THE PRESSURE IS STILL ON!
Current and Emerging Therapies for Managing Glaucoma

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ACTIVITY DESCRIPTION
Glaucoma continues to be the leading cause of irreversible blindness worldwide. New methods of assessing patient risk have been identified, and new therapies for decreasing intraocular pressure (IOP) have been developed. One new therapeutic mechanism for glaucoma involves the role of nitric oxide on IOP regulation. In addition, alternative drug delivery methods have been invented. The purpose of this activity is to update ophthalmologists on the mechanisms of action of current and emerging glaucoma therapies and to assess traditional and emerging risk factors for disease progression.

TARGET AUDIENCE
This educational activity is intended for ophthalmologists caring for patients with glaucoma.

LEARNING OBJECTIVES
Upon completion of this activity, participants will be better able to:
- Outline the relationship between the sites of action and selection of IOP-lowering therapies
- Discuss the role of nitric oxide in IOP regulation
- Describe the mechanism of action of current and emerging topical glaucoma therapies
- Evaluate the clinical relevance of safety and efficacy data for emerging topical therapies for the treatment of glaucoma
- Assess traditional and emerging risk factors for progression in patients with ocular hypertension or glaucoma

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INTRODUCTION

Glaucoma is a leading cause of irreversible blindness that affects millions of people worldwide.\(^1\) New risk factors and new therapies for glaucoma have emerged. Low ocular perfusion pressure (OPP) and low cerebral spinal fluid pressure (CSF-P) may be indicators of disease progression. Current therapies aim to lower intraocular pressure (IOP) by aqueous suppression or by increasing uveoscleral outflow. Furthermore, pilocarpine, which works indirectly on the trabecular meshwork (TM) via ciliary body contraction, is still used in some patients. There are no available therapies targeting outflow through direct action on the TM, a major contributor to aqueous outflow in normal eyes. Emerging therapies, such as latanoprostene bunod (LBN) and netarsudil, may change the treatment landscape of this disease by lowering IOP in patients with glaucoma through this mechanism. Herein, the current state of glaucoma management is described.

DEFINING GLAUCOMA: AN UPDATE FROM THE AMERICAN ACADEMY OF OPHTHALMOLOGY

In the September 2015 Preferred Practice Pattern updates, the American Academy of Ophthalmology defined primary open-angle glaucoma (POAG) as “…a chronic, progressive optic neuropathy in adults in which there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. This condition is associated with an open anterior chamber angle by gonioscopy.”\(^2\)

RISK FACTORS OF GLAUCOMA

The American Academy of Ophthalmology Glaucoma Preferred Practice Pattern guidelines recognize several risk factors that have been identified in carefully conducted population-based studies. Intraocular pressure, age, race, and family history are long-standing glaucoma risk factors. The potential role of IOP has long been recognized as important in the pathophysiology of glaucoma. Furthermore, lowering IOP has been found to decrease the risk of optic nerve damage and blindness. Older age is also a known risk factor for the development of POAG; it has been estimated that 31% of patients with POAG in the United States are aged 70 to 79 years.\(^3\) Prevalence of glaucoma in the siblings of patients is 10.4%, and 1.1% in the offspring of patients.\(^4\) Overall, first-degree relatives of patients with glaucoma have a 9.2-fold higher relative risk of developing glaucoma.\(^4\) With regard to race, African Americans and Latinos are at a higher risk of developing glaucoma than are whites.\(^5,6\) The rising Hispanic population in the United States is expected to make up the largest group of patients with this disease by 2035.\(^3\)

Particular structural and functional abnormalities in the eye may also be a risk factor. Measuring central corneal thickness is an important component of a complete ocular examination.\(^7\)
A measurement of < 555 μm is associated with a greater risk of glaucoma development than a central corneal thickness of ≥ 588 μm. Large studies have identified an increased prevalence of POAG in patients with myopia; this occurrence has been proposed to be caused by weaker scleral support, which may cause patients to be more susceptible to retinal and optic nerve damage.

Emerging risk factors include low CSF-P and low OPP, both of which correlate with optic nerve damage. The optic nerve can be affected by 2 pressurized regions: the pressure of the intraocular space (ie, IOP) and the pressure from the subarachnoid space, which is caused by cerebrospinal fluid. The lamina cribrosa is in between these 2 opposing regions, and the pressure difference between them (translaminar pressure difference) can cause structural alterations to the optic disc. Similarly, the optic nerve cupping observed in patients with elevated IOP could also occur in patients with low CSF-P. Both a prospective and a retrospective study showed that CSF-P was significantly lower in patients with glaucoma (P < .001). In the prospective study, loss of vision was positively correlated with translaminar pressure difference and negatively correlated with CSF-P. However, performing a lumbar puncture does not necessarily represent CSF-P, and such a procedure may not be a practical part of an ophthalmological evaluation. Noninvasive methods of measuring CSF-P are under development.

The Baltimore Eye Survey, Egna-Neumarkt Study, Proyecto VER, and Barbados Eye Survey all identified low OPP as a significant risk factor for POAG. Ocular perfusion pressure represents the relative pressure at which blood perfuses the eye and is the difference between systemic blood pressure (BP) and IOP. Either low BP or high IOP can lead to low OPP and an increased risk of developing POAG. In a study that measures the relation between OPP and glaucoma, it is impossible to separate the individual effects of IOP and BP when measuring OPP unless there is simultaneous control for both IOP and BP.

In the Barbados Eye Study, use of a multivariable model did demonstrate an inverse relation between OPP and POAG, even after controlling for BP and IOP. On the other hand, the Rotterdam Study strongly supports that controlling for IOP resulted in a null association between OPP and incident open-angle glaucoma.

It is possible that treatment of systemic hypertension could modify the risk of POAG. In considering this matter, one must account for the type of BP treatment (diet, drugs, and type of drugs) and the effectiveness of that treatment. In the Egna-Neumarkt Study, hypertension was adversely associated with POAG, but not with being on medication. Conversely, the Blue Mountains Eye Study showed that untreated hypertension was not a strong risk factor for glaucoma, but that patients who had hypertension, despite being treated with antihypertensive medication, were at risk for POAG. Although there are studies that did not find a correlation with antihypertensive medication and POAG, the European Glaucoma Treatment Study showed that the diuretic dorzolamide may be a risk factor for glaucoma.

**PATHOPHYSIOLOGY OF GLAUCOMA**

There is still much to be elucidated regarding the pathophysiology of this disease. Glaucoma is a multifactorial disease that results in structural and functional damage to the retina and optic nerve. Aqueous humor production by the ciliary body and its drainage through uveoscleral outflow and the TM modulate IOP. Blockage or resistance to aqueous outflow...
increases IOP, leading to damage to the lamina cribrosa and, eventually, to the optic nerve fibers.27

On a cellular level, many contributing mechanisms have been proposed to explain how ocular degeneration occurs in glaucoma (Figure 2).25 The axonal damage induced by high IOP prevents the transport of molecules that nourish the retinal nerve fibers, which further stresses posterior eye structures.26 Ocular hypertension may cause microcirculation to be blocked (hypoxia/schemia), and the increasing pressure surrounding the ocular tissue could cause the ganglion cells to be deprived of necessary nutrients to survive.27 In response to the stress and pressure, surrounding cell types, such as glial cells and astrocytes, may release factors that induce apoptotic cell death.20 High IOP may cause retinal ganglion damage and death by inducing an inflammatory response.22 However, some patients with normal IOP who have glaucoma have been shown to also have altered adaptive immunity, supporting the hypothesis that inflammatory damage can cause glaucoma, dependent or independent of IOP levels.30

To complicate the matter, IOP has been shown to change over 24 hours, and body position during measurement also contributes to fluctuations in IOP.31 Twenty-four–hour monitoring showed that IOP levels are higher at night than during the day.21 Physicians who consider how therapeutic options control diurnal and nocturnal IOP may be better able to elect the best treatment plan for a patient.

THERAPEUTIC TARGETS FOR GLAUCOMA TREATMENT

The goals for managing POAG include lowering IOP and maintaining a target range, preventing further damage to the optic nerve and the retinal fiber layer, and stabilizing vision.2 Decreasing a patient’s IOP by ≥25% can slow glaucoma progression,23 and clinicians are recommended to begin treatments that can reduce IOP by 20% to 30% from baseline.2 There are multiple sites of action for lowering IOP. Decreasing aqueous production, lowering episcleral venous pressure, and increasing uveoscleral and trabecular outflow (decrease outflow resistance) are all mechanisms that can be targeted by current drug therapies or drugs that are in late-phase clinical development (Figure 3).
IOP of 26.5 mm Hg; after treatment, the mean IOP was reduced (Table 1). LBN was 26.7 mm Hg and IOP was reduced by 8 to 9 mm Hg.

In the APOLLO trial, the mean baseline IOP of patients given timolol, 0.5%, twice daily (8 pm and 8 am). Both treatment arms experienced similar adverse events. Conjunctival hyperemia occurred in 9% of the patients receiving LBN, 0.024%, and in 0.7% of the patients receiving timolol, 0.5%.

In the LUNAR trial, the mean baseline IOP was 26.5 mm Hg. This measurement was reduced by 7.5 to 8.8 mm Hg in the group receiving LBN, 0.024%, and by 6.6 to 7.9 mm Hg in the group receiving timolol, 0.5% (Table 1). Both treatment arms experienced similar adverse events. Conjunctival hyperemia occurred in 9% of the patients receiving LBN, 0.024%, and in 0.7% of the patients receiving timolol, 0.5%.

A long-term efficacy and safety open-label 12-month extension study was conducted to further assess the results of the APOLLO and LUNAR trials. After patients completed treatment from their respective trials, all were treated with LBN for an additional 9 months (APOLLO) or 3 months (LUNAR). Patients who crossed over from timolol treatment had an additional 6.3% to 8.3% decrease in diurnal IOP. The mean reduction in IOP for all patients was 32% to 34%. The most common adverse events were conjunctival hyperemia (5.9%), eye irritation (4.6%), and eye pain (3.5%).

Phase 2 VOYAGER Trial: Latanoprostene Bunod vs Latanoprost

Although phase 3 studies compared LBN to timolol, a phase 2 study on 413 patients with POAG or ocular hypertension (mean baseline IOP was approximately 26 mm Hg) was conducted to test the safety and efficacy of different doses of LBN compared with latanoprost. In this study, the investigators compared the additive effect NO had on patients by comparing these 2 molecules. All 4 doses of LBN tested (0.006%, 0.012%, 0.024%, 0.040%) reduced IOP, with the efficacy plateauing at 0.024% to 0.040%. A significantly greater reduction in mean diurnal IOP was demonstrated after a 28-day treatment regimen with LBN, 0.024%, (-9.00 mm Hg) than with latanoprost, 0.005% (-7.77 mm Hg) (P = .005) (Table 1). The most common adverse events were pain at the instillation site (12% in the LBN, 0.024%, group and 6.1% in the latanoprost, 0.005%, group) and hyperemia (2.4% in the LBN, 0.024%, group and 8.5% in the latanoprost, 0.005%, group).

Phase 2 Constellation Trial: Latanoprostene Bunod vs Timolol Over 24 Hours

Significant reduction of nocturnal IOP with latanoprost was shown in a previous study. To demonstrate that LBN has a similar effect, a crossover phase 2 study evaluated the efficacy of LBN, 0.024%, over 24-hour IOP compared with that of timolol, 0.5%. The mean baseline IOP during the day in the sitting position was 21.6 mm Hg, whereas the measurement in the supine position was 24.7 mm Hg. Nocturnal mean IOP measured in the supine position was 25.7 mm Hg. Both LBN and timolol reduced daytime mean IOP by 2.3 to 3.9 mm Hg (P < .001) in either position, but only LBN sustained a more effective control of IOP at night compared with baseline (-2.5 mm Hg) (P = .002) and timolol (-2.3 mm Hg) (P = .004).

RHO KINASE INHIBITORS

Rho kinases modulate structural components of various cell types, including those in the TM and Schlemm canal. Rho kinases can be inhibited directly through the use of...
of pharmacologic inhibitors (netarsudil and ripasudil) or indirectly through NO signaling.\textsuperscript{25} The NO–cyclic guanosine monophosphate pathway activates protein kinase G, which inhibits Rho kinase (Figure 5).\textsuperscript{26} Inhibiting Rho kinase prevents myosin light chain phosphorylation, which prevents the interaction of actin and myosin and halts muscle contraction.\textsuperscript{26} As the muscles relax, resistance in the TM decreases and aqueous humor outflow increases, which in turn lowers IOP.\textsuperscript{26}

Netarsudil

Netarsudil (AR-13324) is an inhibitor of Rho kinase and a norepinephrine transporter. By inhibiting Rho kinase, the compound works through 3 sites of action: decreasing aqueous humor production, decreasing episcleral venous pressure, and increasing aqueous humor outflow through the TM.\textsuperscript{51,52} Netarsudil is currently undergoing review by the FDA. Results of recent phase 3 trials, ROCKET 1 and ROCKET 2, were reported at the 2016 Annual Meeting of The Association for Research in Vision and Ophthalmology (Table 2).\textsuperscript{53} In each trial, netarsudil, 0.02%, was compared with timolol, 0.05%, in both untreated patients and in those previously treated with PGAs. Overall, netarsudil was noninferior to timolol in unmedicated patients with a baseline IOP < 25 mm Hg. The most common adverse event reported for a daily dose of netarsudil in ROCKET 2 was conjunctival hyperemia (50.2%). Data from the phase 3 trial, ROCKET 4, were presented at the 2017 Annual Meeting of The Association for Research in Vision and Ophthalmology (Table 2).\textsuperscript{54} The baseline IOP for that study was 20.7 to 22.4 mm Hg. Netarsudil reduced IOP to 16.3 to 17.8 mm Hg, whereas timolol reduced IOP to 16.7 to 17.6 mm Hg.\textsuperscript{54} A netarsudil/latanoprost fixed combination, 0.02%/0.005%, has been evaluated in several clinical trials. Two phase 3 trials (Mercury 1 and Mercury 2) showed that the netarsudil/latanoprost fixed combination was statistically superior to netarsudil or latanoprost monotherapy. The combination lowered IOP 1 to 3 mm Hg more than did each of its components.\textsuperscript{55} The most common adverse event for the fixed combination was conjunctival hyperemia (53.4%).\textsuperscript{56}

Table 1. Clinical Trials Comparing Efficacy and Safety of LBN vs Timolol or Latanoprost\textsuperscript{44,45,47}

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LBN, 0.024% (n = 264)</th>
<th>Timolol, 0.5% (n = 123)</th>
<th>LBN, 0.024% (n = 259)</th>
<th>Timolol, 0.5% (n = 128)</th>
<th>LBN, 0.024% (n = 83)</th>
<th>Latanoprost, 0.005% (n = 82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP reduction, mm Hg</td>
<td>8-9</td>
<td>6.7-7.4</td>
<td>7.5-8.8</td>
<td>6.6-7.9</td>
<td>9</td>
<td>7.77</td>
</tr>
<tr>
<td>Common adverse events</td>
<td>LBN, 0.024% (n = 283)</td>
<td>Timolol, 0.5% (n = 135)</td>
<td>LBN, 0.024% (n = 277)</td>
<td>Timolol, 0.5% (n = 135)</td>
<td>LBN, 0.024% (n = 83)</td>
<td>Latanoprost, 0.005% (n = 82)</td>
</tr>
<tr>
<td>Eye irritation</td>
<td>3.9%</td>
<td>2.2%</td>
<td>7.2%</td>
<td>4.4%</td>
<td>3.6%</td>
<td>0</td>
</tr>
<tr>
<td>Conjunctival hyperemia</td>
<td>2.8%</td>
<td>1.5%</td>
<td>9.0%</td>
<td>0.7%</td>
<td>4.8%</td>
<td>0</td>
</tr>
<tr>
<td>Ocular hyperemia</td>
<td>NR</td>
<td>NR</td>
<td>2.5%</td>
<td>0.7%</td>
<td>2.4%</td>
<td>8.5%</td>
</tr>
</tbody>
</table>

Table 2. Clinical Trials With Netarsudil Comparing Efficacy and Safety vs Timolol\textsuperscript{53,54}

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Rocket 1 (Phase 3)</th>
<th>Rocket 2 (Phase 3)</th>
<th>Rocket 3 (Phase 3)</th>
<th>Rocket 4 (Phase 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP reduction, mm Hg*</td>
<td>3.3-5.0</td>
<td>3.7-5.1</td>
<td>3.3-4.6</td>
<td>3.7-5.1</td>
</tr>
<tr>
<td>Common adverse event</td>
<td>Netarsudil (n = 203)</td>
<td>Timolol (n = 208)</td>
<td>Netarsudil (n = 251)</td>
<td>Timolol (n = 251)</td>
</tr>
<tr>
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Abbreviations: IOP, intraocular pressure; LBN, latanoprostene bunod; NR, not reported.

![Figure 5. Nitric oxide derived from endothelial cells can diffuse into smooth muscles and induce conversion of GTP to cGMP, which activates PKG. PKG decreases intracellular calcium levels and inhibits the Rho kinase signaling pathway, resulting in smooth muscle relaxation. Abbreviations: cGMP, cyclic guanosine monophosphate; NO, nitric oxide; NOS, nitric oxide synthase; PKG, protein kinase G.](image)

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**Ripasudil**
Ripasudil is a Rho kinase inhibitor that has been shown in clinical studies to be safe and effective. It has been approved for use in Japan since 2014. As monotherapy, ripasudil lowered IOP by 2.6 to 3.7 mm Hg at 52 weeks of treatment. Combination therapy with compounds such as PGAs and beta blockers resulted in additive effects. There was a relatively high number (85%) of adverse drug reactions in patients. Conjunctival hyperemia (74.6%), blepharitis (20.2%), and allergic conjunctivitis (17.2%) were the most frequent adverse reactions documented. The cases of conjunctival hyperemia were noted to be mostly mild (97%) and resolved on their own (78%).

**Nitric Oxide–Donating Bimatoprost**
Bimatoprost, a prostaglandin F2α receptor analogue, lowers IOP by increasing uveoscleral outflow. NCX 470 is a dual-action molecule that combines bimatoprost with an NO-donating moiety. Ocular treatment with NO has been shown to relax the Schlemm canal and TM. In preclinical studies, NCX 470 increased levels of cyclic guanosine monophosphate (Figure 5) in ocular tissue and is more effective at decreasing IOP than is bimatoprost at equivalent doses. The first in-human phase 2 trials are expected to start early in 2018.

**Nitric Oxide–Donating Carbonic Anhydrase Inhibitors**
The CAIs dorzolamide and brinzolamide are topical drugs that lower IOP and prevent ischemic damage by inhibiting aqueous humor production in the ciliary body. Carbonic anhydrase inhibition has also been shown to vasodilate blood vessels in the retina and optic nerve of animals. To enhance the effects of CAIs, NO moieties have been added to dorzolamide and brinzolamide, and preclinical studies have been conducted.

**EMERGING DRUG DELIVERY METHODS**

**Sustained-Release Bimatoprost and Travoprost Implants**
A phase 1/2 dose-ranging study described the efficacy of a sustained-release (SR) biodegradable implant containing bimatoprost. At 16 weeks, eyes treated topically with bimatoprost had an average IOP reduction of 8.4 mm Hg. During this same time point, patients who received bimatoprost SR (6, 10, 15, or 20 μg) experienced an IOP reduction of 7.2, 7.4, 8.1, and 9.5 mm Hg, respectively. At 6 months, 71% of patients receiving bimatoprost SR did not require rescue or retreatment. The most common adverse event for both treatments was conjunctival hyperemia. Conjunctival hyperemia with an onset later than 2 days after the injection procedure occurred more often with topical bimatoprost (17.3%) than with the SR implant (6.7%).

There are phase 2 trials under way that are evaluating the safety and efficacy of intracanal travoprost implants compared with timolol. Both a biodegradable and a removable titanium implant are being investigated by their respective companies.

**Bimatoprost Ring**
The bimatoprost insert is a silicone ring loaded with bimatoprost. It is inserted around conjunctival fornices of the eye and replaced every 6 months. A phase 2 randomized trial compared the bimatoprost ring with timolol during a 6-month treatment period. Intracocular pressure was reduced by 3.2 to 6.4 mm Hg and by 4.2 to 6.4 mm Hg with the bimatoprost ring and timolol, respectively. Adverse events were similar to those seen with other types of bimatoprost delivery methods. Alternative delivery methods such as this can help increase the poor adherence to POAG medication, which has been documented in patients receiving PGA and beta blocker therapy.

**Key Take-Home Messages**
- POAG is a complex and incompletely understood multifactorial disease
- Many risk factors are known; emerging risk factors may include OPP and CSF-P
- Treatments are in development, with new... - Methods of action (NO, Rho kinase inhibition) - Sites of action (TM) and episcleral venous pressure - Drug delivery platforms (SR implants and conjunctival rings)
- Reduction in IOP remains the only established treatment goal

**REFERENCES**


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56. Serio J. 3-month interim report of a prospective 12-month safety and efficacy study of topical PG324 (fixed combination of netarsudil 0.02% and latanoprost 0.005%) compared to the individual components in subjects with elevated intraocular pressure (MERCURY 1). Paper presented at: 2017 Annual Meeting of The Association for Research in Vision and Ophthalmology; May 7-11, 2017; Baltimore, MD.


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CME POST TEST QUESTIONS
To obtain AMA PRA Category 1 Credit™ for this activity, complete the CME Post Test by writing the best answer to each question in the Answer Box located on the Activity Evaluation/Credit Request form on the following page. Alternatively, you can complete the CME Post Test online at http://tinyurl.com/glaucomapressureCME.

See detailed instructions at To Obtain AMA PRA Category 1 Credit™ on page 2.

1. For the treatment of POAG, which of the following is the correct pairing of drug class and site of action?
   a. Beta blocker: decreasing episcleral venous pressure
   b. PGA: decreasing aqueous humor production
   c. CAI: increasing uveoscleral outflow
   d. Rho kinase inhibitor: increasing trabecular outflow

2. How does LBN decrease IOP?
   a. By decreasing aqueous production and increasing trabecular outflow resistance
   b. By decreasing uveoscleral outflow and opening the iridocorneal angle
   c. By decreasing trabecular outflow resistance and increasing uveoscleral outflow
   d. By opening the iridocorneal angle and decreasing aqueous production

3. Nitric oxide lowers IOP by decreasing:
   a. Episcleral venous pressure
   b. Resistance to trabecular outflow
   c. Aqueous fluid production
   d. Uveoscleral outflow

4. Which therapy increases trabecular and uveoscleral outflow?
   a. LBN
   b. Timolol
   c. Bimatoprost
   d. Netarsudil

5. A phase 3 trial compared an NO-donating formulation of latanoprost, LBN, with timolol. Which of the following is TRUE regarding this trial?
   a. The study population excluded patients with ocular hypertension
   b. The study design was open label
   c. Patients treated with LBN achieved more IOP reduction than those treated with timolol
   d. The most common treatment-emergent adverse events were mild to moderate and included conjunctival hyperemia in both treatment groups

6. A phase 3 trial compared a Rho kinase inhibitor, netarsudil, with timolol. Which of the following is TRUE regarding this trial?
   a. The study population included only patients with previously untreated glaucoma
   b. Netarsudil was shown to be superior to timolol in patients with a baseline IOP < 25 mm Hg
   c. Patients who had a baseline IOP < 25 mm Hg achieved an IOP reduction of ≥ 3.3 mm Hg after receiving netarsudil
   d. Among patients with a baseline IOP < 25 mm Hg, timolol treatment lead to conjunctival hyperemia in < 5% of patients

7. Which therapies promote smooth muscle relaxation of the TM?
   a. Netarsudil and bimatoprost ring
   b. NO-donating bimatoprost and CAIs
   c. Latanoprost and netarsudil
   d. LBN and netarsudil

8. Which of the following decreases the risk for developing glaucoma?
   a. Being Hispanic
   b. Increasing intake of dietary nitrates
   c. Having a corneal thickness < 555 μm
   d. Having high myopia
THE PRESSURE IS STILL ON! CURRENT AND EMERGING THERAPIES FOR MANAGING GLAUCOMA

To receive AMA PRA Category 1 Credit™, you must complete this Evaluation form and the Post Test. Record your answers to the Post Test in the Answer Box located below. Scan this completed page and return via e-mail to cme-nyee@nyee.edu or fax it to 212-870-8128. Your comments help us to determine the extent to which this educational activity has met its stated objectives, assess future educational needs, and create timely and pertinent future activities. Please provide all the requested information below. This ensures that your certificate is filled out correctly and is e-mailed to the proper address. It also enables us to contact you about future CME activities. Please print clearly or type. Illegible submissions cannot be processed.

PARTICIPANT INFORMATION (Please Print)  ☐ Home  ☐ Office

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Specialty __________________________ Degree ☐ MD ☐ DO ☐ OD ☐ PharmD ☐ RPh ☐ NP ☐ RN ☐ PA ☐ Other

Institution __________________________

Street Address ____________________________________________

City __________________________ State ___________ ZIP Code ___________ Country __________________________

E-mail __________________________ Phone __________________________ Fax __________________________

Please note: We do not sell or share e-mail addresses. They are used strictly for conducting post-activity follow-up surveys to assess the impact of this educational activity on your practice.

Learner Disclosure: To ensure compliance with the US Centers for Medicare and Medicaid Services regarding gifts to physicians, New York Eye and Ear Infirmary of Mount Sinai for CME requires that you disclose whether or not you have any financial, referral, and/or other relationship with our institution. CME certificates cannot be awarded unless you answer this question. For additional information, please e-mail NYEE CME at cme-nyee@nyee.edu. Thank you.

☐ Yes ☐ No I and/or my family member have a financial relationship with New York Eye and Ear Infirmary of Mount Sinai and/or refer Medicare/Medicaid patients to it.

☐ I certify that I have participated in the entire activity and claim 1.5 AMA PRA Category 1 Credits™.

Signature Required __________________________ Date Completed __________________________

OUTCOMES MEASUREMENT

☐ Yes ☐ No Did you perceive any commercial bias in any part of this activity? IMPORTANT! If you answered “Yes,” we urge you to be specific about where the bias occurred so we can address the perceived bias with the contributor and/or in the subject matter in future activities.

Circle the number that best reflects your opinion on the degree to which the following learning objectives were met:

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<th>5 = Strongly Agree</th>
<th>4 = Agree</th>
<th>3 = Neutral</th>
<th>2 = Disagree</th>
<th>1 = Strongly Disagree</th>
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<tr>
<td>Outline the relationship between the sites of action and selection of IOP-lowering therapies</td>
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<td>Discuss the role of nitric oxide in IOP regulation</td>
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<tr>
<td>Describe the mechanism of action of current and emerging topical glaucoma therapies</td>
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<tr>
<td>Evaluate the clinical relevance of safety and efficacy data for emerging topical therapies for the treatment of glaucoma</td>
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<tr>
<td>Assess traditional and emerging risk factors for progression in patients with ocular hypertension or glaucoma</td>
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1. Please list one or more things, if any, you learned from participating in this educational activity that you did not already know.

________________________________________________________________________________________

2. As a result of the knowledge gained in this educational activity, how likely are you to implement changes in your practice?

4 = definitely will implement changes  3 = likely will implement changes  2 = likely will not implement any changes  1 = definitely will not make any changes

Please describe the change(s) you plan to make: ____________________________________________ 4 3 2 1

3. Related to what you learned in this activity, what barriers to implementing these changes or achieving better patient outcomes do you face?

4. Number of patients with glaucoma I see per week

☐ 0  ☐ 1-5  ☐ 6-10  ☐ 11-25  ☐ More than 25

5. Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced for you through participation in this activity.

☐ Patient Care  ☐ Practice-Based Learning and Improvement  ☐ Professionalism

☐ Medical Knowledge  ☐ Interpersonal and Communication Skills  ☐ Systems-Based Practice

6. What other topics would you like to see covered in future CME programs?

________________________________________________________________________________________