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Travoprost Intracameral Implant: A Review on the Novel Treatment Modality for Open-Angle Glaucoma and Ocular Hypertension

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Abstract

Objective: This article reviews the published data encompassing the development, pharmacology, efficacy, and safety of travoprost, intracameral implant, a treatment for reduction of intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension. **Data Sources:** A literature search was conducted from drug discovery until September 2024 through PubMed, MEDLINE, and National Institutes of Health Clinical Trials Registry utilizing the following search terms: iDose, travoprost, intracameral implant, OTX-TIC, open-angle glaucoma, and ocular hypertension. **Study Selection and Data Extraction:** All relevant English-language studies, or studies that could be appropriately translated into English, containing the pharmacology, pharmacokinetics, safety, and efficacy of travoprost intracameral implant were selected for review. **Data Synthesis:** Travoprost implants showed significant reductions in IOP compared with other treatment options with fewer limitations often associated with topical medications resulting in travoprost implant patients favoring reduced concomitant use of topical IOP-lowering medications (with 81% of patients being medication free). **Relevance to Patient Care and Clinical Practice in Comparison with Existing Drugs:** Due to limited compliance with topical treatment modalities, the travoprost implant presents a promising alternative pathway for drug delivery. With a duration of 3 years and removal of the need for patient dexterity and application compliance, the travoprost implant serves an unmet need for patients and prescribers. **Conclusion:** Travoprost intracameral implant is a safe and effective delivery system for intracameral travoprost administration for patients with OAG or ocular hypertension.

Keywords

iDose, travoprost, intracameral implant, OTX-TIC, open-angle glaucoma, ocular hypertension

Introduction

Glaucoma is the leading cause of irreversible blindness worldwide. Studies of prevalence estimate that glaucoma will affect around 112 million people by 2040.[1] Elevated intraocular pressure (IOP) remains the primary modifiable risk factor in treating glaucoma. IOP-lowering topical medications are effective and have an excellent risk profile making them the first-line treatment; however, compliance with such medication routines remains an area of primary concern among glaucoma specialists. It has been shown that nearly 50% of patients who were prescribed IOP-lowering drops discontinued usage within 6 months and just one third had refilled their medications after 3 years.[2]

Among the numerous classes of IOP medications, prostaglandin analogues (PGAs) are the most frequently prescribed class due to their once-daily dosing regimen along with remarkable IOP-lowering effects. The proposed mechanism of IOP lowering is thought to be the increase in drainage of aqueous fluid through the uveoscleral pathway. Studies have shown an average of 6 to 8 mmHg decrease in IOP with PGA usage.[3] However, despite their excellent safety profile and IOP-lowering effects, PGAs often present

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Table 1. Phase II and III Clinical Study Results.

Reference	Phase	Study number	Duration	Population size (*n*)	Comparator	Primary endpoint results
Berdahl[6]	IIb	GC-009	36 months	154	Travoprost FE implant, travoprost SE implant, timolol eye drops 0.5% twice daily	CFB mean reductions in IOP; 7.6 to 8.8 mmHg for the travoprost FE group, 7.3 to 8.0 mmHg for the travoprost SE group, 7.3 to 7.9 mmHg for the timolol group
Sarkisian[7]	III	GC-010	3 months	590	Travoprost FE implant, travoprost SE implant, timolol eye drops 0.5% twice daily	CFB in time-matched diurnal IOP at 8 AM and 10 AM; –6.6 to –8.4 mmHg for the travoprost FE group, –6.6 to –8.5 mmHg for the travoprost SE group, –6.5 to –7.7 mmHg for the timolol group
Clinicaltrials.gov[8], Glaukos[9]	III	GC-012	3 months	560	Travoprost FE implant, travoprost SE implant, timolol eye drops 0.5% twice daily	CFB in diurnal IOP; –6.21 to –8.26 mmHg for the travoprost FE group, –6.79 to –8.40 for the travoprost SE group, –6.76 to –7.17 mmHg for the timolol group

Abbreviations: CFB, change from baseline; FE, fast-eluting; IOP, intraocular pressure; *n*, population size; SE, slow-eluting.

users with unwanted adverse effects, including ocular surface irritation and hyperemia, iris color changes, eyelash changes, and periorbital fat atrophy, which hinder compliance rates. In addition, studies have also demonstrated the difficulty that elderly patients experience with remembering and instilling eye drops. On average, patients require 1.4 to 1.8 drops to properly get the medication to the eye and approximately one third of patients are unable to instill drops in the eye.[3] Numerous studies have shown poor medication compliance increases disease severity and progression leading to irreversible blindness.[4,5]

Due to adverse effect profile, compliance concerns, and lifestyle burden of topical IOP-lowering medications, many extraocular and intraocular drug delivery mechanisms have been proposed and explored. These devices have the advantage of continuous delivery to avoid the peaks and troughs of topical treatment and help with difficulties of compliance. Extraocular devices, such as drug-eluting contact lenses and punctal plugs can help with continuous dosing, but they are plagued with concerns of being easily displaced. Among intraocular eluting mechanisms, the bimatoprost sustained release intracameral implant (Durysta, bimatoprost intracameral implant, 10 μg; Allergan Corp, Irvine, CA) was approved by the Food and Drug Administration (FDA) in 2020 to reduce IOP in patients with glaucoma and ocular hypertension (OHT). The bimatoprost intracameral biodegradable implant was intended to last 3 to 4 months between applications. The implant has shown promising IOP reductions, but there have been concerns of endothelial cell degradation due to the polymer delivery systems remaining in the iridocorneal angle. Due to this, current recommendations are for one implant to be injected per eye, limiting the duration of effect achieved.[6]

A newer entrant into the intracameral drug eluting device group is the travoprost intraocular implant (Glaukos Corp., Aliso Viejo, CA). The travoprost implant consists of a miniature medical grade titanium reservoir (1.2 mm in length by 0.5 mm in diameter) and anchor (0.6 mm in length), which secures the implant through the trabecular meshwork and into the sclera in the iridocorneal angle. The reservoir holds 75 micrograms of proprietary, preservative-free travoprost formulation that is held in place by a titanium cap with a nanoporous ethylene-vinyl acetate membrane to facilitate continuous, long-duration (3 years) elution of travoprost directly into the anterior chamber.[6]

Study Selection and Data Abstraction

A literature search was conducted from drug discovery until September 2024 through PubMed, MEDLINE, and National Institutes of Health Clinical Trials Registry utilizing the following search terms: iDose, travoprost, intracameral implant, OTX-TIC, open-angle glaucoma, and ocular hypertension. All relevant English-language studies, or studies that could be appropriately translated into English, containing the pharmacology, pharmacokinetics, safety, and efficacy of travoprost intracameral implant were selected for review and are summarized in Table 1.

Clinical Pharmacology

Mechanism of Action

The trabecular pathway for aqueous humor outflow streams through specific channels (conventional pathway). While the complete mechanism of travoprost is not fully understood, it has demonstrated selective activity at the prostaglandin F prostanoid (FP) receptor. Due to travoprost implant's nanoporous ethylene-vinyl acetate membrane facilitating continuous elution, its mechanism assists with increasing the uveoscleral outflow. This enhanced drainage of aqueous humor bypasses the trabecular system (unconventional pathway), overall contributing to IOP reduction.[10]

Pharmacokinetics

Travoprost (prodrug) undergoes hydrolysis intraocularly, producing its active free acid structure. The active acid then reaches peak concentration after about 2 hours post-administration before undergoing further transformation within the tissues. The final process involves beta-oxidation of the α (carboxylic acid) chain, oxidation of the 15-hydroxyl area, and reduction of the 13, 14 double bonds.[10] Continuous elution of travoprost via the implant provides a steady dose, therefore eliminating peak and trough concentrations. Fluctuations in IOP that can lead to poor outcomes are lessened with this drug delivery method.[6]

Clinical Studies

A phase IIb study, GC-009, included 154 participants with open-angle glaucoma (OAG) or OHT to evaluate the safety and efficacy of IOP lowering of travoprost intraocular implants with 2 different elution rates. The study included participants taking 3 or less preoperative ocular hypotensive medications, a visual field with a mean deviation of no worse than –12 dB, a cup/disk ratio ≤ 0.8, and best corrected visual acuity (BCVA) of +0.6 logMAR or better (in each eye). Participants were not included if they were diagnosed with retinal disorders unassociated with glaucoma. Participants were randomized 1:1:1 to receive the fast-eluting (FE) or slow-eluting (SE) travoprost implant or timolol eye drops 0.5% twice daily. Of note, baseline characteristics were similar across treatment groups, however, a larger number of participants in the travoprost FE group were on fewer (0-1) IOP-lowering medications than in the travoprost SE or timolol groups, 82.4%, 68.5%, and 61.2%, respectively. To ensure blinding throughout the study, participants randomized to the implant groups received placebo eye drops to administer at the same dosing regimen as the timolol eye drops; those randomized into the timolol control group, underwent a sham implant procedure. Mean IOP reductions from baseline to month 36 were as follows, 7.3 to 7.9 mmHg for the timolol group, the travoprost FE group showed mean reductions of 7.6 to 8.8 mmHg, and the travoprost SE group had mean reductions of 7.3 to 8.0 mmHg.[6,11] Participants in the travoprost implant groups maintained IOP control with the same or fewer IOP-lowering medications compared with screening that was significantly greater than those in the timolol group; 86% for the FE group, 92% for the SE group, and 58% for the timolol group achieving IOP control on the same or fewer topical IOP-lowering medications. Compared with baseline measurements, mean IOP reductions for those on the same or fewer IOP-lowering medications at months 12, 24, and 36 were statistically significant for each of the groups at each of the 3 study visits ($P < 0.0001$).[6] While both travoprost implants showed IOP reduction and the need for fewer topical medications compared with the timolol group for many of the participants, the conclusion of this study and results lead to the decision to move forward with the commercialization of only the SE implant.[6]

GC-010, a phase III, double-masked, prospective study, analyzed travoprost FE and SE implants effectiveness compared with twice-daily timolol 0.5% for use in the reduction of IOP in patients with OAG or OHT. While the phase II study determined that only the SE implant would move forward to commercialization, the FDA requires 2 implant arms for masking purposes, and thus, the FE implant was also studied here. The study included 590 participants in 3 treatment groups randomized 1:1:1; travoprost 75 mcg FE implant, travoprost 75 mcg SE implant, and timolol 0.5% groups, respectively. Treatment groups were well balanced regarding baseline characteristics and unmedicated mean IOP. The primary outcome measure was the change from time-matched baseline diurnal IOP at 8 AM and 10 AM at day 10, week 6, and month 3. Participants in the implant groups showed a consistently greater reduction in diurnal IOP compared with the timolol group across 6 time points (day 10, week 6, and month 3 at 8 AM and 10 AM). Changes from baseline in IOP were –6.6 to –8.4, –6.6 to –8.5, and –6.5 to –7.7 mmHg for the FE implant group, SE implant group, and timolol group, respectively. Statistical and clinical criteria for noninferiority were met for both implant groups compared with timolol. At month 3, only 5.1 % of participants in the FE implant group and 4.2% of participants in the SE implant group were receiving additional topical IOP-lowering medications compared with 7.0% in the timolol group. While the study did not address data related to long-term safety and efficacy, it did demonstrate that the travoprost implant is effective at reducing IOP and maintaining IOP reductions up to 3 months.[7]

The phase III study, GC-012, compared the travoprost implants with a sham surgery and active comparator eye drops of timolol 0.5% to assess the same dosage and outcome criterion as the GC-010 study, however, it focused on patients utilizing less than 2 IOP-lowering medications, as opposed to the maximum of 3 medications used in the GC-010 study. Five hundred and sixty participants were randomized to the travoprost FE implant group, travoprost SE implant group, or timolol 0.5% control group. Change from baseline in diurnal IOP ranged from –6.21 to –8.26 mmHg for the FE implant, –6.79 to –8.40 for the SE implant, and –6.76 to –7.17 mmHg in the timolol group across all time points on the 3 different time occasions (8 AM and 10 AM on day 10, week 6, and month 3). Like GC-010, GC-012 also provided favorable data indicating both travoprost implants were efficacious and provided a consistently safe and tolerable profile.[10,8,9]

Safety

Administration of travoprost via implant has provided compelling data expanding into events related to endothelial cell loss, periorbital fat atrophy, and change to the descemet membrane (specifically, DSAEK and DMEK).[10] In full, safety was measured through the presence of adverse events (AEs) and ophthalmic criteria. Use of either travoprost implant was deemed as favorably safe and well tolerated for patients with OAG or OHT. The GC-010 study resulted in the SE and FE implant groups presenting as noninferior to the timolol ophthalmic solution group. Minor treatment-emergent adverse events (TEAEs) in the SE implant group included retinal detachment and increased IOP. Conjunctival hyperemia, in particular, occurred in 2.6% of the SE implant group that was a significant reduction compared with the 30% to 50% in topical travoprost administration in previous studies. AEs typically associated with topical PGAs were significantly reduced by changing to an intracameral administration method. There was no clinical difference amongst any of the groups regarding BCVA, visual field outcomes, nor AEs typically paired with topical travoprost (evidence of iris hyperpigmentation nor periorbital fat atrophy). Serious TEAEs, notably endophthalmitis, presented with minimal difference between all groups (with one patient's condition resolving with treatment): travoprost SE group had 1.5% (3 patients), travoprost FE group had 2.5% (5 patients), and the timolol group had 1% (2 patients). The SE implant group also exhibited some cases of retinal detachment and increased IOP while the FE implant group solely demonstrated a serious TEAE of an elevated IOP. Deaths reported in the GC-010 study were deemed unrelated to treatment.[11] Of note, there have not been observable differences regarding safety or effectiveness for elderly populations and other specialty populations (ie, pregnancy, lactation, and pediatrics) have not been evaluated at this time.[10]

Dosing/Administration

The 1.8 mm × 0.5 mm travoprost intracameral implant comprised a titanium reservoir with a membrane that regulates the sustained release of travoprost.[10,12] It is pre-loaded in a sterile, single-dose inserter and administered intracamerally through a small, clear corneal incision, and anchored into the sclera on the nasal side at the iridocorneal angle. Administration of the implant should be performed by a surgeon under aseptic conditions. Pupillary dilation should be avoided and an intracameral miotic may be injected to deepen the angle prior to the procedure. The patient's head should be turned away from the surgeon at a 15 to 25 degree angle and the scope should be tilted toward the surgeon at around a 35 degree angle to create a total combined angle of 50 to 60 degrees. Using a gonioscope, the anterior chamber angle and trabecular meshwork should be clearly visualized. The single-dose inserter should be held with the index finger on the implant release button and should be inspected to ensure that the implant is present at the tip. A 2.2 to 2.4 mm clear corneal incision should be made at the temporal limbus. The inserter tip should be entered into the incision, advanced to the pupillary margin avoiding contact with the lens and cornea, advanced to the anterior chamber angle, implanted through the trabecular meshwork and anchored to the sclera. To ensure that the implant is securely attached, slight pressure should be applied to the implant with the inserter tip. If the implant is not fully anchored to the sclera after implantation, the graspers on the inserter should be used to reposition. It should not be re-implanted in the same location. After insertion, a high magnification examination should be performed to ensure that the implant is positioned with the proximal end in the anterior chamber and with an unobstructed membrane. The anchor should be embedded within the sclera.[10]

The therapeutic effects of the implant generally last around 4 to 5 years.[12] As per the FDA package insert, re-administration of the travoprost implant to an eye that has previously received it is not recommended.[10] However, the implant is designed to be replaced with a new one, and recent studies have shown that the implant can be exchanged safely. During the exchange procedure, the surgeon should ensure that the new implant is positioned at least 30 degrees away from the previous implant site.[12]

Cost Analysis

Starting in the first quarter of 2024, Glaukos announced a wholesale acquisition cost of $13 950 for their novel travoprost intracameral implant. Alongside this, the iDose Your Dose initiative was begun and pledges an equal number of travoprost implant units sold to be donated to eligible recipients in the United States and abroad.[9] Furthermore, effective from July 1, 2024, the travoprost implant utilizes a permanent J-code (J7355), which allows for a clear and consistent billing and reimbursement process. Glaukos also announced that the travoprost implant has been classified as an ambulatory payment classification that should provide a standardized and higher quality level of care for patients undergoing this procedure.[13]

Of note, the other implantable glaucoma device, Durysta, only lasts 6 months compared with the 3 years of the travoprost implant and costs about $2100 per implant. In addition, travoprost itself in its topical form is around $64 for a 2.5 ml bottle, which roughly covers 1 eye twice daily for a month. Over 3 years, this would equate to $2300. Overall, it is noted that the novel travoprost implant has a higher price point than other market alternatives yet it provides a higher level of convenience and stability for the patient in ensuring medication compliance.[14,15]

Relevance to Patient Care and Clinical Practice in Comparison with Existing Drugs

With a projected increase in the prevalence of glaucoma-related blindness worldwide, continuous exploration of new treatment modalities is of utmost importance. Estimates show that OAG accounts for greater than 80% of glaucoma cases in the United States and with the aging population, prevention and treatment are pertinent.[16] Topical medications have been the primary treatment modality for years and maintain an excellent safety profile, but they are plagued by unwanted adverse effects, compliance concerns, and difficulty with application.

For more advanced cases of glaucoma, filtration surgeries, such as trabeculectomies and tube shunts have had the highest success at lowering IOP, but they are relatively invasive procedures that include a life-long risk of complications. Modalities, such as selective laser trabeculoplasty and minimally invasive glaucoma surgeries, have been developed over the last decade to bridge the gap between topical medications and more serious filtration surgeries. With newer entrants into the field of intracameral drug eluting devices, patients are provided with further means of easier and less invasive treatments. For clinicians to have more tools to prevent progression in the early phases of the disease would greatly reduce the burden to the patient and the possible need for an invasive procedure in the future. Adding a new and effective minimally invasive treatment to the glaucoma specialists' therapeutic options has the potential to have profound impacts on patients' quality of life.

Both FE and SE membranes were tested in phase II clinical studies with the SE demonstrating a better benefit to risk profile.[7] The 3-year phase II clinical study showed well-controlled IOP with the same or less medications at 36 months in 69% of subjects in the SE group and 63% in the FE group. Current phase III clinical studies are underway, which are comparing the efficacy and safety of travoprost intracameral implants versus twice–daily-dosed timolol 0.05% topical drops. After 3 months of the study, early analysis is showing a mean IOP reduction from baseline of 6.6 to 8.4 mmHg in the FE group, 6.6 to 8.5 mmHg in the SE group, and 6.5 to 7.7 mmHg in the timolol group.[7] With noninferior IOP-lowering effects, patients who receive this one-time implant can achieve lower IOP while also avoiding the issues of irritation and compliance that typically plague topical medications and is far less invasive than progressive surgeries.

Conclusion

While the travoprost implant is not the first IOP-lowering implant to the market, it has the benefit of longitudinal efficacy. Travoprost intracameral implant has been shown to be safe and effective at IOP lowering with the ultimate goal of preventing or reducing occurrence of glaucoma.

Declaration of Conflicting Interests

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