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REVIEW

Bimatoprost Intracameral Implant (Durysta®): A New Era in Glaucoma Management Through Sustained-Release Innovation

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Abstract: The bimatoprost intracameral implant (Durysta®) offers a sustained-release approach to glaucoma management, providing consistent intraocular pressure (IOP) reduction over several months and reducing the need for daily topical therapies. This review evaluates its pharmacology, efficacy, and safety, using data from pivotal clinical trials and recent real-world studies. The implant achieves IOP reductions comparable to topical prostaglandin analogs, with benefits for patient adherence and fewer common side effects. However, repeat administrations are associated with adverse effects such as endothelial cell loss, highlighting the need for optimized re-dosing schedules. Future research should explore its use in advanced glaucomas, cost-effectiveness, and combination with other IOP-lowering treatments. The bimatoprost intracameral implant represents a promising innovation in glaucoma therapy with potential for improved patient outcomes.

Keywords: bimatoprost intracameral implant, glaucoma, intraocular pressure reduction, sustained-release therapy, primary open-angle glaucoma, ophthalmic drug delivery, patient adherence, prostaglandin analogs, endothelial cell safety, real-world evidence, cost-effectiveness, combination therapy in glaucoma

Introduction

Glaucoma is a progressive optic neuropathy and one of the leading causes of irreversible blindness globally.[1,2] The most frequent subtype of glaucoma is primary open-angle glaucoma (POAG) with a 2.4% worldwide prevalence.[3] The primary objective of glaucoma treatment is to prevent disease progression by reducing intraocular pressure in the affected eye. This can be accomplished through the use of topical anti-glaucoma medications, laser interventions, and incisional or filtration surgical procedures.[4,5] Topical eye drops are the initial treatment of choice for managing POAG and ocular hypertension.[6,7] Since their FDA approval in 1996, prostaglandin analog (PGF2α) eye drops have been the first line of treatment in POAG and ocular hypertension due to their increased intraocular pressure (IOP)-lowering efficacy, once a day application, and minimal systematic side effects.[8–11] Despite advancements, preservative-free topical treatments still pose challenges for adherence due to side effects and the burden of daily administration, prompting exploration into sustained-release options like intracameral implants.[12–14] Bimatoprost, approved by the US Food and Drug Administration (FDA) in 2001 as a topical antiglaucoma agent, is classified as a prostamide.[10] Although it shares structural similarities with prostaglandin F2α analogs, it demonstrates unique pharmacological properties in both in vivo and in vitro studies.[15] Since 2020, a new intracameral administration for bimatoprost in the form of a sustained intracameral release implant has been implemented.[16] This method ensures perfect adherence to the therapy and reduces the medication burden by minimizing the topical adverse effects by employing a novel administration approach. While

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intracameral implants, like the bimatoprost implant, offer promising improvements in adherence by reducing the daily burden of topical therapy, the potential for unique side effects and the need to establish a long-term safety profile remain important considerations for widespread clinical adoption.

The aim of this narrative review is to evaluate the potential of the bimatoprost implant in glaucoma by examining the key research that supported its development and approval, along with recent real-world evidence assessing its clinical application.

Materials and Methods

A search was conducted across the scholarly databases: PubMed, Google Scholar, ScienceDirect, and Cochrane, using the keywords: "Durysta", "Bimatoprost intracameral implant", "Intracameral implants". The search included studies published until September 2024. The inclusion criteria included both experimental animal trials and clinical Phase I/II and III trials, as well as real-world evidence studies.

Pharmacology of Bimatoprost Intracameral Implant: Molecular Characteristics and Pharmacokinetics

Bimatoprost is classified as a prostamide, a distinct prostaglandin analog, in which the conventional carboxylic acid group is replaced by a neutral ethylamide substituent. This modification leads to unique and distinct pharmacological properties compared to PGF2α affecting both the conventional (trabecular meshwork) and the non-conventional (uveoscleral) outflow.[17] The presence of an agonist effect on FP prostaglandin receptors, as observed with other PGF2α analogs, has been the subject of controversy.[18–21] It has been proposed that the non-conventional outflow is affected by an increase in remodeling enzymes, such as matrix metalloproteinases, which modify the extracellular matrix of the ciliary muscle and sclera.[10,20,22] Additionally, bimatoprost has been associated with ciliary muscle relaxation, which further contributes to the reduction of IOP by affecting conventional trabecular outflow through the relaxation of the trabecular meshwork.[23] Although the presence of an exact receptor for the action of bimatoprost has been controversial, a study suggested that bimatoprost binds to and inhibits prostamide receptors in the trabecular meshwork, which may also contribute to an increase in conventional outflow through this mechanism.[15] However, findings related to these effects have been inconsistent across studies, and the precise mechanism of bimatoprost' s action has yet to be defined.[10,24,25]

The intracameral implant (Durysta; Allergan, an AbbVie company, North Chicago, IL, USA) is a biodegradable device containing 10 μg of bimatoprost, which is gradually released in a non-pulsatile manner over 3 months into the anterior chamber. Composed of biodegradable polymers, the implant undergoes hydrolysis and metabolism, breaking down into carbon dioxide and water.[26–28] The intracameral implant is preloaded in a single-use 28-gauge applicator, utilizing the NOVADUR drug delivery platform, which has been previously approved for the sustained release of dexamethasone since 2009.[27,29] This direct delivery method produces higher, dose-dependent concentrations of the drug specifically at the ciliary body receptors, surpassing the concentrations observed with the topical application of bimatoprost 0.03% in animal models.[30–32] Furthermore, an in vivo study conducted on beagle dogs demonstrated that the reduction in IOP is maintained for a minimum of 3 months, with 99.8% of the bimatoprost load released by day 80.[30] The localized delivery enhances the upregulation of metalloproteinases, which promotes sustained tissue remodeling and a prolonged and greater reduction of IOP, while minimizing distribution to other tissues that could cause side effects.[26,30,33] With the topical administration of bimatoprost, bimatoprost acid is detected in the ciliary body and aqueous humor of humans and some animal models. In contrast, the direct intracameral route delivers intact bimatoprost molecules to these tissues, which may further enhance the reduction of the IOP.[26] Additionally, in an animal study involving normotensive cynomolgus monkeys treated with both topical and intracameral bimatoprost, an enhanced reduction in IOP was observed in the monkeys receiving intracameral bimatoprost. This suggests that the intracameral route may provide an additional mechanism of action beyond that of topical administration.[33] The effect on uveoscleral outflow with the intracameral bimatoprost was further elucidated in an animal model study involving beagle dogs, which demonstrated a sustained dilation of aqueous outflow vessels. This dilation resulted in a decrease in episcleral venous

pressure and an increase in uveoscleral outflow.[34] Regarding the implant's pharmacokinetics, an animal study found that drug concentration in the aqueous humor increases with higher implant concentrations. However, despite the dose-dependent concentrations of the drug no systematic absorption of bimatoprost was observed, suggesting zero-order kinetics.[31] Zero-order kinetics refer to the implant's ability to release bimatoprost at a consistent rate, regardless of concentration fluctuations in the surrounding tissue, which aids in sustained IOP reduction without peaks and troughs in drug delivery.

Intracameral Implant Administration Procedure

The proposed administration procedure (Figure 1) follows protocols established in the Phase I/II trial and the Durysta Summary of Product Characteristics (SPC), emphasizing the importance of each step to minimize complications and

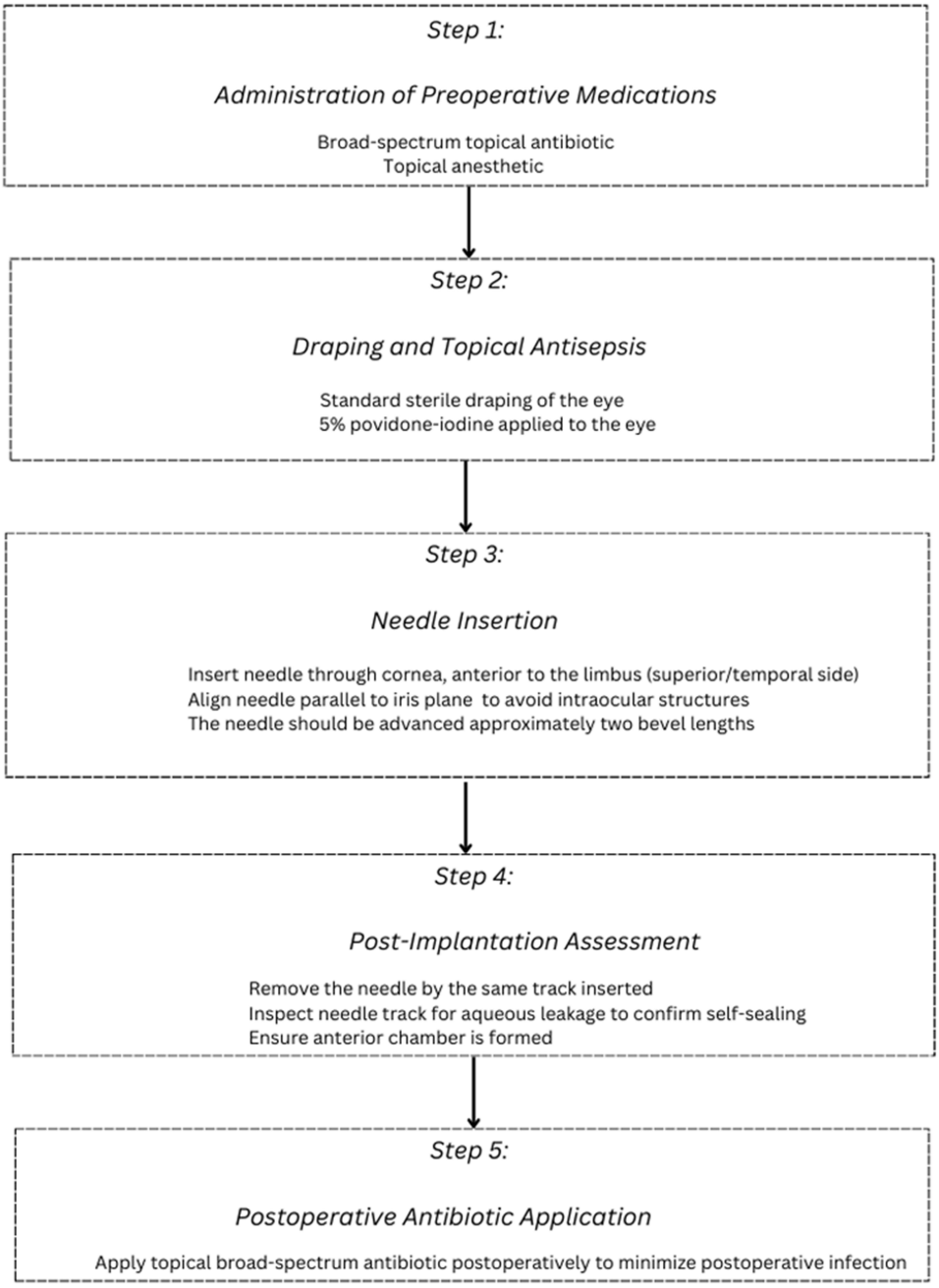

Figure 1 Durysta step by step administration procedure.

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enhance the efficacy of intraocular drug delivery, drawing upon established methods in classical intraocular drug administration.[27,35]

Randomized Clinical Trials

Clinical Phase I/II trials

The safety and efficacy of the bimatoprost implant in lowering IOP in humans were first assessed in the Phase I/II clinical trial, APOLLO, which was conducted from 2010 to 2016.[27,29] This 24-month, multinational, double-blind trial enrolled 75 subjects with well-controlled, with topical prostaglandins, bilateral primary open-angle glaucoma or ocular hypertension, who underwent a washout period from their previous topical treatments before participating. More specifically, the inclusion criteria for the study briefly included adults with open-angle glaucoma or ocular hypertension, a history of at least a 20% IOP reduction in response to topical prostaglandin analogs gonioscopically open angles, a baseline IOP of 22–36 mmHg after washout, and an inter-eye IOP difference of less than 3 mmHg. Exclusion criteria included narrow-angle or closed-angle glaucoma, posterior capsule tear, recent intraocular or any refractive surgery, conjunctival hyperemia or other ocular surface abnormalities, iris color changes associated with topical PGA treatment, central corneal thickness <470 μm or >630 μm (or inter-eye differences >70 μm), and a central endothelial cell count <2000 cells/mm² determined by specular microscopy. The trial evaluated different doses of intracameral bimatoprost implants (ranging from 6 to 20 μg) in a head-to-head comparison with topical bimatoprost, with each patient receiving the implant in one eye and topical bimatoprost in the other. The baseline IOP after the washout period ranged from 24.5 to 26.6 mmHg. A rescue treatment consisting of either an additional topical IOP-lowering medication or a second bimatoprost implant was offered to patients who received less than 15 μg of the intracameral implant and had refractory IOP measurements. The primary outcome, defined as the mean IOP reduction from baseline at 24 months, showed a dose-dependent effect, with a reduction of 7.5 mmHg for the 6 μg dose and up to 8.9 mmHg for the 20 μg dose, compared to an 8.2 mmHg reduction with topical bimatoprost. The use of rescue therapy was time dependent, with 32% of eyes receiving a second bimatoprost implant within 6 months and 72% requiring a second dose by 24 months.

Interestingly, this need for additional treatment was not solely linked to the degradation rate of the implant, as 6 eyes that maintained controlled IOP without the use of topical medication and did not require rescue therapy, despite having no visible implant on gonioscopy at 24 months. Patient compliance was high, with only 12 patients discontinuing the study—one due to cataract development, which was attributed to the implant, and one due to lack of efficacy. Adverse events, none of which were serious, were reported in 64% of eyes treated with the implant and 48% of those receiving topical bimatoprost, with conjunctival hyperemia being the most common in both groups. However, many of the adverse events in the implant group occurred within the first two days, were mild, and resolved quickly, largely related to the intracameral administration procedure. Notably, when the first two days post-administration were excluded, the incidence of adverse effects was lower in the implant group compared to the topical group. Typical side effects associated with prostaglandin drops, such as eyelash growth and iris hyperpigmentation, were not observed in any patients receiving the implant. Moreover, the implant demonstrated an excellent safety profile, even after a second administration in the rescue treatment group. Importantly, no reduction in endothelial cell count, a potential concern given the proximity of the implant to the corneal endothelium, was observed in any patient during the study.

This clinical trial demonstrated promising outcomes, with the bimatoprost implant showing non-inferiority in terms of IOP reduction compared to topical bimatoprost, and an excellent safety profile, notably reducing the classical adverse effects associated with prostaglandin analogs. However, as a Phase I/II trial, its results should be interpreted cautiously when considering everyday clinical practice. The strict inclusion criteria may have introduced selection bias, as only ideal patients were enrolled. Specifically, patients with poorly controlled glaucoma or those using drops other than prostaglandins were excluded. Additionally, regarding endothelial cell loss, all participants had deep anterior chambers and a minimum of 2000 endothelial cells/mm², limiting insights into the implant's impact on patients who do not meet these criteria. Other forms of glaucoma were also excluded from the study, leaving the implant's efficacy in such cases undetermined. Furthermore, while the trial was multinational, 71% of the participants were white, potentially limiting the generalizability of the findings to more diverse populations.

Clinical Phase III Trials

To further validate the results of the Phase I/II trial on a larger scale, two identical, randomized, double-masked, multinational Phase III clinical trials, ARTEMIS 1 and ARTEMIS 2, were conducted.[36,37] These trials included 594 and 528 patients, respectively, with the primary outcome measure being the change in IOP from baseline at weeks 2, 6, and 12, as well as an assessment of the safety profile of the bimatoprost implant. Briefly, for both studies, the inclusion criteria included a baseline IOP of 22–32 mmHg following washout, gonioscopically open inferior angles, and a central corneal endothelial cell density of at least 1800 cells/mm². Key exclusion criteria included a history of angle-closure or angle-closure glaucoma, a history of non-responsiveness to topical ophthalmic beta-blockers and/or prostaglandin analogs, a history of complicated cataract surgery, and any contraindication to beta-blocker therapy. Based on the dose-dependent IOP-lowering effect observed in earlier studies, both 10 μg and 15 μg doses of the implant were tested. In contrast to the Phase I/II trial, a head-to-head comparison was conducted between the two implant doses and twice-daily (b.i.d). topical timolol, with patients randomized into one of the three treatment groups. Participants in these studies had well-controlled ocular hypertension or open-angle glaucoma and, unlike the previous trial, could be on any topical glaucoma medication prior to enrollment. The bimatoprost implant was administered using the same technique as described earlier, with the implant typically positioned inferiorly in the anterior chamber.[36] After a washout period of prior medications, patients were masked to whether they received a sham injection or sham topical timolol. The baseline IOP for all participants was 24.5 mmHg. Additional bimatoprost implant administrations were performed at week 16 and 32, with a total of three implants given at 16-week intervals for those in the implant groups. Rescue therapy with non-study topical medications was available in refractory cases at the clinician's discretion. At 12 weeks, both dosing regimens of the bimatoprost implant (10 μg and 15 μg) were found to be non-inferior to topical timolol, with a 6–7 mmHg reduction in IOP from baseline. Interestingly, at some specific time points during the study, both bimatoprost implant doses demonstrated superior IOP reduction compared to timolol. The IOP-lowering effect remained consistent with repeated implant administrations across both studies. In ARTEMIS 1, 69% of patients receiving the 10 μg dose and 63% of those receiving the 15 μg dose did not require rescue treatment by week 86, while in ARTEMIS 2, these rates were 82% and 78%, respectively, by week 52. Kaplan–Meier analysis from ARTEMIS 1 estimated that 75.5% of patients (10 μg) and 73% (15 μg) did not need additional treatment for 1 year after the last implant administration, with similar findings observed in ARTEMIS 2. The exact rate of implant biodegradation varied between patients and doses, resulting in uncertainty regarding the optimal timing for re-administration. Notably, the implant size increased between weeks 12 and 28 due to contact with aqueous humor, with 95% of the 10 μg implants being less than 25% of their original size by 20 months.

In both ARTEMIS 1 and 2 trials, adverse effects were reported, the majority of which were of mild-to-moderate severity and dose-dependent, with the most-pronounced effects occurring within the first two days post-administration. These early adverse effects were primarily attributed to the administration procedure itself, consistent with findings from the Phase I/II study. The most common ocular side effect was conjunctival hyperemia, which was more prevalent during the first two days, occurring in 17.7% of patients, compared to only 5.1% of patients after this initial period.[38] Treatment-related adverse events were observed in 57.9% (ARTEMIS 1) and 48% (ARTEMIS 2) of patients receiving the 10 μg dose, compared to 61.1% and 61.9% of patients receiving the 15 μg dose. In contrast, only 25.9% (ARTEMIS 1) and 20.8% (ARTEMIS 2) of those treated with topical timolol experienced adverse effects. However, more serious adverse events, particularly corneal decompensation due to endothelial cell loss, were more frequently observed in the implant groups, particularly with repeated administrations. The incidence of corneal complications increased with higher doses and repeated treatments, leading to implant removal in 3.6% and 2.9% of patients receiving the 10 μg dose, and 8.3% and 10.8% of those receiving the 15 μg dose in ARTEMIS 1 and 2, respectively. Although some endothelial cell loss was also noted in the topical timolol groups, it was more prevalent in the implant groups, especially after multiple implant administrations. The dose-dependent nature of these side effects, along with the impact of repeated treatments, was further highlighted by the fact that many patients did not receive all three planned implants. More specifically, in ARTEMIS 1, 87% of patients receiving the 10 μg dose, and 80% receiving the 15 μg dose completed all three administrations. In ARTEMIS 2, these rates were 88% and 78%, respectively. Notably, no corneal adverse effects

were observed after a single administration of the 10 μg dose, leading to its FDA approval for single-dose use. Additionally, common prostaglandin-associated side effects, such as eyelash growth, were not reported in any patients, and iris hyperpigmentation was only noted in 11 eyes across both studies.

Following the demonstrated non-inferiority and favorable safety profile of the 10 μg bimatoprost intracameral implant in previous studies, as well as its FDA approval, a Phase 3b study was designed to further evaluate its IOP-lowering effects and safety over a one-year period with only a single administration of the implant.[39] Unlike prior studies, this investigation included a 24-hour diurnal IOP assessment, with measurements taken every two hours in both sitting and supine positions using pneumotonometry.[39] After an initial washout and baseline 24-hour IOP measurement, 31 patients with primary open-angle glaucoma or ocular hypertension (20.4%) received a single 10 μg bimatoprost implant. Results showed an hour-matched IOP reduction ranging from 1.7 to 3.7 mmHg in the sitting position and 1.7 to 2.4 mmHg in the supine position, with an overall reduction in IOP fluctuation across the 24-hour period. At two months, no patient required additional topical treatment, and by 12 months, only 8 patients (25.8%) needed supplemental treatment, aligning with the Kaplan–Meier analysis from the ARTEMIS trials.[36,39] The implant's biodegradation rate was corroborated, with initial swelling observed at week 16 in 38.7% of patients, followed by a reduction to less than 25% of the implant's original size in 67.7% of patients by the one-year mark. This single administration of the 10 μg implant demonstrated a strong safety profile, with no serious adverse effects reported. The most common adverse event was conjunctival hyperemia, primarily related to the administration procedure. Unlike the ARTEMIS trials, which involved multiple implant administrations at fixed intervals, this study observed no greater than a 20% reduction in endothelial cell count, further supporting the safety of a single implant dose. Although this study provides a rigorous, diurnal evaluation of the implant's effects, the small cohort size limits the generalizability of these promising results.

Another phase 3b study was conducted to compare selective laser trabeculoplasty (SLT) with a higher dose of the bimatoprost implant (15 μg), which exceeds the currently approved dosage.[40] Briefly, inclusion criteria included patients with open-angle glaucoma or ocular hypertension, a baseline IOP between 22 mmHg and 34 mmHg, an interocular pressure difference of less than 5 mmHg, and the patient being considered a suitable candidate for selective SLT. Gonioscopically open angles and a central total corneal endothelial cell density of ≥1800 cells/mm² were also required. Key exclusion criteria included a history of SLT, evidence of complicated cataract surgery, and the presence of phakic intraocular lenses. While the study established non-inferiority, it included up to three repeated administrations of the implant, which were associated with serious ocular complications in 6.3% of patients, including cataract formation, quadrantanopia, corneal edema, and endothelial cell loss. In contrast, no serious ocular complications were reported in the SLT group. Anterior chamber inflammation occurred in 9.9% of eyes receiving the implant compared to 3.5% in the SLT group, and iritis developed in 3.5% of eyes after a second implant administration. Corneal treatment adverse effects were reported in 19.9% of eyes treated with the implant, compared to 4.3% of eyes treated with SLT. These included serious events such as corneal endothelial cell loss and corneal edema, as well as less serious events like punctate keratitis. Notably, 10% of patients experienced a reduction of more than two lines in best-corrected visual acuity (BCVA), ultimately resulting in the discontinuation of the bimatoprost 15μg implant's development.

An ongoing Phase 3b multicenter clinical trial (NCT03850782), initiated in 2019, is currently underway and demonstrates promising results.[41,42] This trial employs a pro re nata (PRN) approach using the FDA-approved dosage, aligning more closely with routine clinical practice.[42] Preliminary findings were presented at the 2024 ARVO annual meeting, with 211 of the 423 enrolled patients completing the one-year follow-up period. The IOP reduction was significant, with an 8.1 mmHg decrease from baseline observed at 12 weeks, with a declining effect leading to a 6.3 mmHg reduction at the end of the first year. However, the decline in effect was deemed acceptable for over half of the patients, as cumulative probability analysis indicated that 56.5% of participants did not require additional implants or supplemental topical therapy by the conclusion of the first year. Furthermore, the implant maintained an acceptable safety profile up to the point at which these data were collected (1 year for almost half patients).

While the results of the clinical trials are promising, the patient pool's limited diversity in both age and ethnicity and the exclusion of other glaucoma types, such as pseudoexfoliation, may restrict the generalizability of these findings.

FDA Approval

The intracameral bimatoprost implant, with a dosage of 10 µg, received FDA approval in March 2020 based on the efficacy and safety profiles reported in the ARTEMIS 1 and 2 studies.[43] Its approved indication is for the treatment of primary open-angle glaucoma and ocular hypertension, and it is approved only for a single administration, as repeated administrations in Phase 3 clinical trials were associated with corneal adverse effects. The implant is contraindicated in patients with ocular or periorbital inflammation, corneal abnormalities such as endothelial dystrophy, and those with a history of prior corneal transplantation due to the potential for a decline in endothelial cell count. Additionally, it is contraindicated in individuals with an absent or ruptured posterior lens capsule, including those with aphakia, due to the risk of posterior chamber migration, as well as in patients with hypersensitivity reactions to any of its components.[35]

Real World Studies

While randomized clinical trials are considered the gold standard for reliability, real-world evidence studies are essential in complementing their findings.[44] They capture clinical outcomes in a broader patient population reflective of everyday clinical practice, unrestricted by the strict inclusion and exclusion criteria often present in clinical trials.[44]

Since the FDA approved the use of 10 µg intracameral bimatoprost in 2020, seven retrospective real-world studies have been conducted to date.[45–51] An observational retrospective study corroborated the promising, long-lasting efficacy and safety profile demonstrated in Phase 3 trials.[46] It reported a sustained intraocular pressure (IOP) reduction of 3.3 mmHg from a lower baseline IOP of 16.6 mmHg, attributed to the absence of a washout period compared to the Phase 3 trials, over a 12-month period.[46] Additionally, the mean number of topical medications decreased from 1.4 to 0.2 at the 12-month mark, further supporting the implant's durable effect.[46] No severe corneal adverse effects or instances of implant removal were reported.[46] Another retrospective study explored the implant's potential in a specific population of American Indian patients with high, uncontrolled baseline IOP (26.25 mmHg).[47] Results showed that 75% of patients achieved a 20% reduction in baseline IOP by the end of the first year.[47] Additionally, at the six-month mark, 73% of eyes required at least one fewer medication, and by the end of the first year, 40% of eyes were medication-free.[47] The findings of another retrospective study were even more promising, with 68.4% of patients not requiring a return to their initial topical therapy by the end of the first year.[51] The efficacy of the implant in severe POAG appears limited, as suggested by a retrospective study conducted at Duke Eye Center, which more than half of the patients included had severe POAG (54%).[45] Unlike the clinical trials, which did not evaluate the implant's effectiveness in severe cases, this study found a significant reduction in the number of medications for up to six months in mild and moderate POAG.[45] However, in eyes with severe disease, this reduction was sustained only up to one month, with 20.7% of cases requiring additional procedures, including filtration surgery, to achieve adequate IOP control.[45] An alternative approach to implant administration has been proposed, employing a slit-lamp setting rather than a dedicated operating theater, as conducted in clinical trials.[48] Despite this change in setting, the same procedural steps were followed, resulting in a favorable safety profile, with only 3 of 129 patients reporting mild, transient adverse effects.[48] At one year, 27.8% of eyes maintained adequate IOP control with the implant alone, requiring no additional medications.[48] Additionally, there was a mean reduction of 0.5 medications per eye, with half of the eyes requiring one or fewer medications at 12 months compared to baseline.[48] The effect of the implant on patients with a history of glaucoma surgery and even chronic angle closure glaucoma (3.4%), including filtration and minimally invasive procedures, was notable, despite the absence of a significant reduction in IOP.[49] This lack of reduction may be attributed to the lower baseline IOP and the absence of a washout period.[49] Nevertheless, there was a decrease in medication use, with only 4 out of 41 eyes requiring additional surgery.[49] The effect of the implant on eyes with a history of SLT, according to a retrospective study was consistent with findings from the Phase 3 trials, demonstrating a significant decrease in IOP.[38,50] Additionally, patients with prior SLT who received the implant experienced a noteworthy reduction of one medication.[50] However, this study did not prove whether the combination of the bimatoprost implant and SLT is superior to bimatoprost administered alone.[50]

Overall, all of the retrospective studies demonstrated a reduction in medication burden, effective IOP reduction, and an adequate safety profile in a broader patient population, including those with previous glaucoma surgery, various types of glaucoma, and specific populations not included in the clinical trials. However, due to the recent FDA approval, the longest follow-up period recorded was approximately one year, highlighting the need for longer-term studies.

Additionally, the patient cohorts were relatively small, ranging from 46 to 197 eyes, indicating that larger cohorts are necessary to establish more robust data. Furthermore, no meta-analyses have been conducted to provide valuable insights into the safety and efficacy of the implant. Most studies were conducted at single centers, with the administration procedure performed by a limited number of experienced practitioners, which restricts the generalizability of their results. It is noteworthy that none of the studies addressed the optimal time point for a second bimatoprost administration following the waning effect of the first administration. These studies underscore the need for more extensive data in advanced glaucoma types, where the implant's effectiveness and safety profile over multiple administrations remain less understood.

A comprehensive summary of all studies investigating the use of the bimatoprost implant is presented in Table 1.

Table 1 Summary of the Studies on Bimatoprost Intracameral Implant (DURYSTA®)

Study	Year	Design	Number of Patients	Key Findings
Shen et al[31]	2020	Pre-clinical study	44 male normotensive dogs	• The PK/PD relationship supports sustained IOP lowering with SR implants, with good tolerance and stable drug release over 3 months
Lee et al[33]	2019	Pre-clinical study	6 female, normotensive cynomolgus monkeys	• Efficacy: Compared with topical bimatoprost, intracameral BimSR may have an additional mechanism of action of IOP lowering.
Lee et al[34]	2018	Pre-clinical study	7 normotensive beagle dogs	• Efficacy: The bimatoprost SR implant lowered EVP in the treated dogs. By reducing EVP, the implant could lead to a more sustained reduction in IOP, offering an effective alternative to conventional glaucoma treatments
Seal et al[30]	2019	Phase 1/2, comparative animal study	24 beagle dogs	• Efficacy: The bimatoprost SR implant significantly improved the delivery of bimatoprost to the iris-ciliary body compared to the topical administration
APOLLO[27,29]	2022	Phase I/II, 24-month, multinational, clinical trial	75 adult patients diagnosed with POAG or OHT	• Efficacy: 6μg dose: 7.5mmHg reduction, 20μg dose: 8.9mHg reduction, Topical bimatoprost: 8.2mmHg • Adverse events: 64% of eyes receiving the implant reported adverse events compared to 48% in topical bimatoprost.
ARTEMIS 1[37]	2021	Phase 3, 20-month, randomized, multicenter	594 patients diagnosed with OAG or OHT	• Efficacy: 10μg and 15μg doses of bimatoprost implant demonstrated noninferiority to twice daily topical timolol 0.5%. Mean IOP reductions from baseline ranged from 7.2–9.5mmHg in the 10μg group and 7.4–9.7 in the 15μg group, compared to 6.6–8.4mmHg in the timolol group. • Adverse events: mild to moderate, most occurring the first 2 days post-administration
ARTEMIS 2[36]	2023	Phase 3, 20-month, randomized, multicenter	528 patients diagnosed with OAG or OHT	• Efficacy in IOP: 10μg and 15μg doses of the bimatoprost implant showed significant IOP reduction, maintaining noninferiority to topical timolol. • Adverse events: mild to moderate, with most occurring the first 2 days post-administration

(*Continued*)

Table 1 (Continued).

Study	Year	Design	Number of Patients	Key Findings
Teymoorian et al[46]	2024	Phase 3 observational, retrospective study	105 patients with OAG or OHT	• Efficacy: mean IOP reduction of 7.5mmHg from baseline at the 12-week follow-up. This reduction was sustained with a mean decrease of 6.8mmHg at the 24-week mark • Adverse events: mild irritation or conjunctival hyperemia
Ali et al[48]	2024	Phase 3 retrospective interventional case series	129 eyes of 81 patients	• Efficacy: The bimatoprost SR implant effectively reduced IOP over a sustained period in a non-surgical setting, indicating that slit-lamp implantation can achieve similar efficacy to traditional methods. • Adverse events: mild to moderate
Medeiros et al[38]	2022	Phase 3 clinical trials 20-month, parallel-group,	747 patients with OAG or OHT	• Efficacy: The 10μg bimatoprost implant demonstrated sustained IOP reductions from 4.9–-7mmHg over 15 weeks. The IOP reduction was measured from a baseline of 24.5mmHg in patients with OAG and OHT
Christie et al[40]	2023	Phase 3b, 12-month, randomized, multicenter study	138 glaucoma patients	• Efficacy: noninferiority of the bimatoprost implant compared to SLT • Adverse events: Serious ocular complications occurred in 6.3% of patients. Corneal adverse effects in 19.9%, higher than with SLT • 10% experienced a reduction of more than 2 lines in BCVA
Moster et al[42]	2024	Phase 3b	423 patients with 211 completing the one-year follow up period	• Efficacy: 8.1 mmHg decrease from baseline at 12 weeks • 56.5% of participants did not require additional implants or supplemental topical therapy by the end of first year • Safety profile: The implant maintained an acceptable safety profile • Efficacy: The IOP-lowering effect of the initial bimatoprost implant administration was well maintained for >1 year
Wong et al[50]	2023	Retrospective study	84 patients	• The mean post-treatment IOP at the most recent f/up was 16.6±5.3mmHg, compared to a pretreatment IOP of 18.5±5.7mmHg
Xu et al[51]	2023	Retrospective study	38 patients	• Efficacy: Mean IOP reduction from baseline was as follows: 1.26±2.53mmHg at 3 months, 0.93 ±4.71mmHg at 6 months and 1.35±5.24mmHg at 12 months • Implant failure: 32.6% of eyes experienced implant failure, which was defined as the need to restart IOP-lowering eye drops or undergo surgical intervention

(*Continued*)

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Table 1 (Continued).

Study	Year	Design	Number of Patients	Key Findings
Bowers et al[49]	2024	Observational, retrospective study	118 from 86 patients with a diagnosis of OAG, chronic angle closure glaucoma, or ocular hypertension	• Efficacy: The reduction in IOP was maintained over the study period, indicating the implant's utility as an adjunctive treatment for patients who may need additional IOP control post-surgery
Sarkisian Jr. and Mitchell[47]	2024	Retrospective study	156 eyes from adult patients	• At 6 months, eyes with baseline IOP≥21 mmHg had a significantly lower mean IOP (19.85±8.01 versus 26.25±4.84 mmHg). • One year after implantation, 73.58% of eyes had a ≥20% reduction in IOP, 41.51% were medication-free and 30.19% were receiving at least one fewer medication. • No major safety issues were reported

Abbreviations: OAG, Open Angle Glaucoma; POAG, Primary Open Angle Glaucoma; OHT, Ocular Hypertension; IOP, Intraocular Pressure; BCVA, Best Corrected Visual Acuity; SLT, Selective Laser Trabeculoplasty; EVP, Episcleral Venous Pressure; PK, Pharmacokinetic; PD, Pharmacodynamic.

Conclusion

The bimatoprost intracameral implant introduces a novel route of administration that effectively reduces IOP, alleviates the burden of daily medications, and maintains a favorable safety profile. This innovative approach shows promise for improving adherence and minimizing common side effects associated with prostaglandins. However, further research is essential to fully understand its role in broader clinical practice, particularly for advanced and secondary types of glaucoma, such as pseudoexfoliative and angle-closure glaucoma. Future studies should focus on establishing optimal timing and criteria for repeat administrations, as the implant's effect duration may vary between individuals. Additionally, exploring alternative dosing strategies and adjunct therapies may help enhance efficacy while minimizing risks associated with multiple administrations. Cost-effectiveness studies are also necessary to determine the economic feasibility of this treatment compared to conventional therapies, especially in long-term management. Real-world studies with diverse and larger cohorts, as well as longer follow-up periods, will be key to providing robust data on the implant's long-term safety and effectiveness. Finally, investigating the implant's combination with other IOP-lowering therapies, such as selective laser trabeculoplasty or minimally invasive glaucoma surgery, could offer insights into complementary approaches that optimize IOP control and patient safety.

Disclosure

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