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TREATING PRESBYOPIA:

New Approaches to a Familiar Problem

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Treating Presbyopia: New Approaches to a Familiar Problem

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CONTENT SOURCE

This continuing medical education (CE/CME) activity captures content from a live symposium at ASCRS.

ACTIVITY DESCRIPTION

Based on a live symposium held during the American Society for Cataract and Refractive Surgeons Annual Meeting, this supplement summarizes the presentations on how to manage presbyopic changes with a variety of current and newly emerging treatment options, and how strategies may work synergistically.

TARGET AUDIENCE

This certified continuing medical education activity is designed for ophthalmologists and optometrists involved in the care of patients with presbyopia.

LEARNING OBJECTIVES

Upon completion of this activity, the participant should be able to:

- **Differentiate** the underlying mechanisms of presbyopic changes.
- **Interpret** the clinical trial experience published in the literature with pharmaceutical and nonpharmaceutical presbyopia-correcting options.
- **Distinguish** among the pharmacological properties of newly emerging presbyopia-correcting drops and their mechanisms of action.
- **Explain** how presbyopia-correcting drops are likely to affect categories of patients based on individual characteristics.
- **Describe** the side effects of pharmaceutical approaches to presbyopia correction with other treatment options to **debate** the pros and cons of each strategy.

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PRETEST QUESTIONS

PLEASE COMPLETE PRIOR TO ACCESSING THE MATERIAL AND SUBMIT WITH POSTTEST/ACTIVITY EVALUATION/ SATISFACTION MEASURES FOR CE/CME CREDIT.

1. **Please rate your confidence in your ability to distinguish among the pharmacological properties of newly emerging presbyopia-correcting drops and their mechanisms of action (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).**
   A. 1
   B. 2
   C. 3
   D. 4
   E. 5

2. **A 51-year-old white woman with manifest refraction of +0.75 sphere OU presents with increased frustration with near work. Her uncorrected distance visual acuity is 20/30 and uncorrected near is J9. Slit lamp and fundus examination are unremarkable. She does not want to wear glasses for distance or for near work. What would be the best course of action to help achieve this patient's goal of spectacle independence in the near range?**
   A. Monovision with keratorefractive procedure after a successful trial with contact lenses
   B. Refractive lens exchange with multifocal lens
   C. Trial of presbyopia pharmaceuticals
   D. Discuss risks and benefits of each modality and give patient the opportunity to choose what may work best

3. **What is the mechanism of action of the current pharmaceutical being studied to restore lens function?**
   A. Increasing aqueous antioxidant concentrations
   B. Breaking disulfide bonds within the lens
   C. Absorbing UV light that induces lens damage
   D. Restoring natural chemical concentrations of the aqueous humor to restore lens nutrition

4. **Known optical disadvantages of multifocal spectacles include:**
   A. Decreased depth perception
   B. "Cob web" effect
   C. Decreased edge-contrast sensitivity
   D. All of the above
   E. Options A and C

5. **By age 50, accommodative amplitude has decreased to approximately how many diopters?**
   A. 0.50 D
   B. 1.00 D
   C. 2.00 D
   D. 3.00 D

6. **Which of the following are features of stage 3 dysfunctional lens syndrome?**
   A. Mild presbyopia
   B. Mild lens opacity
   C. Higher order aberrations
   D. Dry eye

7. **Which of the following statements regarding multifocal spectacles and fall risk is TRUE?**
   A. Patients wearing multifocal spectacles are more likely to fall than patients who do not wear multifocal spectacles
   B. Patients who do not wear multifocal spectacles are more likely to fall than patients who wear multifocal spectacles
   C. There is no known association between fall-risk and multifocal spectacles
   D. Patients wearing bifocal spectacles are less likely to fall than patients wearing single vision spectacles

8. **According to one study, performing cataract surgery in one eye is associated with what percentage reduction in risk of falling over 1 year?**
   A. 14%
   B. 24%
   C. 34%
   D. 44%

9. **According to one study, what reduction in fall risk can be achieved from switching from multifocal spectacles to single-vision spectacles?**
   A. No reduction in fall risk
   B. 20% reduction
   C. 40% reduction
   D. 60% reduction

10. **According to studies, what reduction in pupil size is optimal for maximizing both distance and near vision?**
    A. 10-20%
    B. 20-30%
    C. 30-40%
    D. 40-50%

11. **According to studies involving AGN-190584 for pharmacological treatment of presbyopia, all of the following were nonserious adverse events EXCEPT:**
    A. Headache
    B. Conjunctival hyperemia
    C. Blurred vision
    D. Cataract formation

12. **According to phase 2b studies evaluating the efficacy and safety of CSF-1, which of the following statements is TRUE?**
    A. Patients enrolled in the treatment arm achieved a statistically significant improvement in distance-corrected near visual acuity over patients in the control arm
    B. Patients enrolled in the control arm achieved a statistically significant improvement in distance-corrected near visual acuity over patients in the treatment arm
    C. Patients enrolled in the treatment arm had the same distance-corrected near visual acuity compared to patients in the treatment arm
    D. CSF-1 was found to be ineffective in improving distance-corrected near visual acuity

13. **Which of the following statements regarding pinhole occlusion and near vision is TRUE?**
    A. The closer the pinhole is to the patient's iris, the less his or her peripheral vision will be reduced
    B. The farther the pinhole is to the patient's iris, the less his or her peripheral vision will be reduced
    C. Peripheral vision is not related to distance of pinhole occlude from the iris
    D. Pinhole occlusion does not impact peripheral vision

Treating Presbyopia:
New Approaches to a Familiar Problem

For some ocular conditions, only a single company thinks creatively and executes effective research on an outside-the-box technology to disrupt the treatment landscape. For presbyopia, however, several companies are harnessing the power of innovation to address the need for new solutions to an old problem.

Given changing dynamics in presbyopia management and the treatment pipeline, my colleagues and I thought it would be best to address the state of presbyopia as it stands today. I moderated a live event with guests Marguerite B. McDonald, MD, FACS, and George O. Waring IV, MD, FACS, during which we reviewed the prevalence of presbyopia, modern treatment strategies, promising pipeline candidates, and (should they be approved by regulatory bodies) how those candidates could be used by clinicians. Our respective areas of discussion have been adapted to print for your convenience.

Keeping track of the latest developments in this rapidly evolving field can be difficult for busy eye care providers tasked with any number of responsibilities. We hope this digest helps you in your efforts to stay up-to-date on the state of presbyopia.

— Francis S. Mah, MD, Program Chair

PRESBYOPIA: PREVALENCE, IMPACT, AND TREATMENT OPTIONS

BY GEORGE O. WARING IV, MD, FACS

Statistics regarding the global burden of presbyopia demonstrate why it is among one the biggest areas of unmet need in eye care. Presbyopia combined with crystalline lens–derived higher order aberrations (HOA) defines the first stage of the dysfunctional lens syndrome (stage 1 DLS), followed by mild lens opacity, moderate presbyopia, and HOA; and finally, severe presbyopia, HOA, and opacities adversely affecting daily activities, or cataract (stage 3 DLS).[1,2] Fricke et al have estimated that 1.8 billion people had presbyopia in 2015, meaning that presbyopia has a 25% prevalence globally.[3] The number of patients with near vision impairment due to no or inadequate vision correction was estimated at 826 million in 2015.[3] Further, it has been estimated that the global unmet need for presbyopia correction in 2015 was 45%.[3]

A 2020 systemic literature search found that presbyopia resulted in a reduction of quality of life (QOL) scoring by 22% compared with patients who did not have presbyopia.[4] Approximately 80% of patients with presbyopia have difficulty with daily near-vision tasks.[5] Day-to-day activities affected by presbyopia include reading, writing, and use of mobile phones, and difficulties with blurred vision and use of navigation platforms have been reported among patients with presbyopia.[4] Patients have reported inconveniences related to presbyopia, such as the need to carry, swap, and clean glasses and contact lenses.[6,7]

Economic burden related to presbyopia is significant. For patients, these costs are monetary (ie, money spent on glasses and contacts) and career-oriented (ie, alterations to working ability and career choices).[6,7] Societally, the global productivity loss associated with presbyopia is estimated to be USD$11 billion among people who are younger than 50 years; among those who are younger than 65 years, the estimated global productivity loss is USD$25.3 billion.[8] Holden et al observed that regionally, Europe has the highest rate of presbyopic correction in the world with 96% correction.[5] If this rate were achieved globally, then global productivity loss due to presbyopia would shrink to USD$1.4 billion.[8]

Zebardast et al estimated that 1 in 8 Americans has near-vision impairment.[9] Based on the latest data from the US Census Bureau, that means that approximately 41.6 million Americans have presenting near-vision impairment.[10] The prevalence of presbyopia among Americans who are at least 45 years is 83 to 89%.[4] Among Americans aged 40 to 55, 96% report they are somewhat affected by presbyopia and 46% report that they are extremely affected by presbyopia.[11]

The dynamics of Americans between 40 and 55 years are important. The Millennial generation, loosely defined as being born between 1981 and 1996, aged into this bracket starting in 2021; it should be noted that Millennials surpassed Boomers as a share of the US population in 2020.[12] Most people in this age bracket are at the height of their earning potential, and visual demands—especially in the digital age—increase during this time period. The ubiquity of screens in contemporary American life means that American adults spend more than 11 hours per day watching, reaching, and interacting with electronic

devices.[13,14] The growing preference for text messaging, which requires sharp near vision, in lieu of voice calls suggests that mediums of interpersonal communication are affected by rates of presbyopia.[15]

The patient frustration factor with presbyopia remains high: approximately 90% of patients between the ages of 40 and 55 report frustration with presbyopia.[11] Approximately 62% of presbyopic patients aged 40 to 55 visited an eye care provider (ECP) in the past 12 months, and 79% of those who saw an ECP initiated a discussion about near-vision loss.[11] Still, only 52% of those who saw an ECP received the information they needed.[11]

ECPs can leverage a number of tools to address presbyopia. Nonsurgical treatment options include glasses and contact lenses, and surgical options include kerato-refractive surgery, corneal inlay implantation, and IOL implantation.

Many patients' introduction to a nonsurgical correction for presbyopia comes with spectacles. Single-vision spectacles may be inconvenient for patients who otherwise require correction, and patients using bifocal or trifocal spectacles may experience decreased edge contrast sensitivity or reduced depth perception.[16] Lord et al found that patients aged 63 to 90 years wearing multifocal lenses (ie, bifocal, trifocal, or progressive lenses) were approximately 2.3 times more likely to fall during a 1-year period than patients who did not wear multifocal spectacles, even after adjusting for age, poor vision, reduced lower limb sensation and strength, slow reaction time, and increased postural sway.[16] Among patients using multifocal spectacles, falls were significantly associated with being outside the home, using stairs, and tripping.[16] Lord et al found that "the population attributable risks of regular multifocal glasses use were 35.2% for any falls, 40.9% for falls due to a trip, and 40.9% for falls outside the home."[16]

The incidence of falling is 1 in 4 among patients older than 65, and increases to 1 in 2 among those older than 70.[17,18] Approximately 1 in 3 of these falls may be attributed to use of multifocal lenses.[16] The US Centers for Disease Control and Prevention estimated that, among Americans in 2014, 29 million falls occurred, resulting in 7 million injuries and costing Medicare USD$31 billion.[19] Post-fall anxiety syndrome occurs in approximately one-third of patients who fall. Functional decline, depression, feelings of helplessness, social isolation, increased risk of falling, reduced activities of daily living, lower QOL scoring, and increased institutionalization are all linked with post-fall anxiety syndrome.[16-18]

Given the links between multifocal spectacle use and injury, it should be obvious that ECPs should provide alternative options to patients experiencing presbyopia. One of the solutions we can offer in some of our older patients is cataract surgery. Harwood et al observed that first-eye cataract surgery was significantly associated with a 34% reduced risk of falling compared with patients who have not received first-eye cataract surgery at 1 year.[20] Improvements in activity, anxiety, depression, confidence, visual disability, and handicap were observed at 1 year in patients with first-eye cataract surgery compared with control patients, and a significantly lower rate of fracture occurred in the surgery group.[20] Similar observations were reported by Palagy et al.[19]

Nonsurgical options exist as well. Elimination of multifocal spectacles can prove effective in keeping patients safe from injury. In the VISIBLE study, researchers observed a reduction in fall rates of 40% among patients who switched from multifocal spectacles with single vision spectacles.[20] Still, the aforementioned limitations associated with spectacle use (ie, inconvenience) leave something to be desired when it comes to nonsurgical solutions for presbyopia.

Presbyopia correction does more than just eliminate the need for patients to carry reading glasses. Evidence suggests that improving presbyopia in patients could have significant economic, societal, and health care–associated cost benefits. Overall health improvements—both via reduction in fall and fracture rates and prevention of declining QOL, activity, and independence—may be realized if widespread presbyopia correction could be achieved without the use of multifocal spectacles.

PANEL DISCUSSION: MANAGING PATIENTS WITH PRESBYOPIA

George O. Waring IV, MD, FACS: Engaging patients with presbyopia requires empathy and patience. What reaction do patients have to hearing that they are presbyopic?

Marguerite B. McDonald, MD, FACS: Patients are generally frustrated, depressed, and resigned by presbyopia, which mirrors the data you cited. In many cases, patients are unaware of their options and have been relying on spectacle correction. Or, if they are aware that other options may soon exist, they usually cannot describe them in great detail. I educate my patients that, while presbyopia is a natural process, our field has expanded our understanding of its mechanisms and is innovating to improve the offerings for patients. This news is almost universally well received.

Francis S. Mah, MD: Some patients understand they are experiencing visual complications due to natural aging, but a significant number of patients visiting my clinic for routine eye care learn of their presbyopic diagnosis for the first time while sitting in the chair. For these patients, a sense of defeat often sets in, as there is not much we can do for them other than direct them to purchase over-the-counter spectacles. For patients aging into presbyopia, they suddenly feel old. They used to think of presbyopia as something that affects older relatives and colleagues, and they do not respond well to learning they now share characteristics with that age group.

It is important that providers have empathy for patients when this occurs. From our perspective, it is unsurprising that a patient needs reading glasses. From our patients' perspectives, however, it often comes as a shock.

Dr. Waring: Eye care as a whole should reframe its mindset around presbyopia. We should think of presbyopia correction as an opportunity to improve a patient's QOL rather than as a way to eliminate or mitigate an inconvenient sign of aging. By owning presbyopia correction in its various stages of the DLS, we can expand our practice offerings and allow patients to enter the middle phase of their lives with a sense of direction and control. ■

1. Fricke TR, Tahhan N, Resnikoff S, et al. Global prevalence of presbyopia and vision impairment from uncorrected presbyopia: systematic review, meta-analysis, and modelling. *Ophthalmology.* 2018;125(10):1492-1499.
2. Berdahl J, Bala C, Dhariwal M, et al. Patient and economic burden of presbyopia: a systematic literature review. *Clin Ophthalmol.* 2020;14:3439-3450.
3. Holden BA, Fricke TR, Ho SM, et al. Global vision impairment due to uncorrected presbyopia. *Arch Ophthalmol.* 2008;126(12):1731-1739.
4. Kandel H, Khadka J, Goggin M, Pesudovs K. Impact of refractive error on quality of life: a qualitative study. *Clin Exp Ophthalmol.* 2017;45(7):677-688.
5. Kandel H, Khadka J, Shrestha MK, et al. Uncorrected and corrected refractive error experiences of Nepalese adults: a qualitative study. *Ophthalmic Epidemiol.* 2018;25(2):147-161.
6. Frick KD, Joy SM, Wilson DA, Naidoo KS, Holden BA. The global burden of potential productivity loss from uncorrected presbyopia. *Ophthalmology.* 2015;122(8):1706-1710.
7. Zebardast N, Friedman DS, Vitale S. The prevalence and demographic associations of presenting near-vision impairment among adults living in the United States. *Am J Ophthalmol.* 2017;174:134-144.
8. United States Census Bureau. US and World Population Clock. Accessed August 17, 2021. Available at: https://www.census.gov/popclock/?intcmp=w_200x402.
9. Data on file, Allergan; Full Qualitative Summary.
10. Fry R. Millennials overtake Baby Boomers as America's largest generation. Pew Research Center. Published April 28, 2020. Accessed August 17, 2021. Available at: https://www.pewresearch.org/fact-tank/2020/04/28/millennials-overtake-baby-boomers-as-americas-largest-generation.
11. People spend most of their waking hours staring at screens. MarketWatch website. Available at: https://www.marketwatch.com/story/people-are-spending-most-of-their-waking-hours-staring-at-screens-2018-08-01. Published August 4, 2018. Accessed March 17, 2020.
12. The Nielsen Total Audience Report Q1 2018. Nielsen Company website. Available at: https://www.nielsen.com/us/en/insights/report/2018/q1-2018-total-audience-report/. Accessed March 17, 2020.
13. Americans check their phones 96 times a day [press release]. Nashville, TN: PRNewswire; November 21, 2019. https://www.asurion.com/about/press-releases/americans-check-their-phones-96-times-a-day/. Accessed March 17, 2020.
14. Lord SR, Dayhew J, Howland A. Multifocal glasses impair edge-contrast sensitivity and depth perception and increase the risk of falls in older people. *J Am Geriatr Soc.* 2002;50(11):1760-1766.
15. Peel MN. Epidemiology of falls in older age. *Can J Aging.* 2011;30(1):7-19.
16. Masud T, Morris RO. Epidemiology of falls. *Age Ageing.* 2001;30 Suppl 4:3
17. US Centers for Disease Control and Prevention. Falls are leading cause of injury and death in older Americans. Published September 22, 2016. Accessed August 18, 2021. Available at: https://www.cdc.gov/media/releases/2016/p0922-older-adult-falls.html.
18. Harwood RH, Foss AJE, Osborn F, et al. Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial. *Br J Ophthalmol.* 2005;89(1):53-59.
19. Palagy A, Morlet N, McCluskey P, et al. Visual and refractive associations with falls after first-eye cataract surgery. *J Cataract Refract Surg.* 2017;43(10):1313-1321.
20. Haran MJ, Cameron ID, Ivers RQ, et al. Effect on falls of providing single lens distance vision glasses to multifocal glasses wearers: VISIBLE randomised controlled trial. *BMJ.* 2010;340:c2265.

EMERGING PHARMACEUTICAL OPTIONS FOR PRESBYOPIA

BY FRANCIS S. MAH, MD

Informing patients of forthcoming technologic advances related to presbyopia can be challenging for modern clinics. Busy clinical schedules may not allow eye care providers (ECPs) the time to provide details of pipeline candidates, and, given that over-the-counter spectacles are an adequate (if imperfect) solution, it is not as though our patients are left untreated. Still, it behooves us to provide our patients with a top-line review of some of the treatment options under investigation. In this section, I will review a number of investigational therapies that may soon reach regulatory approval for the treatment of presbyopia.

THE PINHOLE EFFECT

One approach to correcting presbyopia involves employing the eye's own iris to create a pinhole effect, which extends depth of focus without restricting peripheral vision.[1] By not restricting peripheral vision, we ensure our patients do not swap one visual complication for another. European surgeons have used the IC-8 IOL (AcuFocus) to leverage small-aperture technology in patients who are eligible for surgery, and a recent study found this technology resulted in high degrees of patient satisfaction.[2] Some investigational approaches leverage pharmacologic miosis

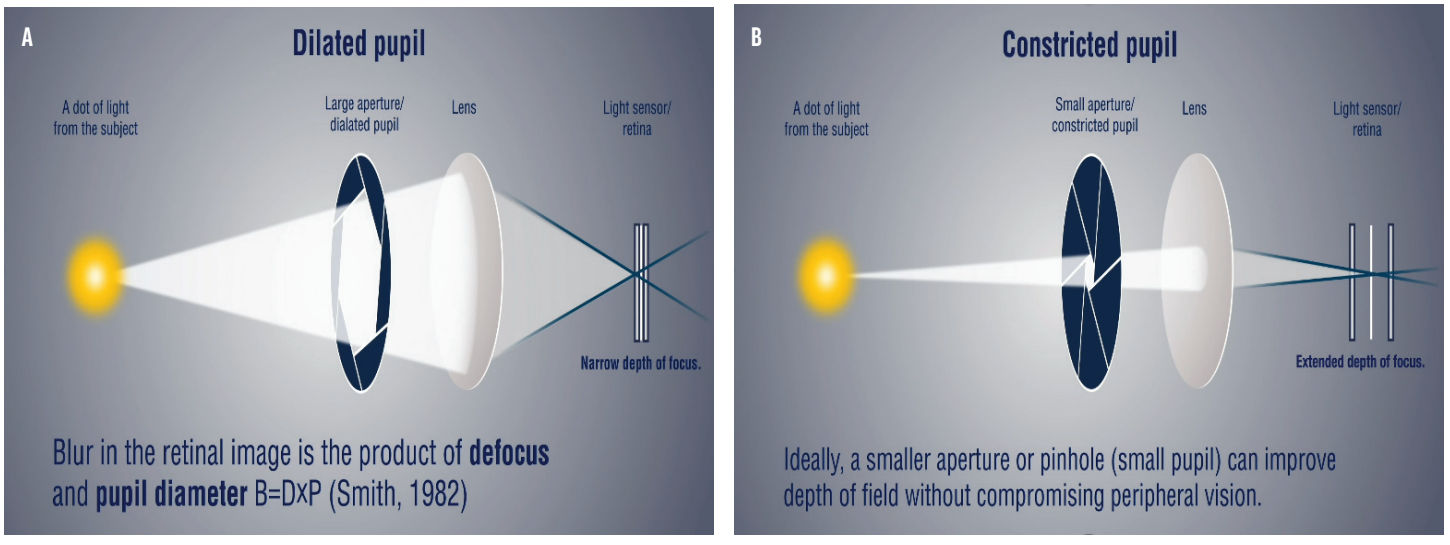


Figure 1. Blur is the product of defocus and pupil diameter. A dilated pupil (A) results in a less focused image than a constricted pupil (B).

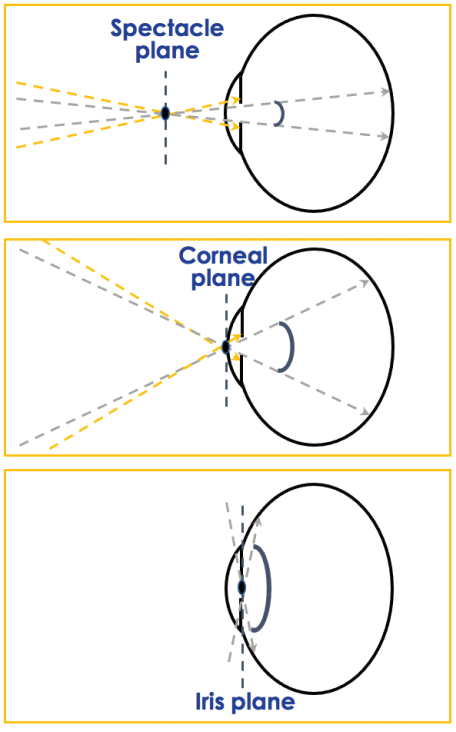


Figure 2. Small aperture technology restricts more peripheral vision the farther away the aperture is from the iris plane. In this illustration, the green dotted lines represent the limits of peripheral vision. Iris plane placement results in negligible reduction of peripheral vision.

to create this effect, which, if approved by regulatory bodies, would expand access to miotic approaches to presbyopia correction via a nonsurgical route.

When unfocused light enters through a large aperture (ie, a dilated pupil) and passes through a lens, an image reaches the light sensor on which it is focused (ie, the retina). Blur, which is the product of aperture diameter and defocus, is more intense when either factor increases in value. When defocus remains a constant, reduction of aperture diameter results in a less blurred image with an enhanced depth of focus (Figure 1). In this instance, peripheral vision remains intact.

In my experience, patients with presbyopia who use pinhole ocular occluders in the clinic are surprised by the degree to which their vision is enhanced. They are sometimes (and understandably) puzzled by the counterintuitive nature of this technology; "How can I have better vision if I am looking through a pinhole?" is a common question. In some cases, patients turn to purchasing pinhole spectacles for daily use, which I advise against because peripheral vision is restricted. The closer the pinhole is to the iris plane, the less peripheral vision is restricted (Figure 2).[1]

When discussing the physics of this visual phenomenon, I have found that it is effective to use a keyhole analogy. I ask patients to imagine they are looking through a keyhole into a room. The closer they get to the keyhole, the more of the room they can see. Therefore, the closer the pinhole is to the patient's iris, the less his or her peripheral vision will be reduced.

There is no universal pupil diameter that will render this technique effective, as patient heterogeneity and situation-specific factors, such as lighting, will affect visual outcomes. Rather than thinking about an absolute reduction in pupil size, clinicians should frame pupil diameter reduction in terms of a percentage in order to maximize results.

Xu et al found that a reduction in typical pupil size by 40 to 50% may be the range for optimizing distance and near vision among 3 different common lighting conditions (Figure 3).[3] The Table details natural pupil size and optimal pupil

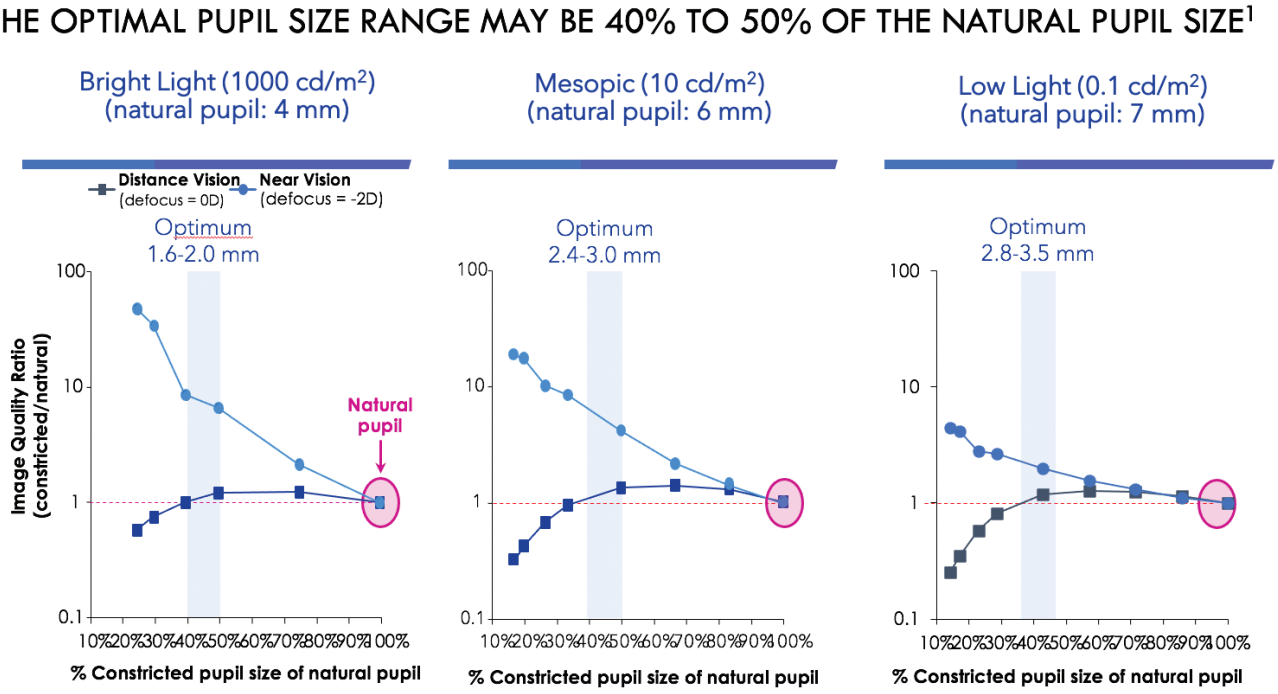


Figure 3. The range of optimal reduction in pupil size is approximately 40% to 50% in bright light, mesopic, and low light conditions. Note that natural pupil size is different in each of these lighting scenarios. (Adapted from Xu R, Thibos L, Bradley A. Effect of target luminance on optimum pupil diameter for presbyopic eyes. *Optom Vis Sci.* 2016;93(11):1409-1419.)

TABLE. OPTIMIZING PUPIL DIAMETER IN VARIED LIGHTING CONDITIONS

Lighting Condition (Candela per square meter)	Natural Pupil Diameter	Optimal Pupil Diameter Range
Bright light (1000 cd/m2)	4 mm	1.6 to 2.0 mm
Mesopic (10 cd/m2)	6 mm	2.4 to 3.0 mm
Low light (0.1 cd/m2)	7 mm	2.8 to 3.5 mm

Adapted from: Xu R, Thibos L, Bradley A. Effect of target luminance on optimum pupil diameter for presbyopic eyes. *Optom Vis Sci.* 2016;93(11):1409-1419.

size in various lighting scenarios, showing that the optimal pupil diameter range is between 1.6 and 3.5 mm in three common lighting conditions.

If (and when) we are able to offer miosis-based solutions for presbyopia, I suspect some patients will be eager to adopt it due to the nonsurgical nature of therapy, the nonfixed reduction in pupil size, and the short duration of treatment effect. For our patients, it could mean that the visual requirements of going to dinner and a movie—reading a menu in low light, watching a screen at distance, and driving home—could be easily satisfied.

ADDRESSING ACCOMMODATION

In some cases, innovators are designing new miotic agents that may be used to address presbyopia via small-aperture approaches. In other cases, researchers have reexamined agents with which ECPs are already familiar and have known effects on the eye's accommodation capacity. One such instance is pilocarpine.[4]

Pilocarpine is an agent commonly in glaucoma treatment. As a cholinomimetic drug, pilocarpine works to facilitate trabecular outflow via direct stimulation of muscarinic cholinergic receptors. The mechanism of action for pilocarpine is thought to be connected to biomechanical ciliary muscle contraction in patients with glaucoma, which directly leads to accommodation. Until recently, the accommodative effects of agents used to lower IOP in patients with glaucoma were not researched. However, they have received renewed interest given their direct effect on accommodation.

DESIGNING AN IDEAL PHARMACOLOGIC AGENT FOR PRESBYOPIA

Given what we know about small-aperture dynamics and drugs that may affect the eye's accommodative abilities, there are a few features that an ideal pharmacologic agent for treating presbyopia would have. In addition to extending the depth of focus, an agent that interacts with the iris plane rather than any area in front of the iris plane and an agent that allows the pupil to return to its natural size may be ideal.

Minimizing adverse events is also key to creating an effective miotic agent for presbyopia. Miotic agents available to ECPs may be effective at enhancing depth of focus, but they often result in patient discomfort and have a limited duration. Given that presbyopia is not a blinding disease, our tolerance for adverse events should be very low. Therefore, even side effects such as brow ache or headache are undesirable. Decreased discomfort will also motivate patients to use a new therapy, a crucial aspect to therapeutic uptake among our patients. An ideal drop that addresses presbyopia would be used once every 6 to 8 hours, which would allow daytime work to be completed while still optimizing pupil size for nighttime driving.

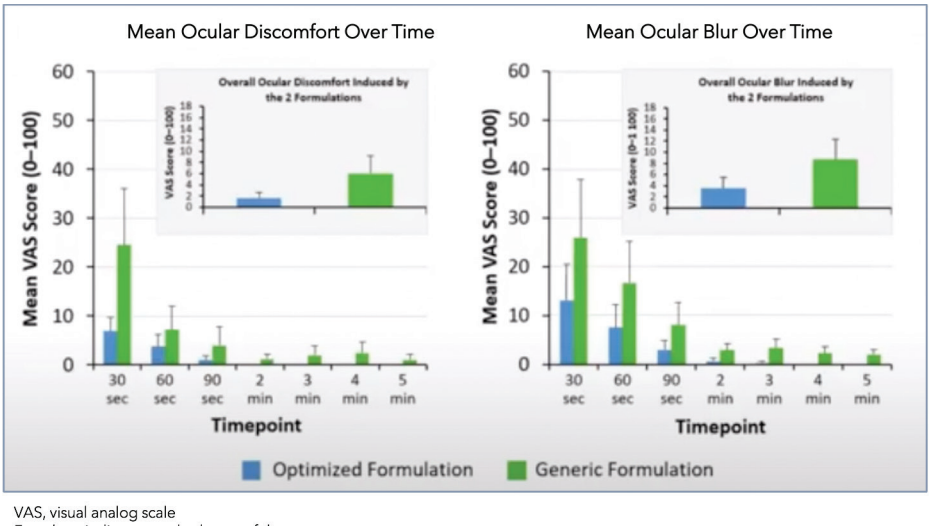
THE PIPELINE

A number of drug candidates are under investigation for the pharmacologic treatment of presbyopia. I will review several that are furthest along in their research phases.

AGN-190584

AGN-190584 (pilocarpine 1.25%, Allergan) is an optimized topical formulation of pilocarpine that is under investigation for the treatment of presbyopia.[5] It is designed for daily bilateral administration. AGN-190584 aims to achieve pupil modulation via iris sphincter contraction, as well as improved accommodation via contraction of the ciliary muscle.[5]

Researchers optimized AGN-190584 by evaluating various formulations with and without oxymetazoline compared with a generic pilocarpine solution (Figure 4). The final formulation demonstrated less discomfort (P = .097) and significantly less ocular blur (P = .016) than the generic formulation. It should be



VAS, visual analog scale
Error bars indicate standard error of the mean

Figure 4. Researchers arrived at the optimized formulation of AGN-190584 by comparing it to generic formulations, and aiming to decrease discomfort and mean ocular blur within a 5-minute window after administration.

noted that decreased discomfort was not statistically significant compared with the generic formulation.[5]

The safety and efficacy of this formulation was evaluated in the phase 3 GEMINI 1 and GEMINI 2 studies.[5] A total of 750 patients with presbyopia were randomly assigned 1:1 to receive AGN-190584 or placebo administered once daily in a bilateral fashion for 30 days.

The primary endpoint in these studies was the proportion of patients who gained at least 3 lines in mesopic, high contrast, binocular distance-corrected near visual acuity (DCNVA) at day 30, hour 3. After comparing the treatment and placebo arms, both studies met the primary endpoint. Secondary endpoints that were met include significant improvement in patient-reported outcomes such as improved vision-related reading ability and reduction in presbyopia's deleterious effects on daily living.

Further details of GEMINI 1 were presented in Q3 2021.[6] In GEMINI 1, patients in the treatment arm showed no loss of distance vision, a rapid onset of action, and sustained vision gains of up to 6 hours. At day 30, hours 3 and 6, 22.5% ($P < .001$) and 9.7% ($P = .011$) of patients, respectively, achieved at least 3 lines of vision in mesopic, high contrast, binocular DCNVA.[6]

The safety profile was positive in both studies. No treatment-emergent serious adverse events occurred during the study among patients in the treatment arm. Among the treatment-emergent nonserious adverse events that occurred at a rate of at least 3% were headache, conjunctival hyperaemia, blurred vision, and eye pain.[5]

Allergan has submitted a New Drug Application (NDA) to the FDA, which is under review.[6] The FDA is expected to act before the end of 2021.

CSF-1

CSF-1 (Orasis Pharmaceuticals) is an agent comprised of low-dose pilocarpine and a propriety multifaceted vehicle designed to address the effects of presbyopia. The drug is intended to be administered twice daily.

The drug's safety and efficacy were evaluated in a phase 2b clinical trial, which met its primary endpoint.[7,8] In that study, 166 patients with presbyopia were randomly assigned 1:1:1 to receive any of three different combinations of CSF-1; patients in the first two arms switched therapy at the start of week 2, and patients in the third arm maintained their regimen and dosing throughout the 3-week study.

DCNVA was assessed 1 hour after drop instillation. Among those in the treatment arms, 47% experienced a 3-line gain in DCNVA compared with 16% in the treatment arm ($P < .001$; Figure 5). Statistical significance was also observed among 2-line gainers, with 80% of treatment patients and 43% of vehicle-treated patients gaining at least 2 lines in DCNVA ($P < .001$). No reported complications of distance vision and night vision were present. Safety was unremarkable in the study.[9]

The drug is under investigation in the phase 3 NEAR-1 and NEAR-2 studies.[10-12] Those studies are multi-center, double-masked, parallel-group clinical trials enrolling approximately 600 participants with presbyopia. The primary endpoint in the phase 3 studies is proportion of patients with 3-line improvement in near VA without loss of at least 1 line of distance-corrected VA; secondary endpoints include 2-line improvements in near vision, effects on night vision, and various safety and tolerability measurements.

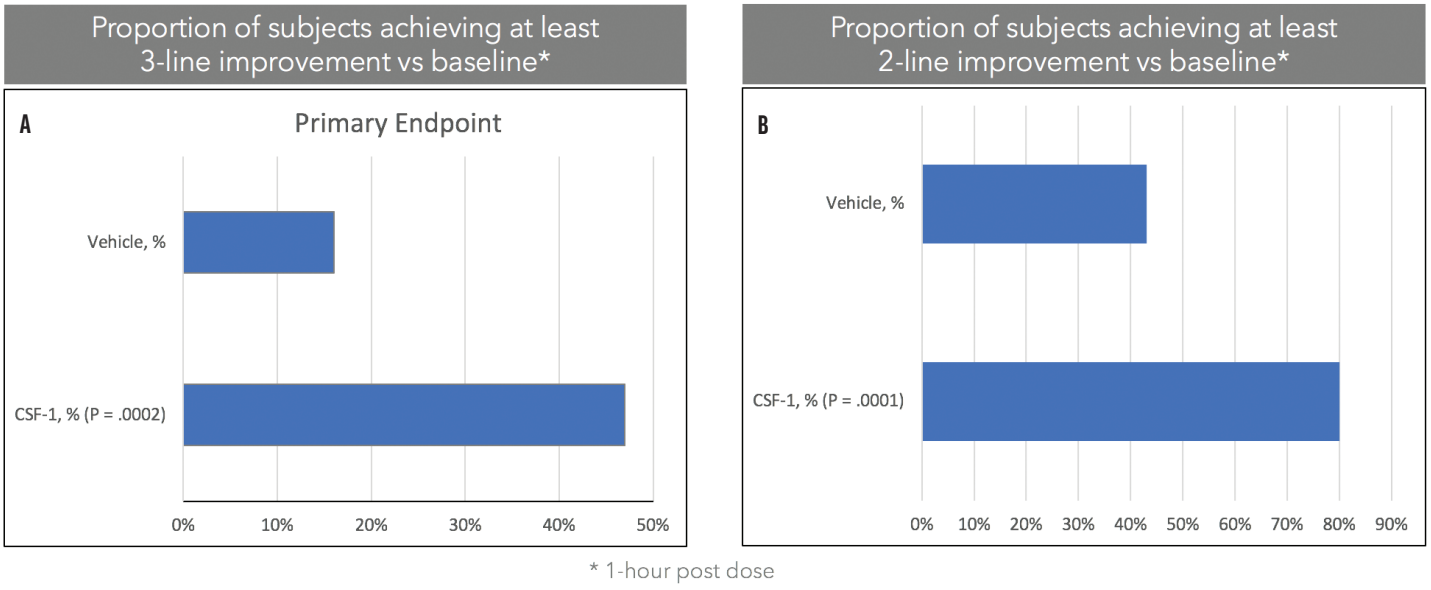


Figure 5. In a phase 2b study evaluating the safety and efficacy of CSF-1, researchers found that the percentages of patients who achieved at least a 3-line (A) and 2-line (B) vision improvement in distance-corrected near visual acuity were significantly higher among patients who were enrolled in the treatment arms compared with those enrolled in the vehicle arms.

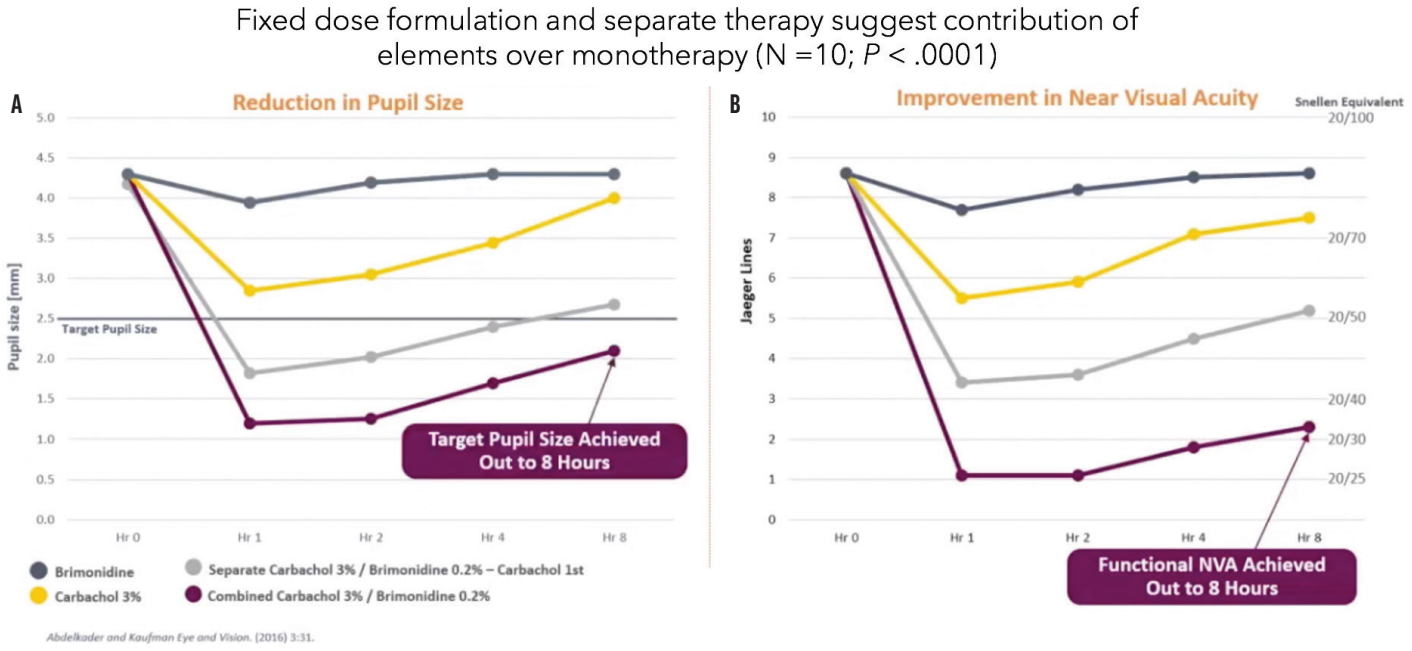


Figure 6. In a 2016 study, a single-drop formulation of 3% carbachol and 0.2% brimonidine performed the best compared with brimonidine monotherapy, carbachol monotherapy, and successive administration of both brimonidine and carbachol in separate drops. The combination drop was the only regimen to allow maintenance of target pupil size at hour 8 (A) and demonstrated superior near visual acuity outcomes at hour 8 (B).

Carbachol/brimonidine tartrate combination drop

A drop by Visus Therapeutics that is a novel combination of carbachol and brimonidine tartrate is currently undergoing a phase 2 safety and efficacy study.[13] The exact makeup of the drop has yet to be announced.

A 2016 study found that a combination of 3% carbachol and 0.2% brimonidine in a single drop resulted in statistically significant improvements in mean near visual acuity (NVA) compared with 3% carbachol alone, 0.2% brimonidine alone, or successive individual instillation of carbachol and brimonidine (Figure 6).[14] These results underscored the findings from a 2015 study that compared a single combination drop of 2.25% carbachol and 0.2% brimonidine to a placebo drop, and found that patients in the treatment arm experienced a statistically significant improvement in NVA.[15]

Among the most recent data related to the drop is a 2019 study that assessed the safety and efficacy of two different single-drop combinations of carbachol and brimonidine.[16] Patients were randomly assigned to group 1 (2.25% carbachol and 0.2% brimonidine) or group 2 (3% carbachol plus 0.2% brimonidine). Researchers assessed pupil size, NVA, and distance visual acuity at hours 1, 2, 4, 8, and 12. It was determined that all eyes demonstrated statistically significant improvements in NVA, with patients in group 2 experiencing sustained improvement. No serious adverse ocular effects were observed among the study patients.

UNR844-CL

UNR844-CL (Novartis) is a disulfide bonds modulator that aims to improve the elasticity of the hardened crystalline lens in patients with presbyopia, thereby allowing improved natural accommodation. It should be noted that this approach is different from the candidates described previously, all of which rely in part on small-aperture approaches to address the effects of presbyopia.

A pair of registered clinical trials found that twice daily instillation of UNR844-CL in patients (N = 125) with presbyopia resulted in improved DCNVA compared with placebo, with 82% of patients demonstrating at least 20/40 DCNVA and 36% of patients demonstrating at least 20/25 DCNVA at month 3.[17,18]

It was reported that a phase 2a study found no statistical difference in the DCNVA measurements at month 3.[19,20] Richdale et al reported that, due to high variability in DCNVA measurements during the study, a post-hoc analysis was performed.[20] Although median difference in DCNVA was not statistically significant among treatment and placebo groups in the post-hoc analysis, researchers felt the post-hoc data were informative enough to move forward with a phase 2b dose-finding study.

THE NEXT ERA OF PRESBYOPIA CORRECTION

We may be on the cusp of offering our patients a novel therapy to address visual disturbances associated with presbyopia. If some of the drugs discussed in this article are deemed safe and effective, then the era of pushing our patients toward spectacle correction could be ending. ■

1. Charman WN. Correcting presbyopia: the problem of pupil size. *Ophthalmol Physiol Opt.* 2017;37:1-6.
2. Schojai M, Schultz T, Jerke C, Böcker J, Dick HB. Visual performance comparison of 2 extended depth-of-focus intraocular lenses. / *Cataract Refract Surg.* 2020;46(3):388-393.
3. Xu R, Thibos L, Bradley A. Effect of target luminance on optimum pupil diameter for presbyopic eyes. *Optom Vis Sci.* 2016;93(11):1409-1419.
4. Renna A, Vejarano LF, De la Cruz E, Alió JL. Pharmacological treatment of presbyopia by novel binocularly instilled eye drops: a pilot study. *Ophthalmol Ther.* 2016; 5:63–73.

5. Allergan, an AbbVie Company, Announces Positive Phase 3 Topline Results for Investigational AGN-190584 for the Treatment of Presbyopia [press release]. Allergan; North Chicago, IL; October 28, 2020. Available at: https://news.abbvie.com/news/press-releases/allergan-an-abbvie-company-announces-positive-phase-3-topline-results-for-investigational-agn-190584-for-treatment-presbyopia.htm.
6. New Data Presented on the Safety and Efficacy of Investigational AGN-190584 as a Potential Novel Treatment for Presbyopia, a Common and Progressive Eye Condition [press release]. Allergan; North Chicago, IL; July 25, 2021. Available at: https://news.abbvie.com/news/press-releases/new-data-presented-on-safety-and-efficacy-investigational-agn-190584-as-potential-novel-treatment-for-presbyopia-common-and-progressive-eye-condition.htm.
7. A Multi-Center, Double-Masked Evaluation of the Efficacy and Safety of CSF-1 in the Treatment of Presbyopia. ClinTrials.gov. ClinicalTrials.gov Identifier: NCT03885011. Accessed August 30, 2021.
8. Orasis Pharmaceuticals Announces CSF-1 Eye Drop Successfully Met Primary Endpoint in Phase 2b Clinical Study in Presbyopia [press release]. Orasis Pharmaceuticals; Herzliya, Isreal; October 10, 2019.
9. McKinney S. Can Patients Just Drop Presbyopia? Review of Ophthalmology. Published August 10, 2021. Accessed September 13, 2021. Available at: https://www.reviewofophthalmology.com/article/can-patients-just-drop-presbyopia.
10. Orasis Pharmaceuticals Announces Initiation of Phase 3 Clinical Studies of Novel Eye Drop Candidate for the Treatment of Presbyopia [press release]. Orasis Pharmaceuticals; Herzliya, Isreal; October 28, 2020.
11. An Evaluation of the Efficacy and Safety of CSF-1 in the Temporary Correction of Presbyopia (NEAR-1) (NEAR-1). ClinTrials.gov. ClinicalTrials.gov Identifier: NCT04599933. Accessed August 30, 2021.
12. An Evaluation of the Efficacy and Safety of CSF-1 in the Temporary Correction of Presbyopia (NEAR-2) (NEAR-2). ClinTrials.gov. ClinicalTrials.gov Identifier: NCT04599972. Accessed August 30, 2021.
13. Visus Therapeutics Initiates Phase 2 Clinical Trial of Brimochol for the Treatment of Presbyopia [press release]. Visus Therapeutics; Seattle, WA; March 25, 2021.
14. Abdelkader A, Kaufman HE. Clinical outcomes of combined versus separate carbachol and brimonidine drops in correcting presbyopia. *Eye Vis (Lond).* 2016;3:31.
15. Abdelkader A. Improved presbyopic vision with miotics. *Eye Contact Lens.* 2015;41(5):323-327.
16. Abdelkader A. Influence of different concentrations of carbachol drops on the outcome of presbyopia treatment - a randomized study. *Int J Ophthalmic Res.* 2019;5(1):317-320.
17. A Study to Evaluate the Safety and Efficacy of EV06 Ophthalmic Solution in Improving Vision in Subjects With Presbyopia. ClinTrials.gov. ClinicalTrials.gov Identifier: NCT02516306. Accessed August 30, 2021.
18. A Study of Safety and Efficacy of UNR844 Chloride (UNR844-Cl) Eye Drops in Subjects With Presbyopia. ClinTrials.gov. ClinicalTrials.gov Identifier: NCT03809611. Accessed August 30, 2021.
19. Further study planned based on positive results for presbyopia drug. Ocular Surgery News. Published October 12, 2020. Accessed August 30, 2021. Available at: https://www.healio.com/news/optometry/20201012/further-study-planned-based-on-positive-results-for-presbyopia-drug.
20. Richdale K. UNR844 ophthalmic solution for the topical treatment of presbyopia: results of a phase ii randomised controlled trial. American Academy of Optometry. Accessed August 30, 2021. Available at: https://www.aaopt.org/detail/knowledge-base-article/papers-novel-pharmaceutical-treatments.

POTENTIAL CLINICAL USE OF PIPELINE CANDIDATES THAT ADDRESS PRESBYOPIA

BY MARGUERITE B. MCDONALD, MD, FACS

In the first installment of this series, George O. Waring IV, MD, FACS, outlined the state of presbyopia in the modern age, with emphasis on how patient safety and convenience could be maximized if a pharmaceutical agent that addressed decreased visual function due to presbyopia were to be approved. Francis S. Mah, MD, then explained how approaches leveraging small-aperture strategies and improved accommodation could provide relief to patients with presbyopia, and summarized the pipeline candidates furthest along in their research cycle.
How might these pharmaceutical approaches, if they are approved by regulatory bodies, affect the day-to-day practice of ophthalmologists and optometrists? To learn how we might best prepare our clinics for a possible change in the treatment landscape, I led a discussion with Drs. Mah and Waring. Our discussion, reproduced below, has been edited for brevity and clarity.

— Marguerite B. McDonald, MD, FACS

Marguerite B. McDonald, MD, FACS: Presbyopia patients are not a homogenous population. Patients experiencing early visual changes related to the natural aging of the eye may forgo spectacle correction altogether, or may find that spectacles with low power are enough for their needs. As patients age, however, they generally find that the power of their lenses increases, and that the visual issues created by presbyopia are more apparent.

Eye care providers (ECPs) can sense a patient's dread or anxiety associated with an initial presbyopia diagnosis; most patients see it as an unwelcome sign of aging. If pharmacologic agents are approved for use, it will fall on ECPs to succinctly describe to patients the options available to them and to advise how spectacles and drops may be used in a two-pronged approach in presbyopia management.

It is likely that these pharmaceutical options will be deemed nonessential for human health and therefore not covered by health insurance plans. In this instance, patients will probably be selective about when they choose to employ drops that obviate their need for spectacles. For example, we can envision a patient who might be fine with wearing readers while working from a home office on a weeknight, but who wants to use drops during work hours and for social events on the weekend.

Which patients do you think are most likely to benefit from the regulatory approval of a drop that addresses presbyopia?

George O. Waring IV, MD, FACS: Incipient presbyopic patients will likely respond positively to a drop. The anxiety associated with presbyopia diagnosis may be alleviated by an option that eliminates the need for spectacle use in a patient's 40s and 50s.

Francis S. Mah, MD: Older patients will likely find great benefit to using a presbyopia-correcting drop, too. Pseudophakic patients who are able to improve their depth of field when using a drop that initiates a pinhole effect could improve patient mobility and reduce fall rates.

Dr. McDonald: ECPs specializing in contact lenses may find that presbyopia-correcting drops will appease patients who have been dissatisfied with multifocal contact lenses. With a drop, these patients will be able to wear contact lenses that address their distance vision and use a drop as needed to adjust their near vision. Cataract surgeons may also recommend drops to patients who underwent surgery with a premium IOL and are dissatisfied with their near vision. There is now an option for cataract patients who want full, aberration-free distance correction with monofocal

IOLs in both eyes, but who still want to be free of reading glasses. The range of patients who might benefit from this technology is wide, and an offering such as a presbyopia-correcting drop may keep patients in a practice as their ocular needs change with age.

In fact, I suspect that practices with several ECPs on staff will seek to build their patient base by creating a specialty division within their clinic that exclusively manages patients with presbyopia. This division would evaluate patients, work with patients to strategize the best balance between spectacle use and drop use, and track patient responses to therapy.

Clinicians who are dedicated to a practice's presbyopia growth will need to remember that, in some cases, they will be encountering patients who have not seen an ECP in their entire lives—and that this population may compose a significant percentage of their patient population. Finding a way to make the first encounter with these patients as successful as possible will be fundamental to continued practice building.

Dr. Mah: Both optometrists and ophthalmologists will be tasked with helping guide presbyopic patients through a new treatment landscape. Creating an algorithm that directs patients into general groups—those who are eligible for surgery, those who are best suited for drops, etc.—may mitigate the disruption to clinical workflow that the arrival of new pharmaceutical options could create.

Dr. Waring: Even among clinics that already employ algorithms for treating presbyopia, adjustments will need to be made to ensure that patients with mild presbyopia are correctly directed toward proper care. Algorithms currently used may not be equipped to capture these patients.

Dr. McDonald: Our clinics need to be prepared for an influx of patients seeking drops for presbyopia. When the industry's formal direct-to-patient marketing campaigns are underway, patients will begin calling our clinic.

The anticipation is clear to my practice. I conducted an informal survey within my practice, asking if patients would be interested in using a drop to correct presbyopia, and we found that patients were overwhelmingly excited about such a solution. Creating a list of known patients that your clinic can contact when a drop is available will provide your practice with momentum when it starts offering prescription pharmaceutical presbyopia therapy.

Clinics may want to hire extra staff if they feel that patient volume will increase significantly. Also, creating new protocols regarding patients who call an ECP's practice may be needed to ensure that intake flows smoothly. Staff education and training will determine whether this new technology leads to a well-functioning clinic or an overwhelmed one.

Dr. Mah: There is no doubt that a technology such as a presbyopia-correcting drop will be disruptive. It's up to ECPs to ensure that this disruption is a net positive for their patients and their clinics. Clinical models that rely on spectacle dispensaries for cashflow may fear that presbyopia-correcting drops will reduce the sale of spectacles, but I believe this worry is unfounded. Many patients will alternate between drops and spectacles, and a patient who is empowered by a clinician with solutions will likely continue to turn to that clinic for their spectacle needs.

Dr. Waring: Earlier we mentioned that some patients who will present for a presbyopia evaluation will experience their initial encounter with an ECP. During comprehensive examinations, I suspect many ECPs will detect latent disease activity. Clinics should also be prepared to direct these patients to the relevant subspecialist for care.

Dr. McDonald: ECPs can use the opportunity presented by presbyopia-correcting drops to strengthen their relationships with patients, which in turn strengthens their practice. As we move toward the era of pharmacologic presbyopia correction, preparation will be the key to success. ■

TREATING PRESBYOPIA:
New Approaches to a Familiar Problem

CME Release Date: November 2021
CME Expiration Date: December 2022
COPE Release Date: November 5, 2021
COPE Expiration Date: November 5, 2023

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DEMOGRAPHIC INFORMATION

Profession
___ MD/DO
___ OD
___ NP
___ Nurse/APN
___ PA
___ Other

Years in Practice
___ >20
___ 11-20
___ 6-10
___ 1-5
___ <1

Patients Seen Per Week (with the disease targeted in this activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
___ >50

Region
___ Northeast
___ Northwest
___ Midwest
___ Southeast
___ Southwest

LEARNING OBJECTIVES

Did the program meet the following educational objectives?	**Agree**	**Neutral**	**Disagree**
Differentiate the underlying mechanisms of presbyopic changes.	_____	_____	_____
Interpret the clinical trial experience published in the literature with pharmaceutical and nonpharmaceutical presbyopia-correcting options.	_____	_____	_____
Distinguish among the pharmacological properties of newly emerging presbyopia-correcting drops and their mechanisms of action.	_____	_____	_____
Explain how presbyopia-correcting drops are likely to affect categories of patients based on individual characteristics.	_____	_____	_____
Describe the side effects of pharmaceutical approaches to presbyopia correction with other treatment options to **debate** the pros and cons of each strategy.	_____	_____	_____

PLEASE COMPLETE AT THE CONCLUSION OF THE PROGRAM.

1. **Based on this activity, please rate your confidence in your ability to distinguish among the pharmacological properties of newly emerging presbyopia-correcting drops and their mechanisms of action (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).**
   A. 1
   B. 2
   C. 3
   D. 4
   E. 5

2. **A 51-year-old white woman with manifest refraction of +0.75 sphere OU presents with increased frustration with near work. Her uncorrected distance visual acuity is 20/30 and uncorrected near is J9. Slit lamp and fundus examination are unremarkable. She does not want to wear glasses for distance or for near work. What would be the best course of action to help achieve this patient's goal of spectacle independence in the near range?**
   A. Monovision with keratorefractive procedure after a successful trial with contact lenses
   B. Refractive lens exchange with multifocal lens
   C. Trial of presbyopia pharmaceuticals
   D. Discuss risks and benefits of each modality and give patient the opportunity to choose what may work best

3. **What is the mechanism of action of the current pharmaceutical being studied to restore lens function?**
   A. Increasing aqueous antioxidant concentrations
   B. Breaking disulfide bonds within the lens
   C. Absorbing UV light that induces lens damage
   D. Restoring natural chemical concentrations of the aqueous humor to restore lens nutrition

4. **Known optical disadvantages of multifocal spectacles include:**
   A. Decreased depth perception
   B. "Cob web" effect
   C. Decreased edge-contrast sensitivity
   D. All of the above
   E. Options A and C

5. **By age 50, accommodative amplitude has decreased to approximately how many diopters?**
   A. 0.50 D
   B. 1.00 D
   C. 2.00 D
   D. 3.00 D

6. **Which of the following are features of stage 3 dysfunctional lens syndrome?**
   A. Mild presbyopia
   B. Mild lens opacity
   C. Higher order aberrations
   D. Dry eye

7. **Which of the following statements regarding multifocal spectacles and fall risk is TRUE?**
   A. Patients wearing multifocal spectacles are more likely to fall than patients who do not wear multifocal spectacles
   B. Patients who do not wear multifocal spectacles are more likely to fall than patients who wear multifocal spectacles
   C. There is no known association between fall-risk and multifocal spectacles
   D. Patients wearing bifocal spectacles are less likely to fall than patients wearing single vision spectacles

8. **According to one study, performing cataract surgery in one eye is associated with what percentage reduction in risk of falling over 1 year?**
   A. 14%
   B. 24%
   C. 34%
   D. 44%

9. **According to one study, what reduction in fall risk can be achieved from switching from multifocal spectacles to single-vision spectacles?**
   A. No reduction in fall risk
   B. 20% reduction
   C. 40% reduction
   D. 60% reduction

10. **According to studies, what reduction in pupil size is optimal for maximizing both distance and near vision?**
    A. 10-20%
    B. 20-30%
    C. 30-40%
    D. 40-50%

11. **According to studies involving AGN-190584 for pharmacological treatment of presbyopia, all of the following were nonserious adverse events EXCEPT:**
    A. Headache
    B. Conjunctival hyperemia
    C. Blurred vision
    D. Cataract formation

12. **According to phase 2b studies evaluating the efficacy and safety of CSF-1, which of the following statements is TRUE?**
    A. Patients enrolled in the treatment arm achieved a statistically significant improvement in distance-corrected near visual acuity over patients in the control arm
    B. Patients enrolled in the control arm achieved a statistically significant improvement in distance-corrected near visual acuity over patients in the treatment arm
    C. Patients enrolled in the treatment arm had the same distance-corrected near visual acuity compared to patients in the treatment arm
    D. CSF-1 was found to be ineffective in improving distance-corrected near visual acuity

13. **Which of the following statements regarding pinhole occlusion and near vision is TRUE?**
    A. The closer the pinhole is to the patient's iris, the less his or her peripheral vision will be reduced
    B. The farther the pinhole is to the patient's iris, the less his or her peripheral vision will be reduced
    C. Peripheral vision is not related to distance of pinhole occlude from the iris
    D. Pinhole occlusion does not impact peripheral vision

ACTIVITY EVALUATION/SATISFACTION MEASURES

Your responses to the questions below will help us evaluate this CE/CME activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low _____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low _____

This activity improved my competence in managing patients with this disease/condition/symptom _____ Yes _____ No

Probability of changing practice behavior based on this activity: _____ Yes _____ No _____No change needed

If you plan to change your practice behavior, what type of changes do you plan to implement? *(check all that apply)*

_____ Change in pharmaceutical therapy
_____ Change in diagnostic testing
_____ Change in current practice for referral
_____ My practice has been reinforced
_____ Change in nonpharmaceutical therapy
_____ Choice of treatment/management approach
_____ Change in differential diagnosis
_____ I do not plan to implement any new changes in practice

Please identify any barriers to change *(check all that apply)*:

_____ Cost
_____ Lack of consensus or professional guidelines
_____ Lack of administrative support
_____ Lack of experience
_____ Lack of time to assess/counsel patients
_____ Lack of opportunity (patients)
_____ Reimbursement/insurance issues
_____ Lack of resources (equipment)
_____ Patient compliance issues
_____ No barriers
_____ Other. Please specify: _____
_____

The design of the program was effective for the content conveyed. ___ Yes ___ No

The content supported the identified learning objectives. ___ Yes ___ No

The content was free of commercial bias. ___ Yes ___ No

The content was relative to your practice. ___ Yes ___ No

The faculty was effective. ___ Yes ___ No

You were satisfied overall with the activity. ___ Yes ___ No

Would you recommend this program to your colleagues? ___ Yes ___ No

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

_____ Patient Care
_____ Practice-Based Learning and Improvement
_____ Professionalism
_____ Medical Knowledge
_____ Interpersonal and Communication Skills
_____ System-Based Practice

Additional comments:

_____

_____ I certify that I have participated in this entire activity.

This information will help evaluate this activity; may we contact you by email in 3 months to ask if you have made changes to your practice based on this activity? If so, please provide your email address below.

_____