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MODERN GLAUCOMA THERAPY: A NARRATIVE REVIEW

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ABSTRACT

Introduction: Glaucoma is a chronic, progressive optic neuropathy and a major cause of irreversible vision loss worldwide. Because early disease is often asymptomatic, many patients are diagnosed after relevant structural damage has already developed. Lowering intraocular pressure (IOP) remains the primary therapeutic objective and the most established approach to reduce the risk of progression. This review summarizes current advances in glaucoma care, including modern pharmacological strategies, sustained-release therapy, neuroprotection research, microinvasive glaucoma surgery (MIGS), and diagnostic innovations.
Methodology: A narrative review of PubMed, Scopus, and Google Scholar was performed to summarize recent evidence on modern glaucoma therapy and monitoring.
Results: Recent progress in medical therapy includes agents targeting the conventional outflow pathway, updated prostaglandin-based approaches, and fixed-dose combinations that reduce regimen complexity. Long-acting drug delivery systems may decrease the reliance on daily eye drops, although safety and durability remain important considerations. Neuroprotection continues to attract strong research interest, but clinical evidence is still insufficient to support a widely accepted strategy beyond IOP lowering. MIGS provides intermediate surgical options that may reduce IOP and medication burden in selected patients, yet outcomes vary across techniques and study designs. OCT and OCT angiography support objective monitoring of structural and vascular changes and may improve detection of progression over time.
Conclusion: Glaucoma care is becoming increasingly individualized through expanding therapeutic and monitoring strategies. Future research should focus on long-term standardized outcomes, improved progression biomarkers, and validation of disease-modifying approaches, including gene- and regenerative therapies.

KEYWORDS

Glaucoma, Intraocular Pressure, Rho-Kinase Inhibitors, Sustained-Release Implant, MIGS

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Introduction

Glaucoma is a chronic, progressive optic neuropathy defined by degeneration of retinal ganglion cells (RGCs) and their axons, leading to characteristic optic nerve head changes and corresponding visual field defects that are typically irreversible. [1] The disease represents a major cause of permanent vision loss worldwide, and its burden is expected to increase further due to population aging and long-term disease duration. [2] Meta-analytic estimates indicate that glaucoma affects a substantial proportion of adults over 40 years of age, with projections suggesting continued growth in the number of patients living with the condition through 2040.

[2] A key clinical challenge is that early-stage glaucoma may remain asymptomatic, and many individuals are diagnosed only after meaningful structural damage has already occurred. [3] Clinically, glaucoma comprises a heterogeneous group of disorders that are commonly classified as primary or secondary, and further stratified by anterior chamber angle anatomy into open-angle and angle-closure forms. [4] Primary open-angle glaucoma (POAG) is the most frequently encountered subtype in many regions, whereas primary angle-closure glaucoma (PACG) remains highly relevant because of its anatomical basis and potential for a more aggressive course in predisposed eyes. [2] Additional entities of clinical importance include normal-tension glaucoma, where progression may occur despite IOP values within statistically normal ranges, and secondary glaucomas, in which optic nerve damage and/or IOP elevation is related to identifiable causes such as pseudoexfoliation, pigment dispersion, inflammation, or corticosteroid exposure. [5] The pathophysiology of glaucoma is multifactorial and is often conceptualized as an interplay between aqueous humor outflow physiology, optic nerve head biomechanics, and neurovascular susceptibility. In open-angle disease, increased resistance within the trabecular meshwork and Schlemm's canal contributes to IOP elevation or heightened pressure-related stress, and prolonged IOP exposure is thought to promote remodeling processes within the

optic nerve head and lamina cribrosa that can compromise axonal integrity. [3] Experimental and clinical literature also supports a role for connective tissue deformation and lamina cribrosa changes, which may amplify strain on retinal ganglion cell axons and contribute to the typical excavation ("cupping") phenotype observed on optic disc evaluation. [6] In parallel, neurodegenerative mechanisms beyond pressure load—including mitochondrial dysfunction, oxidative stress, excitotoxicity, impaired axonal transport, and altered neurotrophic support—have been repeatedly implicated as contributors to RGC vulnerability, potentially explaining why progression can occur at relatively low IOP values in some patients. [7] Another actively investigated concept involves the translaminar pressure gradient, reflecting the relationship between IOP and cerebrospinal fluid pressure; this hypothesis has attracted particular interest in the context of normal-tension glaucoma, although current evidence remainslargely associative and requires cautious clinical interpretation. [8,9] Despite increasing focus on non–IOP-dependent mechanisms, IOP reduction remains the cornerstone of glaucoma therapy, as it is the most consistently modifiable factor linked to disease onset and progression across major clinical subtypes. [3] Contemporary guidelines continue to prioritize pressure lowering as the primary treatment goal in routine practice, while also acknowledging the need for individualized target IOP selection based on baseline risk and progression patterns. [5] However, real-world outcomes may diverge from clinical trial efficacy because sustained therapeutic benefit depends not only on pharmacologic potency but also on adherence, correct drop instillation, ocular surface tolerability, and long-term persistence. [10] Against this background, the aim of the present review is to summarize recent advances in glaucoma management, with emphasis on modern pharmacological approaches (including novel mechanisms and fixed-dose combinations), long-acting drug delivery systems, neuroprotection as an evolving research domain, and the expanding role of microinvasive glaucoma surgery, while highlighting current evidence strengths as well as limitations relevant to everyday clinical decision-making. [5]

Results

1. Modern Pharmacological

Medical management of glaucoma continues to be centered on sustained intraocular pressure (IOP) reduction, as IOP remains the most consistently modifiable factor linked to glaucomatous disease development and progression across major clinical subtypes. [3]

Although non–IOP-dependent mechanisms have been increasingly investigated; current clinical frameworks and real-world practice still prioritize IOP lowering as the primary therapeutic objective supported by established evidence. [5]

Topical pharmacotherapy remains the most widely used initial approach, with treatment escalation guided by the required magnitude of IOP reduction as well as patient-related factors such as tolerability, comorbidity burden, and adherence. In this context, "real-world effectiveness" may differ from randomized trial efficacy because correct instillation technique, persistence over time, and ocular surface tolerability can determine whether the intended pressure reduction is achieved. [10]

1.1 Rho-Kinase Inhibitors

Rho-kinase (ROCK) inhibitors are considered a major recent pharmacological innovation in glaucoma because they primarily target conventional aqueous outflow rather than relying exclusively on aqueous suppression. [11] At the tissue level, ROCK inhibition is thought to reduce trabecular outflow resistance by modulating cytoskeletal organization and contractility in the trabecular meshwork and Schlemm's canal region. [12] Netarsudil has been extensively evaluated in phase III clinical trials, with pivotal ROCKET studies demonstrating statistically significant IOP reduction in open-angle glaucoma and ocular hypertension.[13] Pooled analyses suggest that the IOP-lowering signal is observed across a range of baseline IOP values, although the magnitude of reduction may be modest in some comparative contexts. [14] Because ROCK inhibitors act via a distinct physiological mechanism, they are often discussed as add-on agents when further IOP reduction is needed on top of established therapies. [11] Treatment-limiting adverse effects are clinically relevant, as conjunctival hyperemia is frequently reported and may reduce persistence in routine practice for a subset of patients. [15] Recent safety-focused literature has reported reticular epithelial edema and occasional corneal verticillata with ROCK inhibitors, supporting individualized use and long-term monitoring. [16]

Ripasudil, approved in selected regions (particularly in parts of Asia), has shown clinically meaningful intraocular pressure–lowering efficacy when used as adjunctive (add-on) therapy, supporting the broader therapeutic potential of the ROCK inhibitor class, while also highlighting regional differences in regulatory approval and real-world clinical adoption. [17]

1.2 Prostaglandin-Pathway Innovations

Prostaglandin analogues remain a cornerstone of glaucoma therapy because they reliably reduce intraocular pressure (IOP) by increasing aqueous humor outflow. [18] Recent prostaglandin-pathway innovations have aimed to enhance either the magnitude of IOP reduction or the range of outflow mechanisms affected, particularly in patients requiring stronger pressure lowering. Nitric oxide–donating prostaglandin analogues were developed to combine the established prostaglandin effect on uveoscleral outflow with nitric oxide–mediated modulation of the conventional trabecular pathway. [19] Nitric oxide signaling is associated with relaxation and functional changes in the trabecular meshwork and Schlemm's canal, which may facilitate aqueous drainage through the conventional outflow system. [20] Latanoprostene bunod is the best-studied representative of this approach, showing greater IOP reduction than latanoprost in the VOYAGER trial and clinically meaningful pressure lowering versus timolol in Phase III studies. [18, 21] Nevertheless, interpretation across trials requires caution because differences in eligibility criteria and follow-up protocols limit direct cross-study comparisons. [22] An alternative prostanoid strategy is EP2 receptor agonism, represented by omidenepag isopropyl, which differs pharmacologically from classical FP-receptor prostaglandin analogues. [23] Omidenepag isopropyl is administered as a topical prodrug converted into an active EP2 agonist, and its IOP lowering is linked to increased outflow through cAMP-related mechanisms that may involve both trabecular and uveoscleral pathways. [24] Randomized Phase III trials (SPECTRUM 3 and 4) demonstrated IOP reduction versus timolol over the trial horizon, although long-term persistence and safety require continued evaluation. [25,24] Tolerability remains a key factor in clinical integration, and safety discussions have also reported cystoid macular edema as a potential issue in predisposed eyes, highlighting the importance of individualized risk assessment. [26]

1.4 Fixed-Dose Combinations Incorporating Newer Mechanisms

Fixed-dose combinations (FDCs) are widely used in glaucoma care because they reduce treatment complexity by decreasing the number of bottles and daily instillations. [27] This strategy is clinically relevant in chronic disease management, where nonadherence and treatment fatigue can reduce real-world effectiveness even when pharmacologic efficacy is high. [28] The netarsudil/latanoprost FDC combines a ROCK inhibitor with a prostaglandin analogue, thereby targeting complementary outflow mechanisms and providing an option for therapy escalation. [29] Phase III MERCURY trials demonstrated greater mean IOP reduction with this combination than with either component alone, and pooled analyses supported a safety profile consistent with known effects of its individual agents. [30,31] However, clinical persistence may be limited by tolerability, as conjunctival hyperemia is frequently reported with netarsudil-containing regimens, and fixed-ratio dosing reduces flexibility when adverse effects necessitate component-specific adjustment. [30,32]

1.5 Long-Acting Drug Delivery Systems

Long-acting drug delivery systems were developed to address limitations of daily topical therapy, including inconsistent adherence, variable instillation technique, and fluctuating drug exposure over time. These challenges are clinically important because glaucoma is often asymptomatic in early stages, which may contribute to reduced motivation for strict long-term adherence despite ongoing risk of progression. [28] Sustained-release platforms aim to provide more consistent IOP control while reducing reliance on patient-dependent daily behaviors. [33] The intracameral biodegradable bimatoprost implant is one of the most advanced sustained-release strategies evaluated for open-angle glaucoma and ocular hypertension. Phase III ARTEMIS trials demonstrated sustained IOP reduction following implantation and assessed repeated administration protocols for longer-term pressure control. [34] Long-term observations indicate variable durability, with some eyes maintaining pressure lowering beyond the nominal drug release period, potentially influenced by differences in biodegradation kinetics. [35,36] Safety remains a key determinant of clinical adoption, particularly because intracameral delivery raises concerns regarding corneal endothelial effects, emphasizing careful patient selection and monitoring. [36,37] Comparative Phase III research has also evaluated sustained-release implantation versus selective laser trabeculoplasty (SLT), supporting its potential role as an alternative drop-sparing intervention in selected patients, although long-term comparative effectiveness remains incompletely defined. [38]

2. Neuroprotection – A Highly Active Area of Research

In glaucoma, neuroprotection refers to strategies intended to preserve retinal ganglion cells and their axons through mechanisms that may extend beyond IOP reduction. Preclinical studies implicate multiple pathways—including excitotoxicity, oxidative stress, mitochondrial dysfunction, and impaired neurotrophic support—in retinal ganglion cell vulnerability. Despite a strong biological rationale, reviews consistently highlight that translation from experimental neuroprotection to reliable long-term clinical benefit has remained challenging. [39] Brimonidine has been investigated due to experimental evidence suggesting potential neuroprotective effects beyond IOP lowering, and clinical studies have explored functional outcomes in addition to pressure reduction. [40] However, systematic reviews emphasize that clinical evidence remains inconclusive, partly because study designs, endpoints, and discontinuation patterns can complicate interpretation [41] Citicoline has been evaluated as an adjunctive strategy, with trials assessing functional or electrophysiological outcomes, although methodological heterogeneity limits firm conclusions. [42] NMDA receptor antagonism has demonstrated neuroprotective effects in animal models, but large clinical development programs did not establish a definitive reduction in glaucoma progression. [43,44] Sustained neurotrophic factor delivery has been explored in early-phase studies, where outcomes primarily inform feasibility and safety rather than confirm clinical efficacy. [45] Overall, the absence of a widely accepted neuroprotective standard is commonly attributed to disease heterogeneity, limitations in endpoints, and challenges separating neuroprotection from IOP-mediated effects. [39]

3. Microinvasive Glaucoma Surgery (MIGS)

Microinvasive glaucoma surgery (MIGS) encompasses a heterogeneous group of procedures designed to lower IOP with reduced tissue disruption and a potentially more favorable safety profile compared with more invasive glaucoma surgeries. A clinically useful way to conceptualize MIGS is to classify procedures by the anatomical outflow pathway they primarily target, including trabecular meshwork/Schlemm's canal–based approaches and subconjunctival (bleb-forming) implants. Because MIGS procedures vary in both mechanism and postoperative management requirements, reviews generally recommend interpreting outcomes on a procedure- or device-specific basis rather than assuming a uniform "MIGS effect." [46] Across systematic syntheses, MIGS are most often positioned for mild-to-moderate glaucoma, frequently combined with cataract surgery, where moderate IOP reduction and/or medication reduction is desired with an emphasis on safety. [47] Systematic reviews indicate that MIGS can lower IOP and reduce medication burden, but effect estimates vary substantially due to heterogeneity in baseline disease severity, outcome definitions, and study design. [48] Because cataract surgery itself can lower IOP, reviews stress that interpretation of combined phaco–MIGS outcomes requires attention to control groups and medication washout protocols. [49]

3.1 iStent family (trabecular micro-bypass)

The iStent devices are trabecular micro-bypass implants designed to reduce resistance at the trabecular meshwork by creating a small direct pathway from the anterior chamber into Schlemm's canal using an ab interno approach. This mechanism is intended to facilitate aqueous humor drainage through the conventional outflow system, which is frequently impaired in open-angle glaucoma due to increased trabecular outflow resistance. In cataract-combined surgery, many clinical series and comparative studies report that iStent implantation can reduce IOP and/or topical medication use, although the size of the effect depends strongly on patient selection and baseline values. [50] Real-world cohorts with longer follow-up also suggest sustained medication reduction in many eyes, but these observations should be interpreted in light of heterogeneous designs and the influence of concurrent cataract extraction. [51] When iStent is performed as a standalone intervention (without phacoemulsification), a systematic review and meta-analysis reported clinically meaningful IOP and medication reductions, but emphasized that the evidence base is smaller than for combined procedures. [52] Because iStent improves conventional outflow rather than creating a new filtration route, its achievable IOP range is partly limited by distal outflow anatomy and episcleral venous pressure, which may constrain utility in eyes requiring very low target pressures. [53]

3.2 Hydrus Microstent (Schlemm's canal scaffold)

Hydrus is an intracanalicular implant intended to scaffold and dilate Schlemm's canal, thereby increasing access to collector channels and supporting conventional outflow over a longer segment than point-bypass stents. By addressing both the trabecular interface and canal patency, this design concept aims to improve outflow efficiency across multiple drainage pathways. A Cochrane review reported moderate-certainty evidence suggesting that Hydrus may yield greater short-term IOP reduction than iStent in some comparative contexts, while also highlighting limited head-to-head trial availability and population dependence. [53] Network meta-analyses focusing on cataract-combined MIGS further show that comparative effectiveness estimates depend on trial inclusion and endpoint definitions, meaning results should be generalized carefully. [54] High-quality long-term data come from the randomized HORIZON trial, where Hydrus combined with cataract surgery was compared with cataract surgery alone, with reported differences over 5 years in IOP- and medication-related outcomes using prespecified criteria. [55] A post hoc analysis of HORIZON visual field outcomes also explored functional progression over the same follow-up period, supporting interest in longer-term disease-modifying implications beyond IOP alone. [56]

3.3 Kahook Dual Blade (KDB) excisional goniotomy (implant-free trabecular procedure)

Kahook Dual Blade goniotomy is an implant-free technique that removes a strip of trabecular meshwork, aiming to decrease outflow resistance by exposing direct access to Schlemm's canal. Unlike micro-bypass stents, which create a localized bypass channel, excisional goniotomy physically excises part of the obstructing tissue, which may influence outflow across a broader segment. A focused literature review of KDB outcomes described consistent reductions in IOP and medication burden across many clinical series, while stressing variation by glaucoma subtype, severity, and whether phacoemulsification is performed concurrently. [57]

Meta-analytic comparisons of KDB-phaco versus iStent/iStent inject-phaco have reported differences favoring KDB for certain success endpoints, but also emphasized heterogeneity and limited standardization of criteria across studies. [58] A separate meta-analysis evaluating phacoemulsification with versus without KDB goniotomy addressed the additive benefit of KDB in cataract settings, again highlighting dependence on study design and baseline disease features. [59] Overall, KDB is frequently positioned as an option for patients in whom avoiding an implant is desirable, but interpretation of comparative superiority should remain cautious due to frequent reliance on retrospective and non-randomized evidence. [58]

3.4 XEN Gel Stent (subconjunctival bleb-forming MIGS)

The XEN Gel Stent is designed to create a controlled outflow pathway from the anterior chamber to the subconjunctival space, which typically results in bleb formation and may enable greater IOP reduction than many trabecular MIGS techniques.This approach resembles the concept of traditional filtration surgery but is performed through a minimally invasive ab interno route, which may reduce surgical trauma compared with trabeculectomy in selected cases.Systematic reviews and meta-analyses consistently report reductions in IOP and medication use after XEN implantation, although pooled results incorporate diverse glaucoma populations and heterogeneous perioperative protocols. [60] A meta-analysis specifically emphasized that postoperative bleb management is common, with needling frequently reported across cohorts, which is clinically important when counseling patients about follow-up intensity. [61] Because results vary substantially by center practices and patient phenotype, narrative syntheses have highlighted that XEN outcomes are context-dependent and support individualized decision-making rather than uniform expectations. [62] In practical terms, XEN is often considered when a stronger IOP-lowering effect is needed than typical trabecular MIGS can provide, while still aiming to reduce the invasiveness of conventional bleb-forming surgery in selected eyes. [60]

3.5 GATT (gonioscopy-assisted transluminal trabeculotomy) and circumferential trabeculotomy concepts

Gonioscopy-assisted transluminal trabeculotomy (GATT) is an ab interno angle procedure that opens the trabecular outflow pathway circumferentially (often approaching 360°), aiming to reduce resistance along a broad length of the trabecular meshwork. Because it does not require implant placement and typically spares the conjunctiva, it may preserve future options for filtering surgery if further escalation becomes necessary. A systematic review and meta-analysis concluded that GATT can lower IOP and reduce medication burden in open-angle glaucoma, with an overall safety profile consistent with angle-based procedures, although complications and success definitions varied between studies. [63] Longer follow-up studies (including cataract-combined cohorts) support sustained outcomes in many eyes but also show that baseline severity and disease subtype likely influence durability and magnitude of effect. [64] From a review perspective, GATT represents a more extensive trabecular intervention than focal micro-bypass, and it may be considered when a broader modification of the conventional outflow pathway is desired. [63]

3.6 OMNI Surgical System

The OMNI Surgical System is used to perform ab interno canaloplasty (dilation of Schlemm's canal) and trabeculotomy (opening of the trabecular meshwork), with the aim of improving conventional outflow through both structural expansion and reduction of trabecular resistance. In contrast to permanent implants, OMNI procedures modify the outflow pathway without leaving a device in place, which may be relevant for surgeons and patients preferring implant-free strategies. A systematic review and meta-analysis focusing on standalone OMNI reported significant IOP reduction across several follow-up time points and improvement in medication burden at one year in open-angle glaucoma populations. [65] Two-year outcomes from ROMEO and other observational studies provide additional real-world context, but interpretation remains constrained by differences in baseline disease, treatment targets, and study design. [66] Overall, OMNI is typically framed as a flexible approach for mild to moderate open-angle glaucoma, especially when reduction of medication burden is a key clinical goal. [65]

3.7 PreserFlo MicroShunt

PreserFlo MicroShunt is a subconjunctival drainage device intended to create a filtration pathway and bleb formation, conceptually aligning it closer to filtration surgery than to conventional outflow MIGS. [67] As with other bleb-forming approaches, postoperative outcomes depend not only on device placement but also on wound healing biology and bleb behavior over time. [68] Randomized evidence comparing PreserFlo with trabeculectomy suggests that both approaches can substantially lower IOP, with differences emerging in efficacy and complication profiles depending on follow-up duration and outcome definitions. [67]

An updated systematic review concluded that trabeculectomy may provide stronger pressure lowering up to two years in uncontrolled glaucoma, while PreserFlo may be associated with a lower risk of certain hypotony-related events, although the number of RCTs remains limited. In a review framework, PreserFlo is commonly discussed as a "middle-ground" option for patients needing greater IOP reduction than typical trabecular MIGS can provide, but where surgeons aim to avoid some aspects of conventional trabeculectomy. [68]

3.8 iStent infinite (third-generation trabecular micro-bypass for broader canal access)

The iStent infinite system uses multiple trabecular micro-bypass stents positioned across a wider span of Schlemm's canal, with the intent of accessing a larger number of collector channels than single focal implants. [69] Regulatory documentation describes its use in adults with primary open-angle glaucoma when prior medical and surgical treatments have failed, reflecting its positioning in more treatment-refractory contexts than cataract-linked first-line MIGS. [70] A multicenter clinical study of standalone iStent infinite reported significant reductions in IOP and medication use with a favorable safety profile in patients with uncontrolled open-angle glaucoma, although the study design and population characteristics should be considered when extrapolating to broader practice. [69] A separate multicenter evaluation of iStent infinite combined with phacoemulsification provides additional evidence on effectiveness in cataract settings, but outcomes remain dependent on baseline IOP and preoperative treatment intensity. [71] In summary, iStent infinite is often presented as an attempt to expand the performance of trabecular bypass strategies by increasing circumferential access, but long-term comparative evidence is still evolving. [69]

3.9 Endoscopic cyclophotocoagulation (ECP) with cataract surgery (inflow reduction approach)

Endoscopic cyclophotocoagulation (ECP) differs mechanistically from the above procedures because it targets aqueous humor production by treating the ciliary processes, thereby reducing inflow rather than improving outflow. [72] When combined with phacoemulsification, ECP is commonly evaluated as a strategy to enhance IOP control and decrease medication reliance during cataract surgery. [73] A systematic review and meta-analysis reported that phaco-ECP can produce sustained reductions in IOP and medication dependence, while also indicating that complication profiles may differ from cataract surgery alone, underscoring the need for balanced risk–benefit discussion. [72] Clinical studies in open-angle glaucoma populations support the concept that phaco-ECP can be effective in selected eyes, particularly when medication reduction is a meaningful clinical objective. [73] From a practical standpoint, ECP occupies a distinct place in treatment algorithms because it can be considered even when the conventional outflow pathway is unlikely to respond strongly, although careful patient selection remains essential. [72]

4. Emerging Technologies in Diagnosis and Monitoring

Optical coherence tomography (OCT) has become central to glaucoma diagnosis and monitoring because it enables quantitative assessment of retinal nerve fiber layer (RNFL) and macular ganglion cell complex (GCC) structure. [74] Macular GCC measures are often discussed as informative in earlier disease stages, although performance depends on segmentation approaches and ocular comorbidities that influence macular anatomy. [75] Longitudinal OCT monitoring supports detection of structural change, yet measurement variability and floor effects can limit sensitivity, particularly in advanced glaucoma. [76] OCT angiography (OCT-A) provides noninvasive information on optic nerve head and retinal microvasculature, and contemporary reviews report associations between vascular metrics and glaucoma severity. [77] At the same time, interpretation of OCT-A progression over short intervals is often cautious due to physiologic variability and device-related measurement noise. [78]

Ongoing longitudinal work is evaluating whether OCT-A metrics predict future structural loss, although routine thresholds for clinical progression monitoring have not been uniformly established. [79]

5. Future Directions in Glaucoma Therapy

Gene therapy strategies aim to influence aqueous outflow regulation or neuronal vulnerability, although most evidence remains preclinical and translational. [80] Trabecular meshwork–directed gene approaches are of particular interest because they could, in principle, modify outflow resistance mechanisms rather than only producing symptomatic pressure reduction. [81]

Recent experimental studies include gene-editing and RNA-targeting concepts with sustained IOP reduction in animal models, while clinical translation will depend on delivery specificity and long-term safety. [82, 83] Cell-based therapies are being explored both for sustained neurotrophic support and for retinal ganglion cell replacement concepts, although major biological challenges remain for functional integration. [84] In parallel, trabecular meshwork regeneration strategies—including stem-cell-derived approaches and extracellular vesicle/secretome concepts—are being investigated as potential routes to restore outflow function in preclinical settings. [85, 86] Overall, future-oriented technologies are generally framed with cautious optimism, and reviews emphasize the need for rigorous long-term validation before broad clinical implementation. [80]

Discussion

The evidence summarized in this review reinforces that intraocular pressure (IOP) reduction remains the central, evidence-supported strategy to slow glaucoma onset and progression across major clinical phenotypes, even as additional disease mechanisms continue to be explored. [3] At the same time, real-world effectiveness is strongly influenced by long-term adherence, tolerability, and persistence, meaning that “best” pharmacology may not translate into stable pressure control if treatment burden and ocular surface issues limit consistent use.[10] Recent pharmacological advances, particularly ROCK inhibition and prostaglandin-pathway innovations, broaden therapeutic options by engaging outflow-related mechanisms and may help address patients who require further IOP lowering beyond classical first-line regimens. [11,18] Fixed-dose combinations represent a practical strategy to reduce regimen complexity and may improve day-to-day feasibility of chronic therapy, although tolerability trade-offs can still limit persistence for certain formulations in routine care. [30] Long-acting delivery systems have important implications for the field because they directly target a major limitation of topical therapy—variability in patient-dependent dosing—while introducing new safety and monitoring considerations related to intracameral administration. [34] Neuroprotection remains a highly active research domain with compelling biological rationale, but current clinical evidence has not yet established a broadly accepted standard that reliably improves long-term functional outcomes independent of IOP effects. [39] In parallel, MIGS has expanded the procedural spectrum between medical therapy and traditional filtration surgery, supporting a more individualized escalation pathway, though comparative effectiveness remains context-dependent and should be interpreted on a device- and population-specific basis. [48] Finally, continued progress in OCT-based structural monitoring and emerging translational approaches such as gene therapy may reshape future management by enabling earlier detection of progression and potentially modifying disease mechanisms, but both require rigorous long-term validation before broad implementation. [76,80]

Conclusions

This review indicates that contemporary glaucoma management continues to rely on sustained intraocular pressure control as the most actionable therapeutic strategy, while the overall treatment landscape is becoming increasingly diversified. Classical topical regimens remain clinically effective, but their long-term impact is often constrained by adherence difficulties, tolerability issues, and cumulative ocular surface burden, which may limit persistence over the disease course. Recent pharmacological advances broaden escalation pathways by introducing alternative mechanisms targeting aqueous outflow and by offering combination strategies that may reduce regimen complexity in selected patients. In parallel, long-acting drug delivery systems represent a clinically relevant attempt to reduce dependence on daily self-administration, although variability in durability and the need for careful safety surveillance remain key barriers to widespread implementation. Microinvasive glaucoma surgery expands procedural options for patients in whom medication burden is problematic or moderate pressure reduction is sufficient, yet outcomes remain heterogeneous and strongly dependent on technique, target pathway, and patient selection. Neuroprotection and regenerative concepts continue to attract research attention and may ultimately complement pressure-based therapy, but current evidence does not yet support their routine use as established disease-modifying standards. Future progress in the field will likely depend on stronger long-term comparative data across modern therapies, improved biomarkers and progression endpoints that better reflect clinically meaningful change, and integrated treatment strategies that prioritize both efficacy and sustainability in real-world care.

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