None; Jason Chien, None; Robert L. Stamper, None

**Support:** Supported in part by Research to Prevent Blindness, The Fortisium Foundation, and That Man May See.

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**Efficacy and safety of a new preservative-free fixed combination latanoprost-timolol (T2347) for open-angle glaucoma or ocular hypertension**

Jonathan C. Clarke1, Cosme Lavin-Dapena2, Tomasz Zarnowski3, Norbert Pfeiffer4, Jean Philippe Nordmann5, Ingeborg Stalmans6, 1Glucoma, Moorfields Eye Hospital, London, United Kingdom; 2Servicio de Optalmología, Hospital La Paz, Madrid, Spain; 3SPSK, LUBLIN, Poland; 4University Medical Center Mainz, Mainz, Germany; 5OPHTHALMOLOGY, CHNO des Quinze-Vingts, PARIS, France; 6Glucoma Unit, University Hospitals, LEUVEN, Belgium.

**Purpose:** To compare the effect on IOP and safety of unpreserved fixed combination latanoprost-timolol (T2347) to established benzalkonium chloride (BAC)-preserved latanoprost-timolol (BPLT, Xalacom®) in patients with ocular hypertension (OHT) or open-angle glaucoma (OAG).

**Methods:** Phase III, randomised, parallel-group, investigator-masked study conducted in 10 countries. Male or female patients aged ≥18 years with OAG or OHT in both eyes controlled with BPLT were randomised at Day 0 (D0) to receive T2347 (N=127) or BPLT (N=115) each evening for 84 days. Efficacy on intraocular pressure (IOP) was measured in the morning of D0, D42, and D84, and non-inferiority of T2347 to BPLT was tested statistically based on the change in IOP from D0 to D84. Safety parameters were also reported.

**Results:** The mean change in IOP from baseline to D84 was -0.49±1.80 mmHg for preservative-free T2347 and -0.49±2.25 mmHg for preserved BPLT. These results met the limits set for non-inferiority. Similar results were observed at D42. T2347 was better tolerated than BPLT in terms of ocular irritation/burning/ stinging on instillation on D42 (p=0.003) and D84 (p<0.001), and itching on D84 (p=0.010). Itching throughout the day was also less severe for T2347 than on BPLT on D84 (p<0.001).

**Conclusions:** Preservative-free fixed combination latanoprost-timolol formulation showed similar efficacy and better tolerability than BPLT, suggestive of a therapeutic advantage of the preservative-free formulation for chronic use in patients with OAG/OHT.

**Commercial Relationships:** Jonathan C. Clarke, Laboratoires THEA (R); Cosme Lavin-Dapena, LABORATOIRES THEA (R); Tomasz Zarnowski, LABORATOIRES THEA (R); Norbert Pfeiffer, Laboratoires THEA (R); Jean Philippe Nordmann, Laboratoires THEA (R); Ingeborg Stalmans, Laboratoires THEA (R)

**Clinical Trial:** 2013-005222-29
in terms of IOP reduction 3 months after TE (adjusted means -8.12 mmHg versus -8.30 mmHg; Difference: 0.18; 95% CI -1.91 to 2.26, p=0.8662). Similar results were found 6 months after TE (-9.13 mmHg versus -9.06 mmHg; p=0.9401). Both groups had similar results concerning the appearance of the filtering bleb, corneal staining, and numbers of treatments with 5-FU, needlings and suture lyses. But more patients reported AEs in the acetazolamide/dexamethasone group than in the dorzolamide/timolol group.

**Conclusions:** Preoperative dorzolamide/timolol is equally effective as preoperative acetazolamide/dexamethasone and has a favourable safety profile. Both groups showed a similar bleb appearance. Quality of life assessment scores favoured treatment with dorzolamide/timolol.

**Commercial Relationships:** Katrin Lorenz, None; Joanna Wasieleca-Podsiadlik, None; Katharina Bell, None; Giulia Renieri, None; Alexander Keicher, None; Christian Rucket, None; Norbert Pfeiffer, None; Hagen Thiem, None

**Support:** MSD SHARP & DOHME GmbH, Germany and Santen Pharmaceutical Co., Ltd., Japan.

**Clinical Trial:** NCT01228149

**Program Number:** 2105 Poster Board Number: A0165
**Presentation Time:** 3:45 PM–5:30 PM

**Pharmacokinetics, Safety and IOP Lowering Profiles of omidenepag isopropyl, a Selective EP2 Agonist in Healthy Japanese and Caucasian Volunteers (Phase I Study)**

Makoto Aihara, Fenghe Lu, Hisashi Kawata, Yuki Tanaka, Kenzo Yamamura, Ryo Iwamura, Kenji Yoneda, Noriko Odani, Naveed Shams. 1. Ophthalmology, University of Tokyo, Bunkyo-ku, Japan; 1Santen Inc., Emeryville, CA; 1Santen Pharmaceutical Co., Ltd., Osaka, Japan; 1Ube Industries, Ltd., Ube, Japan; 1Santen Pharmaceutical Co., Ltd., Ikoma, Japan.

**Purpose:** To evaluate the plasma pharmacokinetics, safety and intraocular pressure (IOP) lowering profiles of omidenepag isopropyl (OMDI) ophthalmic solution 0.0025%, one drop once daily for 7 days, in healthy male adults.

**Methods:** This was a Phase 1 open-label, single center study. Fourteen (14) healthy male volunteers were enrolled including 7 Japanese and 7 Caucasian. OMDI 0.0025% was administrated once daily at 9:00 a.m. for 7 days. The plasma concentrations and pharmacokinetic parameters (C_{max}, T_{max}, T_{1/2}, and AUC_{0-last}) of omidenepag (OMD), the active metabolite of OMDI were determined. Adverse events, ocular and systemic safety parameters were analyzed. IOP was measured.

**Results:** The shapes of the plasma concentration of OMD over time were similar for study Days 1, 3 and 7 in both Japanese and Caucasian subjects. There were no significant differences in pharmacokinetic parameters between Japanese and Caucasian subjects after repeated dosing (7 days). The pharmacokinetic results (mean ± SD) on day 7 for Japanese and Caucasian subjects were, respectively: C_{max} 37.53 ± 15.52 pg/mL vs 33.31 ± 11.81 pg/mL; AUC_{0-last} 24.49 ± 6.43 pg*h/mL vs 20.02 ± 4.81 pg*h/mL; T_{max} 0.20 ± 0.08 hours vs 0.18 ± 0.09 hours; T_{1/2} 0.49 ± 0.07 hours vs. 0.53 ± 0.09 hours. The OMD concentrations were below the limit of quantification (BLQ, < 1.00 pg/mL) after 4 hours of administration for all Japanese and Caucasian subjects on Days 1, 3 and 7. There were no unexpected safety findings. There were 3 (21.4%) subjects with conjunctival hyperemia, 2 (14.3%) subjects with photophobia and 1 (7.1%) subject with AST/ALT increase. This was a phase 1 study and was designed to optimize the dose for future studies.

**Conclusions:** The pharmacokinetic parameters were similar between Japanese and Caucasian subjects. There was no OMD accumulation in plasma after 7 days of repeated dosing. OMDI was well tolerated. OMDI 0.0025% demonstrated good IOP-lowering effect in both Japanese and Caucasian healthy volunteers.

**Commercial Relationships:** Makoto Aihara; Fenghe Lu, Santen Inc. (E); Hisashi Kawata, Santen Pharmaceutical Co., Ltd. (E); Yuki Tanaka, Santen Pharmaceutical Co. Ltd. (E); Kenzo Yamamura, Santen Pharmaceutical Co. Ltd. (E);

Ryo Iwamura, Use Industries Co. Ltd. (E); Kenji Yoneda, Use Industries Co. Ltd. (E); Noriko Odani, Santen Pharmaceutical Co. Ltd. (E); Naveed Shams, Santen Inc. (E)

**Clinical Trial:** NCT02650063

**Program Number:** 2105 Poster Board Number: A0166
**Presentation Time:** 3:45 PM–5:30 PM

**Omidenepag isopropyl, a selective EP2 agonist, shows additive intraocular pressure (IOP)-lowering effects when used concomitantly with existing anti-glaucoma drugs in animal models**

Takazumi Taniguchi, Tomoko Kiriha, Miki Takahashi, Ryo Iwamura, Kenji Yoneda, Noriko Odani, Atsushi Shimazaki, Masaki Ichikawa, Jin-Zhong Zhang, Santen Pharmaceutical Co., Ltd., Ikoma, Japan; Santen Pharmaceutical Co., Ltd., Osaka, Japan; Ube Industries, Ltd., Ube, Japan; Santen Inc., Emeryville, CA.

**Purpose:** Omidenepag isopropyl (OMDI) is a prodrug of omidenepag (OMD), human EP2 receptor agonist with non-prostaglandin structure. Its IOP-lowering effect has been demonstrated in animal models and clinical trials for glaucoma. Here we comprehensively analyzed the receptor binding affinity of OMD, a hydrolyzed form of OMDI, and evaluated additional IOP-lowering effects of OMDI when combining it with existing anti-glaucoma drugs in animal models.

**Methods:** Binding affinities of OMD to prostainoid receptors (DP1, EP1-4, FP and IP) were determined using recombinantly expressed human receptors. The binding activities of OMD to various non-prostanoid receptors (over 100 molecules) were evaluated by calculating inhibition constants. Agonist activity was evaluated for receptors showing strong binding affinity. Ocular hypertensive effects after single topical administration of OMDI (0.001% in rabbit or 0.0006% in monkey) in combination with 0.5% timolol maleate, 0.15% brimonidine tartrate, or 1% brinzolamide were compared with those of monotherapy in ocular normotensive animals. IOP was measured before, and 2, 4 and 6 hrs after the application of each drug(s).

**Results:** OMDI was a highly EP2 receptor-selective compound, exhibiting a strong binding affinity (Ki=3.6 nM) for its receptor with agonist activity (EC50=8.3 nM). When OMDI was used concomitantly with timolol in rabbits, additional IOP-lowering effect was observed throughout the day compared with monotherapy, and with significant difference (p value<0.01) at 6 hrs after drug application. In monkeys, IOP reduction was also greater in OMDI and brimonidine combination compared to monotherapy throughout the day, with significant difference (p value<0.05) at 2 hrs post-administration. The IOP-lowering effect of co-treatment with OMDI plus brinzolamide was numerically greater compared to either drug alone.

**Conclusions:** OMDI has remarkable selectivity for human EP2, suggesting that OMDI acts through this receptor to lower IOP. Our animal studies suggest that OMDI could be useful in new glaucoma
treatments, both as monotherapy as well as combined with existing drugs.

**Commercial Relationships:** Takazumi Taniguchi, Santen Pharmaceutical Co., Ltd. (E); Tomoko Kirihara, Santen Pharmaceutical Co., Ltd. (E); Miki Takahashi, Santen Pharmaceutical Co., Ltd. (E); Ryo Iwamura, Ube Industries, Ltd. (E); Kenji Yonenob, Ube Industries, Ltd. (E); Noriko Odani, Santen Pharmaceutical Co., Ltd. (E); Atsushi Shimazaki, Santen Pharmaceutical Co., Ltd. (E); Masaki Ichikawa, Santen Pharmaceutical Co., Ltd. (E); Jin-Zhong Zhang, Santen Inc. (E)

**Program Number:** 2106 Poster Board Number: A0167

**Presentation Time:** 3:45 PM–5:30 PM

**Repeated dosing of NCX 667, a new nitric oxide (NO) donor, retains IOP-lowering activity in animal models of glaucoma**

Elena Bastia1, Francesco Impagnatiello1, Ennio Ongini1, Janet B. Serle1, Michael V. Bergamini1, 1Nicox Research Institute, Bresso, Italy; 2Icahn School of Medicine at Mount Sinai, New York, NY; 3Nicox Ophthalmics, Inc, Fort Worth, TX.

**Purpose:** NCX 667 is a novel NO-donor proven to effectively lower intraocular pressure (IOP) in rabbit and non-human primate models of glaucoma after single administration. Here we address the IOP-lowering effect of NCX 667 after repeated dosing.

**Methods:** NCX 667 (1%, 30μL dissolved in PBS with cremophor EL 5%, DMSO 0.3%, BAC 0.02%) was administered 4 consecutive times 1 hour apart within 1 day or bid (9AM & 4PM) for 5 days to oculo normotensive New Zealand White rabbits. IOPs were recorded prior to dosing and hourly post-dosing in the first study or 30, 60, 120, 180, and 240min post AM dose on days 1, 3 and 5 in the second study. Laser-induced ocular hypertensive non-human primates were treated bid (9AM & 4PM) for 5 consecutive days and IOPs measured hourly for 6 hours on days 1, 3 and 5. Two-way ANOVA followed by Bonferroni’s multiple comparison test was performed as statistical analysis.

**Results:** In rabbits, NCX 667 resulted in sustained IOP-lowering when administered hourly during 4h (IOP change= -3.11 ± 0.72 and -3.11± 0.74 mmHg, 30-60 min following the first and the fourth administration, respectively). Similarly, on day 1, NCX 667 AM dose rapidly lowered IOP (IOP change= -3.6 ± 1.0 mmHg, p<0.05 vs. vehicle at 30min), and slowly returned to baseline values of 21.2 ± 0.2 mmHg at 240min. NCX 667 was as effective on day 3 (IOP change= -2.7 ± 0.4 mmHg, 30min) and 5 (IOP change= -3.9 ± 0.5 mmHg, 30min) compared to day 1. No signs of ocular discomfort were observed. Similarly, in the primates NCX 667 retained its IOP-lowering effects over 5 days of treatment (IOP change= -8.5 ± 0.6 mmHg, day 1 and -8.6 ± 4.5 mmHg, day 5).

**Conclusions:** Regardless of the experimental paradigm used, repeated dosing with NCX 667 resulted in comparable IOP-lowering activity over time with no signs of tachyphylaxis or ocular discomfort.

**Commercial Relationships:** Elena Bastia, Nicox Research Institute (E); Francesco Impagnatiello, Nicox Research Institute (E); Ennio Ongini, Nicox Research Institute (E); Janet B. Serle, NicoX Research Institute (F); Michael V. Bergamini, Nicox Ophthalmics Inc (E)

**Program Number:** 2107 Poster Board Number: A0168

**Presentation Time:** 3:45 PM–5:30 PM

**Intraocular pressure lowering following topical (ocular) delivery of trabodenoson: Effects of preservative and age in living mice**

David Albers1, Guorong Li2, William K. McVicar3, W Daniel Stamer3, 1Inotek Pharmaceuticals, Lexington, MA; 2William K. McVicar, W Daniel Stamer, None

**Purpose:** Trabodenoson is a selective adenosine A1 mimic typically shown to lower intraocular pressure (IOP) in rabbits, monkeys and humans. We have previously reported that trabodenoson significantly lowers IOP in 3 month old mice by increasing conventional outflow facility. The purpose of the current study was to test IOP-lowering efficacy of trabodenoson in aged mice. Further, we investigated whether a preservative-free formulation of trabodenoson impacts the magnitude of IOP lowering.

**Methods:** Three month or one year old C57Bl6J male and female mice received once daily topical administrations of 6% trabodenoson in the right eye and vehicle in the left eye for 7 days. In experiments involving the evaluation of preservative-free formulation, preservative-free vehicle was used. In all groups of mice, IOPs were measured daily in both eyes by rebound tonometry, 30 min prior to drug/vehicle administration.

**Results:** In one year old mice, a significant lowering in IOP was observed in trabodenoson-treated eyes as compared to vehicle-treated eyes after 7 days of evaluation. IOPs decreased up to 3.0±0.81 mean ± SEM mmHg as compared to vehicle (p<0.05). Despite lower mean IOPs in older mice (16 versus 20 mmHg), this IOP reduction in older mice was similar to IOP changes in 3 month old mice (3.6±0.62 as compared to vehicle, p<0.05). Interestingly, once daily 6% trabodenoson formulated in a preservative-free suspension reduced IOP approximately 3.1±1.86 mmHg as compared to vehicle, similar to the IOP lowering effects of trabodenoson formulated in a preservative-containing suspension.

**Conclusions:** Trabodenoson reduced IOP equivalently in both 3 month and one year old mice. Furthermore, the IOP-lowering capabilities of trabodenoson are similar in preservative-free formulations as compared to preservative-containing formulations.

**Commercial Relationships:** David Albers, Inotek Pharmaceuticals (E); Guorong Li, None; William K. McVicar, Inotek Pharmaceuticals (E); W Daniel Stamer, None

**Program Number:** 2108 Poster Board Number: A0169

**Presentation Time:** 3:45 PM–5:30 PM

**Extended PGA Delivery Results in Significant Drug Sparing Compared to Topical PGAs and Achieves Sustained IOP Lowering for 11 Months without Any Loss of Efficacy**

Tomas Navratil1, Joanny Conley1, Rozenmarijn S. Verhoeven1, Kristin Blackwell1, Akshay Nadkarni1, Leo Trevino1, Benjamin R. Yerxa1, Michael Depenbusch1, Tracey Knox1, Iqbal Ahmad1, Thomas R. Walters1, Steven L. Mansberger1, 1Envisia Therapeutics, Research Triangle Park, NC; 2Arizona Eye Center, Chandler, AZ; 3Keystone Research Ltd., Austin, TX; 4University of Toronto, Toronto, ON, Canada; 5Devers Eye Institute, Portland, OR.

**Purpose:** Topical PGAs are the most utilized glaucoma therapeutics in the US but their administration results in very high transient intraocular drug concentrations that are far above the EC50 value for FP receptor activation. PGA super-therapeutic levels may lead to hyperemia and tachyphylaxis as shown with twice a day bimatoprost administration. Intracameral ENV515 travoprost XR was used to answer whether the long-term, sustained release of PGAs can achieve both significant dose sparing and long term IOP lowering without tachyphylaxis.

**Methods:** Intracameral ENV515 travoprost XR was formulated with > 6 month duration target. To evaluate IOP lowering effect and to measure intraocular levels of travoprost, 17 glaucoma patients previously shown to lower intraocular pressure (IOP) in rabbits, monkeys and humans. We have previously reported that trabodenoson significantly lowers IOP in 3 month old mice by increasing conventional outflow facility. The purpose of the current study was to test IOP-lowering efficacy of trabodenoson in aged mice. Further, we investigated whether a preservative-free formulation of trabodenoson impacts the magnitude of IOP lowering.

**Results:** In one year old mice, a significant lowering in IOP was observed in trabodenoson-treated eyes as compared to vehicle-treated eyes after 7 days of evaluation. IOPs decreased up to 3.0±0.81 mean ± SEM mmHg as compared to vehicle (p<0.05). Despite lower mean IOPs in older mice (16 versus 20 mmHg), this IOP reduction in older mice was similar to IOP changes in 3 month old mice (3.6±0.62 as compared to vehicle, p<0.05). Interestingly, once daily 6% trabodenoson formulated in a preservative-free suspension reduced IOP approximately 3.1±1.86 mmHg as compared to vehicle, similar to the IOP lowering effects of trabodenoson formulated in a preservative-containing suspension.

**Conclusions:** Trabodenoson reduced IOP equivalently in both 3 month and one year old mice. Furthermore, the IOP-lowering capabilities of trabodenoson are similar in preservative-free formulations as compared to preservative-containing formulations.

**Commercial Relationships:** David Albers, Inotek Pharmaceuticals (E); Guorong Li, None; William K. McVicar, Inotek Pharmaceuticals (E); W Daniel Stamer, None

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unilateral dose of ENV515 with timolol used as active comparator in the contralateral eye.

**Results:** In the 28-day study, low and high doses of ENV515 lowered IOP in a dose related manner, with timolol and TRAVATAN®-like efficacy. This IOP lowering effect was achieved at lower aqueous humor levels of travoprost vs the drug levels observed after topical dosing: high dose ENV515 mean ± SD of 95 ± 41 pg/ml travoprost (n=10) vs ~1,800 pg/ml measured in aqueous humor after topical TRAVATAN® Z. In a separate 12-month study, low dose ENV515 demonstrated an IOP-lowering effect for 11 months after a single dose without any loss of efficacy over this period, matching the pre-study PGA and in-study timolol IOP-lowering effects. ENV515 decreased the mean +/- SD 8 AM IOP by 6.7 ± 3.7 mmHg (p < 0.005) or 25% over 11 months (mean of all 8 AM IOPs over 11 months).

**Conclusions:** In a short term study, ENV515 intracameral travoprost XR demonstrated IOP lowering effect similar to TRAVATAN Z at much lower intraocular travoprost levels. In a long term evaluation, ENV515 lowered IOP consistently for 11 months after a single dose without any tachyphylaxis, matching in-study timolol and in-study topical PGAs with a dose that was significantly lower compared to topical TRAVATAN Z needed over the same period.

**Commercial Relationships:** Tomas Navratil, Envisia Therapeutics (E); Jinny Conley, Envisia Therapeutics (E); Rozemarijn S. Verhoeven, Envisia Therapeutics (E); Kristin Blackwell, Envisia Therapeutics (E); Akshay Nadkarni, Envisia Therapeutics (E); Leo Trevino, Envisia Therapeutics (E); Benjamin R. Yerxa, Envisia Therapeutics (E); Michael Depenbusch, None; Tracey Knox, None; Iqbal Ahmad, Envisia Therapeutics (C); Thomas R. Walters, Envisia Therapeutics (C); Steven L. Mansberger, Envisia Therapeutics (C).

**Clinical Trial:** NCT02371746

**Program Number:** 2109 **Poster Board Number:** A0170

**Presentation Time:** 3:45 PM–5:30 PM

**Effectiveness and Safety of Topical Bimatoprost Insert for Primary Open-Angle Glaucoma and Ocular Hypertension**

**Treatment**
Sebastiao Cronemberger1, Juçara R. Franca2, Alan C. Araújo3, Francine R. Cunha2, André A. Faraco3, Anderson Ferreira3, Giselle Foureaux4, 1Ophthalmology, Federal Univ of Minas Gerais, Belo Horizonte, Brazil; 2Pharmacy, Federal University of Minas Gerais, Belo Horizonte, Brazil; 3Pharmacy, Federal University of Minas Gerais, Belo Horizonte, Brazil; 4Morphology, Federal University of Minas Gerais, Belo Horizonte, Brazil.

**Purpose:**
Primary open-angle glaucoma (POAG) is initially treated with daily instillation of eye drops which are effective but may have adverse effects. Polymer systems of extended-release drugs may reduce these effects and improve adherence to treatment. We have developed an insert for sustained release of bimatoprost.

After, we assessed in patients with ocular hypertension (OH) or POAG the efficacy and safety of bimatoprost inserts in one eye compared to Lumigan™ eye drops in the contralateral eye.

**Methods:** All patients underwent the following exams by the same doctor: visual acuity measurement, slit lamp examination, Goldmann applanation tonometry, ultrasonic pachymetry, fundus examination and visual field testing. Inclusion criteria were both eyes with IOP>21mmHg without medication at 8:00 to 9:00 am; normal biomicroscopy; no antiglaucomatous or refractive surgery. Five normal patients with IOP≤14mmHg were also included. An insert of chitosan for prolonged release of bimatoprost was placed in the upper conjunctival fornix of the right eye (Fig. 1). In the left eye, patients instilled one drop of Lumigan™ daily at 9:00 pm. All exams were repeated weekly at 8:00 to 9:00 am for six weeks except the visual field. Anova two-way, Student test and paired-t test were used for statistical analysis. The level of significance was set at 0.05.

**Results:** No intolerance or discomfort with the insert was reported by the patients. In both eyes (insert and eye drop), the average IOP reduction was similar in the initial 3 weeks (insert: 31.2±10.3%, and eye drops: 34.8±10.1%). The percentage of IOP reduction at the end of the 3rd week was of 30% for insert and of 35% for eye drops (Fig. 2). A research conducted by CTIT/UFMG with participants demonstrated that 58% prefer insert; 25% prefer eye drops and 17% have no preference. Insert runs in 83.3% of patients and 58% of them would change the installation of the eye drops to inserts. The reasons are practicality of the insert; forgetfulness (instilling eye drops) and higher price of eye drops.

**Conclusions:** The insert of bimatoprost reduced significantly the IOP, similarly to what happened with Lumigan™ eye drops, for 3 weeks. The use of insert can be an alternative to daily instillation of eye drops for the treatment of POAG or OH.

![Insert (upper fornix)](image)

% of IOP reduction at 3 weeks

**Commercial Relationships:** Sebastiao Cronemberger, None; Juçara R. Franca; Alan C. Araújo, None; Francine R. Cunha, None; André A. Faraco, None; Anderson Ferreira, None; Giselle Foureaux, None.

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Program Number: 2110 Poster Board Number: A0171

Presentation Time: 3:45 PM–5:30 PM

Interim Analysis of Low Dose ENV515 Travoprost XR with 11 Month Duration Followed by Dose Escalation and 28 Day Efficacy Evaluation of High Dose ENV515

Steven L. Mansberger1, Jinny Conley2, Rozemarijn S. Verhoeven1, Kristin Blackwell1, Michael Depenbusch1, Tracey Knox1, Thomas R. Walters1, Iqbal Ahmad1, Benjamin R. Yerxa2, Tommas Navratil2. 1Devers Eye Institute, Portland, OR; 2Envisia Therapeutics, Durham, NC; 3Arizona Eye Center, Chandler, AZ; 4Keystone Research Ltd, Austin, TX; 5University of Toronto, Toronto, ON, Canada.

Purpose: ENV515 travoprost XR is an extended release formulation using nano- and microparticle engineering PRINT technology and a fully biodegradable polymer drug delivery system. Previously, ENV515 demonstrated 8 months of intraocular pressure (IOP) lowering effect after a single dose in nonclinical studies in dogs and sustained IOP lowering effect over 28 days after a single dose in glaucoma patients. To further evaluate ENV515, a 12-month dose escalation study was initiated with low and high doses of ENV515 using a single intracameral administration.

Methods: We enrolled 5 glaucoma patients in a 12-month Phase 2 study of low dose ENV515, and 10 glaucoma patients in a 12-month cohort of high dose ENV515. All enrolled patients were topical prostaglandin analogue (PGA) users at the time of enrollment. After washout, patients were administered a single low or high dose ENV515 in the study eye with timolol maleate 0.5% BID used as active comparator in the contralateral eye. We report 11-month interim analysis of low dose ENV515, and compare the 28-day response of the low vs. high dose of ENV515.

Results: In the low dose cohort, the mean IOP ± SD at the pre-washout visit on a PGA analogue was 19.7 ± 2.7 mmHg, with a post-washout baseline IOP of 26.1 ± 2.2 mmHg at 8 AM. ENV515 decreased the mean ± SD 8 AM IOP from baseline by 6.7 ± 3.7 mmHg (p < 0.005) or 25% over 11 months (mean of all 8 AM IOPs over 11 months). The mean 8 AM IOP after a single low dose of ENV515 was 19.5 mmHg over the 11-month period. There were no serious adverse events and the most common adverse event was early-onset transient hyperemia related to the dosing procedure. The high dose ENV515 demonstrated 1.1 mmHg better IOP lowering effect at 28 days when compared to the low dose ENV515.

Conclusions: Low dose ENV515 was well tolerated over 11 months, and demonstrated sustained IOP-lowering effect for 11 months following a single dose. High dose ENV515 demonstrated a potential to elicit a greater treatment effect compared to the low dose at 28 days and is currently being evaluated for sustained long-term IOP lowering effect.

Clinical Relationships: Steven L. Mansberger, Santen (C), Allergan (F), Envisia Therapeutics (C), Gore (C), National Eye Institute (F), Aerie Pharmaceuticals (C), Alcon (F), Valeant (C); Jinny Conley, envisia therapeutics (E); Rozemarijn S. Verhoeven, envisia therapeutics (E); Kristin Blackwell, envisia therapeutics (E); Michael Depenbusch, envisia therapeutics (E); Thomas R. Walters, envisia therapeutics (C); Iqbal Ahmad, envisia therapeutics (C); Benjamin R. Yerxa, envisia therapeutics (E); Tommas Navratil, Envisia Therapeutics (E)

Clinical Trial: NCT02371746

Program Number: 2111 Poster Board Number: A0172

Presentation Time: 3:45 PM–5:30 PM

Results of A Randomized, Double-Masked, Parallel-Arm Phase 2b Study Evaluating the Safety and Efficacy of OTX-TP (travoprost insert) Compared to Timolol Drops for the Treatment of Patients with Open-Angle Glaucoma or Ocular Hypertension

Christine Wilson1, Kenneth N. Sall1, Shamik Bafna2, Joseph P. Gira1, Eugene B. McLaurin1, Eugene Protzko2, Reginald Sampson1, Navin Tekwani2, Michael Tepedino1, Steven Vold3, Thomas R. Walters1, Jamie Lynne Metzinger1, Deepa Mulani1, Jonathan H. Talamo1. 1Ocular Therapeutix, Bedford, MA; 2Sall Research Medical Center, Artesia, CA; 3Cleveland Eye Clinic, Elyria, OH; 4Ophthalmology Consultants, St. Louis, MO; Total Eye Care PA, Memphis, TN; 5Seidenberg Protzko Eye Associates, Havre de Grace, MD; 6Hull Eye and Surgery Center, Lancaster, CA; 7Tekwani Vision Center, St. Louis, MO; 8Cornerstone Eye Care, High Point, NC; 9Vold Vision, Fayetteville, AR; 10Texan Eye Care PA, Austin, TX.

Purpose: To evaluate the safety and IOP-lowering efficacy of OTX-TP, an extended release travoprost insert, when placed in the canaliculus of the eyelid in patients with open-angle glaucoma (OAG) or ocular hypertension (OH). The study was designed to assess clinically meaningful response to treatment.

Methods: This was a prospective, multicenter Phase 2b trial. Patients diagnosed with OAG or OH were randomized (1:1) to receive either OTX-TP + placebo drops, or Timolol Maleate Ophthalmic Solution 0.5% + placebo vehicle insert (PV). Assigned drops were used twice daily at approximately 8h and 20h for the entire study. Subjects completed follow-up visits at Days 3, 15, 30, 45, 60, 75 and 90. Primary endpoints included the difference in mean change from baseline between treatment groups. Safety evaluations included adverse event (AE) collection and exam findings, including slit lamp, dilated fundus, visual acuity exams, grading of ocular hyperemia and subjective ocular comfort assessment.

Results: A total of 79 (OTX-TP, N=37; Timolol, N=42) subjects were randomized into the study. Demographic characteristics were similar in both treatment groups. IOP reductions from baseline were observed in both treatment groups at all 3 time points (8, 12 and 16h) at the Day 30, 60 and 90 Visits. Reductions in the OTX-TP group ranged from 2.30-5.11 mmHg and in the Timolol group, 5.28-7.23 mmHg, across 9 visits. Post-hoc analyses removing specific cohorts of patients reduced the performance difference between OTX-TP and Timolol. A similar percentage of subjects in both groups were reported to have experienced at least 1 ocular or non-ocular AE. The most frequently reported ocular AEs were dacryocanaliculitis, acquired dacryostenosis and eyelid edema. There were no deaths or other SAEs reported. Two OTX-TP subjects and 2 Timolol subjects discontinued study participation due to an ocular AE.

Conclusions: OTX-TP produced IOP reductions from baseline at Days 30, 60 and 90 and was safe and well tolerated. The performance of the Timolol cohort may have been enhanced by the presence of PV. A study design utilizing longer washout for OTX-TP subjects and absence of punctal occlusion in the presence of an active comparator may result in reduced differences between treatment groups.

Clinical Relationships: Christine Wilson; Kenneth N. Sall, Ocular Therapeutix (F); Shamik Bafna, Ocular Therapeutix (F); Joseph P. Gira, Ocular Therapeutix (F); Eugene B. McLaurin, Ocular Therapeutix (F); Eugene Protzko, Ocular Therapeutix (F); Reginald Sampson, Ocular Therapeutix (F); Navin Tekwani, Ocular Therapeutix (F); Michael Tepedino, Ocular Therapeutix (F); Steven Vold, Ocular Therapeutix (F); Thomas R. Walters, Ocular Therapeutix (F); Jamie Lynne Metzinger, Ocular Therapeutix (E);
Deepta Mulani, Ocular Therapeutix (E); Jonathan H. Talamo, Ocular Therapeutix (E)
Support: Ocular Therapeutix supported this research.
Clinical Trial: NCT02312544

Program Number: 2112 Poster Board Number: A0173
Presentation Time: 3:45 PM–5:30 PM
The Effects of Netarsudil Ophthalmic Solution on Aqueous Humor Dynamics in Humans
Arthur J. Sit1, Arash Kazemi1, Jay W. McLaren1, Casey Kopczynski2, Theresa G. Heah3, Gary D. Novack1,4, 1Ophthalmology, Mayo Clinic, Rochester, MN; 2Aerie Pharmaceuticals, Inc, Durham, NC; 3Ophthalmology and Pharmacology, University of California Davis, Davis, CA; 4PharmaLogic Development, Inc., San Rafael, CA.
Purpose: Netarsudil mesylate (previously AR-13324) lowers intraocular pressure (IOP) in normal subjects, subjects with ocular hypertension, and patients with open-angle glaucoma. It also lowers IOP in a fixed combination with latanoprost. In this study, we determined the effect of netarsudil mesylate ophthalmic solution 0.02%, which inhibits Rho Kinase as well as the norepinephrine transporter, on aqueous humor dynamics (AHD) in healthy human volunteers.
Methods: In this double-masked, vehicle-controlled, paired-comparison study, healthy volunteers were randomized to receive netarsudil 0.02% in one eye and its vehicle in the contralateral eye, once daily in the morning for 7 days. Outflow facility was measured by digital Schiotz tonography. Episcleral venous pressure (EVP) was measured by using an objective, computer-controlled venomanometer and image analysis software. Aqueous humor flow rate was measured by anterior segment fluorophotometry. AHD variables measured at 1 week were compared to those measured at baseline by using two-sample t-tests with statistical significance assumed for P <0.05.
Results: Ten subjects (mean age 39 ± 14 yrs) completed the study. Mean IOP in the netarsudil-treated eyes decreased from 17.0 ± 2.5 to 12.4 ± 2.2 mmHg (mean ± SD), a decrease of 4.6 mm Hg, compared to a decrease of 0.7 mm Hg in the vehicle-treated eyes (Table). Netarsudil-treated eyes showed an increase in outflow facility of 19% (p = 0.02) and a decrease in EVP of 9% (p = 0.01). Outflow facility also increased in netarsudil-treated eyes (p < 0.001). Aqueous humor flow rate and uveoscleral flow rate did not change (p>0.05). For the vehicle treated eyes, there was no change in any AHD variables. Consistent with previous reports, subjects reported conjunctival hyperemia.
Conclusions: In this study of normal volunteers, once-daily dosing of netarsudil mesylate ophthalmic solution 0.02% lowered IOP relative to baseline by increasing outflow facility and decreasing episcleral venous pressure.

Table: Aqueous Humor Dynamics Parameters in Netarsudil Treated Eyes (n=10)

<table>
<thead>
<tr>
<th>Time</th>
<th>IOP (mmHg)</th>
<th>Outflow Facility (µL/min/µmHg)</th>
<th>Episcleral Venous Pressure (mmHg)</th>
<th>Aqueous Humor Flow Rate (µL/min)</th>
<th>Uveoscleral Flow Rate (µL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>17.0 ± 2.5</td>
<td>0.27 ± 0.10</td>
<td>7.90 ± 1.24</td>
<td>2.53 ± 0.90</td>
<td>0.00 ± 1.19</td>
</tr>
<tr>
<td>Day 8</td>
<td>12.4 ± 2.2</td>
<td>0.30 ± 0.11</td>
<td>7.21 ± 1.75</td>
<td>2.13 ± 0.41</td>
<td>0.44 ± 0.92</td>
</tr>
<tr>
<td>Change</td>
<td>-4.6</td>
<td>0.05</td>
<td>-0.69</td>
<td>-0.39</td>
<td>0.36</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001a</td>
<td>0.02a</td>
<td>0.01a</td>
<td>0.08</td>
<td>0.17</td>
</tr>
</tbody>
</table>

* Statistically significant difference vs baseline
4 Statistically significant difference vs vehicle

Commercial Relationships: Arthur J. Sit,
Aerie Pharmaceuticals, Inc. (F); Arash Kazemi, Aerie Pharmaceuticals, Inc. (F); Jay W. McLaren, Aerie Pharmaceuticals, Inc. (F); Casey Kopczynski, Aerie Pharmaceuticals, Inc. (I), Aerie Pharmaceuticals, Inc. (E); Theresa G. Heah, Aerie Pharmaceuticals, Inc. (I), Aerie Pharmaceuticals, Inc. (E);
Gary D. Novack, Aerie Pharmaceuticals, Inc. (C)
Support: Aerie Pharmaceuticals, Inc.
Clinical Trial: NCT02406287

Program Number: 2113 Poster Board Number: A0174
Presentation Time: 3:45 PM–5:30 PM
Evaluation of the XEN45 Gel Stent in Patients with Primary Angle Closure Glaucoma
Francisco Millan1, Maria E. Reveron1, Lilian Gonzalez1, Miguel Siso1, Carelys Suescum1, Gary D. Novack1,4, Susan S. Lee3, Vanessa Vera1. 1Unidad Oftalmológica de Caracas, Caracas, Venezuela, Bolivarian Republic of; 2AVAO Foundation, Baruta-Caracas, Venezuela, Bolivarian Republic of; 3PharmaLogic Development, Inc., San Rafael, CA; 4University of California, Davis, CA.
Purpose: The XEN45 Gel Stent has been evaluated in patients with open angle glaucoma. In this report, we sought to evaluate the use of this device in patients with primary angle closure glaucoma (PACG). Based upon its small size, soft polymer composition, and anterior chamber placement, there is reason to believe it might be useful as a PACG therapeutic option.
Methods: This was a retrospective review of XEN surgical experience between February 2014 and May 2016 of 3 ophthalmologists in South America. Preoperative evaluations, including measurement of intraocular pressure (IOP) and enumeration of medications was performed. Post-operative visits were consistent with standard of care, and typically included 1 day, 1 and 2 weeks, 1, 2, 3, 6, 9 and 12 months. Presented are data available as of early November 2016.
Results: Implanted were 15 eyes of 13 patients, and with the exception of 1 XEN solo procedure, the majority were considered mixed mechanism glaucoma due to XEN placement immediately after cataract extraction in PACG patients. The population consisted of Hispanic females with a mean age of 62.8 ± 10.6 years (range 43 - 80). All received pre-operative mitomycin-c and post-operative dexamethasone.
From a mean pre-operative medicated IOP of 19.5 ± 2.9 mmHg, mean IOP at the first post-operative day decreased to 10.8 ± 6.1 (-8.7 mmHg) and 11.2 ± 3.5 at 1 week (-8.5 mm Hg). Mean IOP remained decreased, with the 8 eyes with data at 12 months having a mean IOP of 13.0 ± 2.6 (-6.5 mmHg). The proportion of the 15 eyes experiencing a decrease in IOP of 20% or more was 100% (8/8) at Month 12. The mean number of medications decreased from 3.3 ± 1.2 pre-operatively to 0.9 ± 1.1 at 12 months. Only one patient was considered an efficacy failure (Month 12), requiring an additional glaucoma surgical intervention.
There were 3 reports of needling procedures performed in 2 eyes. Transient post-operative hyphema (microscopic, 1 eye; Grade I, 2 eyes) was the most common post-operative complication, followed by cystoid macular edema (1 eye post combined surgery).
Conclusions: In this retrospective evaluation of patients with PACG, the XEN gel stent was safe and effective in lowering the IOP ≥20% in the majority of patients at 12 months and medication use from baseline was reduced by approximately two-thirds. Further clinical studies are indicated to evaluate the safety and efficacy of the XEN gel stent in managing patients with PACG.
Commercial Relationships: Francisco Millan, None; Maria E. Reveron, None; Lilian Gonzalez, None; Miguel Siso, None; Carelys Suescum, None; Gary D. Novack, Inotek (C), Deerfield (C), DMS (C), Sun (C), Sylentis (C), Aerie (C), Envisia (C), Allysta (C), Jenivision (C), Nicox (C), Peregrine (C), Eximore (C); Susan S. Lee, Allergan (E); Vanessa Vera, Allergan (C)

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The Effect of Ologen® Collagen Matrix (OCM) in Prevention of Intraocular Pressure spikes after Ahmed Glaucoma Valve Surgery (AGV-FP7): Intermediate results of a 2-Year Follow-up

Meliza Unson, Arkadiy Yadgarov, Robert Ritch, Tak Y. Tai, Reena Garg, Noga Harizman

Purpose: OCM has been shown to reduce and modulate scarring of the conjunctiva. We propose that guided wound healing will allow a thinner wall around the plate to prevent early post-operative intraocular pressure (IOP) spike. The purpose of this study is to evaluate effectiveness of OCM on the prevention of the post-operative hypertensive phase and on long-term IOP control.

Methods: A prospective, randomized, controlled study was done on eyes with refractory glaucoma requiring an AGV-FP7. Eyes with IOP > 20 mmHg on maximum tolerated glaucoma medications were included. In study eyes, a round 12 mm x 1 mm OCM segment was placed flush over the AGV-FP7 plate immediately before conjunctival closure. Student’s t-test was used for statistical analysis.

Results: 18 patients enrolled, 11 were randomized to receive OCM. Mean preoperative IOP was 31.4 ±9.8 mmHg and 39.1 ±9.8 mmHg in the study and control group (p=0.12). At post-operative months 1, 2, and 3, the IOP was lower in the study eyes compared to control (p<0.05 at months 1 and 2; p=0.06 at month 3). At last follow up, there was a statistically significant lowering of post-operative IOP (p<0.05) but there was no significant difference in IOP or medications between groups (16.4 ±7.8 mmHg and 18.5 ±6.3 mmHg for control and study eyes, p=0.53).

Two cases in the OCM group (20%) and one case in the control (17%) did not achieve IOP < 21 mmHg.

No surgical revisions or late complications were noted.

Conclusions: Intraoperative implantation of OCM over an AGV-FP7 may prevent a post-operative hypertensive phase. Intermediate data show no long term difference in IOP control between OCM augmented AGV surgery and AGV surgery alone.

Figure 1. Mean IOP post-operatively after AGV FP7 implantation in control and study eyes. Asterisk denotes statistically significant difference (p<0.05).

Program Number: 2115 Poster Board Number: A0175
Presentation Time: 3:45 PM–5:30 PM

Tear proteome provides basis for patient stratification after switching to a unpreserved glaucoma medication

Antti Jylhä, Janika Nattinen, Ulla Aapola, Matti Nykter, Roger W. Beuerman, Hannu M. Uusitalo

Ophthalmology, Medical School, University of Tampere, Tampere, Finland; BioMediTech, University of Tampere, Tampere, Finland; Singapore Eye Research Institute, Singapore, Singapore; TAYS Eye Center, Tampere University Hospital, Tampere, Finland.

Purpose: Glaucoma patients commonly experience adverse events due to long-term use of benzalkonium chloride (BAK) preserved glaucoma medication. It was hypothesized that the tear proteome would reflect the mechanisms involved in ocular surface adverse reactions such as inflammation. In order to study this concept, the tear proteome was analyzed in patients before and over one year period after switching from a preserved to an unpreserved prostaglandin drug.

Methods: Study consisted of 28 patients and 5 visits: screening/baseline visit and visits at 1.5, 3, 6 and 12 months after the medication switch from preserved latanoprost (Xalatan®) to preservative-free tafluprost (Taflotan®). Clinical evaluation and tear collection using Schirmer’s strips were performed during each visit. Relative quantification of tear proteins was done by NanoLC-TripleMSTOF using SWATH. Statistical and MS data analysis were performed with extensive software by Sciex, R software and Ingenuity pathway analysis (IPA).

Results: SWATH library for 978 proteins was created and 785 proteins were relatively quantified in each sample. We compared protein expression data between the visits and identified 3 distinctive protein clusters with high reliability (p<0.001). One of the clusters consisted of beneficial (lacrimal gland secreted proteins) ocular surface biomarkers, e.g. LYZ, PROL1 and various cystatins. Another two clusters included well-known inflammation related proteins such as ALB, TF and S100A8 and C3, ENO1 and S100A9. Further analysis of the clusters revealed 41 differentially expressed proteins (adjusted p-value < 0.05). Pathway analysis identified ‘inflammation of organ’ as the most enriched function term (p-value = 1.2E-05).

Conclusions: Proteomic analysis stratified patients into three different groups. Two of them showed improvement of tear protein profile while one group showed increase in inflammatory related proteins. In the future, selected protein profiles could be used for the prediction of best therapeutic options for glaucoma patient.

Commercial Relationships: Antti Jylhä, None; Janika Nattinen, None; Ulla Aapola, None; Matti Nykter, None; Roger W. Beuerman, Allergan (C); Hannu M. Uusitalo, Santen (F)
Support: TEKES 40807/12
Clinical Trial: 2010-021039-14

Program Number: 2116 Poster Board Number: A0177
Presentation Time: 3:45 PM-5:30 PM

Shared Medical Appointments in Glaucoma Management at a Tertiary Care Eye Hospital - A Randomized Trial

Rengaraj Venkatesh, kavitha srinivasan, Nazli Sonmez, Ryan Buell, Kamalini Ramdas, Glaucome, Aravind Eye Hospital, Pondicherry, India; 1Harvard Business School, Boston, MA; 2Deolite Institute of Innovation & Entrepreneurship, London Business School, London, United Kingdom.

Purpose: Glaucoma is a chronic disease and highly asymptomatic in early stages. Patients' understanding and knowledge about the disease is important to improve compliance to treatment and follow up, and also to prevent progression. Shared medical appointments (SMAs), in which patients are examined by their physician as a group, have...
been found to be successful in managing chronic conditions like obesity, diabetes. The primary objective of this study was to examine how SMA affects the level of patient’s knowledge and satisfaction in glaucoma care provision.

**Methods:** A prospective randomized trial involving 265 patients was conducted involving primary glaucoma on treatment for one year. Fifty-three groups of five patients were randomly assigned to either the SMA or one-on-one (control) group. While one patient in the SMA group is being examined and treated, the other 4 in the group get to listen to them. Those in the one-on-one group engage with the doctor while the other 4 patients wait outside the consultation suite. During the appointment, patients in both conditions experience an eye examination and receive recommendations from the doctor, and have the opportunity to ask questions. After their examination, patients received a survey that included questions assessing their level of knowledge about glaucoma and their satisfaction level with the experience.

**Results:** One hundred sixty patients were randomized into the one-on-one group while 105 were recruited into the SMA group. Patients randomized in the SMA group were 12% more satisfied with their appointment experience than patients who received a one-on-one appointment (p<0.05). In addition, glaucoma knowledge scores were 5% higher amongst patients randomized to the SMA group when compared to patients attending one-on-one appointments, though the differences were not statistically significant (p=0.31).

**Conclusions:** The results support the use of SMA in glaucoma management since it has a potential for increasing the satisfaction and knowledge level of patients. We believe, this will improve patient compliance and follow up rates, indirectly reducing the burden of glaucoma blindness.

**Commercial Relationships:** Rengaraj Venkatesh, None; Kavitha Srinivasan, None; Nazli Sonmez, None; Ryan Buell, None; Kamalini Ramdas, None

**Support:** London Business School Grant

**Clinical Trial:** REF/2016/11/012659

**Program Number:** 2117 **Poster Board Number:** A0178

**Presentation Time:** 3:45 PM–5:30 PM

**Association between periodontal disease and primary open angle glaucoma**

**Konstantin Astafurov**, **Brian Ibabao**, **Leslie Hyman**, **John Danias**

1Ophthalmology, SUNY Downstate Medical Center, Brooklyn, NY; 2Wills Eye Hospital Philadelphia, Philadelphia, MD; 3SUNY Upstate Medical University, Syracuse, NY; 4SUNY Eye Institute, New-York, NY.

**Purpose:** Chronic inflammation outside the central nervous system in general, and periodontal disease in particular, have been recently suggested to play a role in the pathogenesis of primary open angle glaucoma (POAG). This research work aimed to investigate the association between moderate/severe periodontal disease and POAG in a retrospective claims-based study.

**Methods:** Billing records from patients >40 years old seen at both the Ophthalmology (n=34, 570 visits) and Dental (n=31,194 visits) Clinics of Kings County Hospital from April 2012 to March 2015 were reviewed for presence/absence of POAG and history of periodontal treatment. Patients with ICD-9 codes for non-POAG glaucoma or various inflammatory and pathologic vascular ocular conditions were excluded from further review. Cases had at least 2 visits to the Ophthalmology Clinic for POAG-associated ICD-9 codes (365.10, 365.11). Controls were patients with at least two visits to the Ophthalmology Clinic for common ocular conditions such as dry eye syndrome, age-related cataract, refractive error, etc without glaucoma-associated ICD-9 codes (365.xx). Presence of moderate/severe periodontitis was defined by whether they had undergone at least one periodontal treatment procedure, indicated by specific dental Current Procedural Terminology (CPT) codes during the study period.

**Results:** Of the 7,600 patients identified from the record review 392 met the study eligibility criteria for POAG cases and 2414 were eligible as Controls. 3,025 periodontal dental procedures had been performed during the study period. Moderate/severe periodontitis was present in 11.5% of POAG patients and 7.7% of controls (Odds Ratio (OR): 1.61 95% CI (1.15-2.33), p<0.007). Moderate/severe periodontal disease remained associated with POAG in a multivariate logistic regression model adjusting for age and sex (OR: 1.66, 95% CI (1.17-2.35), p < 0.005).

**Conclusions:** Moderate/severe periodontal disease was associated with POAG in this retrospective claims-based study. Limitations of the study include ascertainment bias, inability to confirm the absence of periodontitis, and possible selection bias. Despite these limitations, the results support a possible link between periodontal disease and POAG.

**Commercial Relationships:** Konstantin Astafurov, Brian Ibabao, Leslie Hyman, John Danias

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