Supplement to

January/February 2023

Supported by Alcon Global Medical Affairs

Alcon

CRST GT

Cataract & Refractive Surgery Today Glaucoma Today

THE EVIDENCE: A CLINICAL PERSPECTIVE ON THE HORIZON TRIAL

Key 2- and 5-year outcomes from the HORIZON Clinical Trial and perspectives on how they apply to real-world practice.

I. Paul Singh, MD

Brian Flowers, MD

Pradeep Ramulu, MD, PhD

THE EVIDENCE: A CLINICAL PERSPECTIVE ON THE HORIZON TRIAL

Key 2- and 5-year outcomes from the HORIZON Clinical Trial and perspectives on how they apply to real-world practice.

INTRODUCTION

It has been a little over a decade since the first standardized definition of micro-invasive glaucoma surgery (MIGS) was introduced.[1] In that time, ophthalmology has seen the release of various devices and surgical techniques within the category that have transformed how glaucoma patients are managed. Taken together, it is fair to say that the introduction of MIGS has revolutionized what we are capable of doing on behalf of our patients; clinical trial data from major studies continue to demonstrate repeatable and predictable IOP responses after MIGS procedures with demonstrated safety. Clinical trials, like the HORIZON trial, show us that MIGS devices are also associated with a greater ability to reduce or eliminate medication burden and achieve long-term IOP stability.[2-4]

It is always relevant to ask to what degree clinical trial data might apply to one's clinical practice. Are the findings limited to the particular study population, or do they represent what you might find in the real world? Data from a well-designed and executed prospective clinical trial conducted within a highly representative population with sufficient enrollment might aid in our interpretation as we attempt to guide our practices by the available evidence. We should also look at MIGS device studies not only for whether they demonstrate statistical significance in favor of one group or the other, but whether those outcomes are truly clinically meaningful.

The HORIZON trial, in which the Hydrus Microstent (Alcon LLC; Fort Worth, TX; USA) plus cataract surgery (CS) was compared to CS alone, may be such a clinical trial from which our field can learn to further improve outcomes for patients with primary open-angle glaucoma (POAG). After 2 years, this pivotal trial led to US FDA approval after it met its primary endpoint in demonstrating a greater percentage of patients achieving a 20% or more reduction in IOP compared to CS alone.[2] The trial sponsor had the great foresight to plan patient enrollment for 5-year follow-up, and in the subsequent years of the study of the device, the long-term safety and efficacy were confirmed.[3,4]

The study shows us the very real impact we can potentially have in our patients' lives. MIGS has allowed us to surgically intervene earlier in the disease continuum, addressing the anatomy of the aqueous drainage pathway to accomplish long-term control of the only known, modifiable, risk factor to prevent progression. These facts are extremely meaningful when sitting with the individual patient explaining the options available for addressing elevated IOP in patients with mild-to-moderate POAG.

Figure 1. From left to right, Drs. Ramulu, Flowers, and Singh sit down to discuss the latest data from the HORIZON trial at AAO 2022 in Chicago.

I sat down with two of my trusted colleagues, Brian Flowers, MD, and Pradeep Ramulu, MD, PhD, to review this impressive data set and to talk about how we each interpret findings from HORIZON in our own clinical practices (Figure 1). The results of this collaboration are included in this supplement. As we reviewed all the evidence and talked through the nuances, it became apparent that the true benefit of MIGS versus cataract surgery was not represented in a single finding from HORIZON; rather, the additive effects of gaining control of the IOP in a way that addresses the significant medication compliance issues our patients face suggests we are doing something fundamental to address the disease course. The evidence makes the difference as we expand MIGS devices and shape our decision-making.

– I. Paul Singh, MD

1. Saheb H, Ahmed II. Micro-invasive glaucoma surgery: current perspectives and future directions. *Curr Opin Ophthalmol*. 2012;23(2):96-104.
2. Samuelson TW, Chang DF, Marquis R, et al; HORIZON Investigators. A schlemm canal microstent for intraocular pressure reduction in primary open-angle glaucoma and cataract: The HORIZON Study. *Ophthalmology*. 2019;126(1):29-37.
3. Ahmed IIK, Rhee DJ, Jones J, et al; HORIZON Investigators. Three-year findings of the HORIZON Trial: a schlemm canal microstent for pressure reduction in primary open-angle glaucoma and cataract. *Ophthalmology*. 2021;128(6):857-865.
4. Ahmed IIK, De Francesco T, Rhee D, et al; HORIZON Investigators. Long-term outcomes from the HORIZON Randomized Trial for a schlemm's canal microstent in combination cataract and glaucoma surgery. *Ophthalmology*. 2022;129(7):742-751.

The Evolving Treatment Paradigm: What it Means for Decision-Making

A change in mindset may be the most important aspect in achieving success with MIGS devices.

BY I. PAUL SINGH, MD; BRIAN FLOWERS, MD; AND PRADEEP RAMULU, MD, PHD

In the formal classification, micro-invasive glaucoma surgery (MIGS) devices are defined by five criteria: (1) use of an *ab interno* approach; (2) minimal trauma to the target tissue with negligible disruption of normal anatomy and physiology; (3) at least modest efficacy; (4) high safety profile; and (5) rapid patient recovery with minimal impact on their quality of life.[1] Since this definition was introduced, several devices and surgeries have broadened the offerings in the MIGS category, and thereby broadened the definition. For example, in some MIGS procedures, the surgeon excises at least a portion of the trabecular meshwork (TM) tissue, with the idea that removing diseased tissue should facilitate improved flow mechanics. Such procedures raise several questions: are they indeed "minimally traumatic to the target tissue," as the formal definition requires? Do goniotomies fall under a separate category compared to trabeculotomy, and as to the latter, is there a difference between removing tissue for 90° versus 180°? More fundamentally, are these procedures desirable options in the armamentarium of glaucoma treatment options if they obviate future options that would otherwise be targeted at the removed tissue?

Ultimately, the pursuit of formal definitions may be more of an academic exercise. Nevertheless, new MIGS devices have added to, and have not necessarily replaced, the options available to the practitioner. In our view, the variety of MIGS devices offers greater ability to personalize the care of each patient. In that context, options for TM removal do not need to fit any sort of definition if the more important question is whether the risk-benefit profile makes sense for the individual patient and whether they preclude future options. Certainly, some forms of glaucoma, such as juvenile or angle-closure glaucoma, might benefit from TM removal, and so it is important to recognize a role for these procedures.

As the above illustrates, clinicians are able to ask a different set of questions than they historically may have with a treatment paradigm that started with drops, moved to laser, and considered invasive surgery as a last resort. MIGS has facilitated the laudable goal of early intervention, with the mindset of performing the best procedure for the patient today with an eye to what future steps may be warranted. As clinicians approach the prospect of individualizing the care of glaucoma patients, an understanding of the relevant data can help guide decision-making. As well, to be truly successful in this regard, clinicians may be challenged to rethink their conventional definitions of a successful outcome.

MECHANISMS OF ACTION

One way to differentiate among MIGS devices is according to where in the aqueous drainage pathway it has an effect. Emerging evidence in the glaucoma literature has expanded the understanding of aqueous flow dynamics. Although a majority of resistance in primary open-angle glaucoma (POAG) occurs in the TM, the juxtacanalicular region and the Schlemm canal (SC) are also important potential areas of blockages.[2] Moreover, these anatomic structures function within the conventional outflow pathway. Recent evidence highlights the important role of collector channels in directing flow to the distal drainage system, ultimately terminating in the episcleral venous system.[3]

Collectively, an evolved understanding of aqueous flow dynamics demonstrate that the entire system is complex, and each component has a function in physiologic flow. Therefore, MIGS options which address multiple potential sources of resistance may offer a distinct advantage. To this point, the trimodal mechanism of action associated with Hydrus Microstent (Alcon LLC; Fort Worth, TX; USA) is notable: the Hydrus Microstent (1) directs aqueous to bypass the TM through the inlet of the device to allow fluid to pass from the anterior chamber into the SC; (2) scaffolds the SC to provide permanent patency in the canal to prevent SC collapse, despite IOP elevation and augment flow; and (3) maintains patency across a 90° span of the canal, providing access to multiple collector channels over time.[4] The device is engineered with a slight contour to match the curvature of the SC and with three open windows along its 8-mm length that face the anterior chamber for unobstructed collector channel access.[5] The latter is a significant consideration, as complete blockages/herniations or collapse of the SC that block the ostia of the collector channels are present in about 50% of eyes with POAG.[6]

New MIGS devices have added to and have not necessarily replaced the options available to the practitioner. In our view, the variety of MIGS devices offers greater ability to personalize the care of each patient.

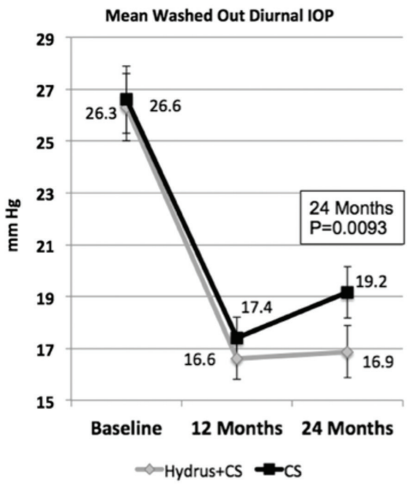

Figure 1. The IOP rebounded at 24 months in the CS group in the Hydrus II study.

There may be an additional aspect to consider after successful implantation of a Hydrus device. Mechanically opening a portion of the canal and scaffolding it open over time potentially restores physiologic function within the aqueous drainage pathway. Moreover, if there is a collapse in the SC, bypassing the canal vis-à-vis a focal stent may be insufficient to undo the collapse.[7] Intuitively, opening and maintaining the patency of SC for 90° are additive to TM bypass in assuring aqueous drainage.

As reviewed in other parts of this supplement, these mechanisms and benefits appear to contribute to better outcomes compared to cataract surgery (CS) alone (see *Reviewing HORIZON 2- and 5-Year Outcomes*). While separating the effects of MIGS and CS on IOP response postoperatively is complicated, there is evidence accumulating from major clinical trials to support that MIGS devices have an additive effect on IOP lowering.[5,8,9] For example, the IOP-lowering effect of CS alone was similar in the comparison groups in each of the COMPASS, HYDRUS II, and HORIZON trials, and deemed greater in each group being studied with a MIGS device.[5,8,9] Consistently better IOP response should tell us something. As well, MIGS devices appear to deliver more durable IOP reduction: in the Hydrus II Study, mean diurnal washed-out IOP in the Hydrus plus CS group was slightly lower when compared to the CS alone group at 12 months, and then the IOP rebounded at 24 months in the CS group (Figure 1).[5]

However, a singular focus on IOP may paint an incomplete picture when judging outcomes after MIGS surgery. As demonstrated in the HORIZON trial, compared to CS alone, Hydrus plus CS resulted in a higher percentage of patients on zero medications at 2 and 5 years and a significant reduction in the need for invasive secondary surgical interventions (SSI), in addition to greater-magnitude reduction in IOP at 2 and 5 years.[9-11]

DIFFERENTIATING THE DATA

The decision-making process in POAG is inherently different for each ophthalmologist, but it is safe to say we are all working from the same library of MIGS studies. A question we must answer is how to compare outcomes from one study to another, and ultimately between one device or surgery and another, so that we can make the best decision for each individual patient.

Although the various MIGS devices and surgeries belong to the same category, the regulatory pathway each one followed is different. Some nonimplantable MIGS devices are classified as Class 1 or 2 devices, whereas implantable MIGS devices require the full premarket approval process associated with Class 3 devices (Table). The distinction may be a factor when considering the evidence associated with a particular device: data requirements for Class 1 or 2 devices may not include clinical data or may be limited to 1 year. If clinical data exist, they will not be of the rigor required for Class 3 devices. As well, with respect to Class 2 devices, the selected predicate devices may be variable; furthermore, Class 3 MIGS devices must be implanted in conjunction with CS.

As clinicians, we want to feel confident in the quality of the data from a clinical trial, and here again is something we see in the HORIZON trial. From our perspective, these are unprecedented data in the context of a 5-year study by design for MIGS implant devices. In brief, the HORIZON trial had a 2-year pivotal phase with the primary endpoint being the percentage of patients with a reduction of at least 20% in mean washed-out diurnal IOP from baseline. The study met this endpoint, and several secondary endpoints also favored the use of Hydrus Microstent plus CS versus CS alone. In years 3-5 of the study, which retained a large majority (80%) of enrollees, patients were followed to assess safety and for monitoring efficacy outcomes; however, medication washout was not continued beyond 24 months. This second phase of the study demonstrated continued durability in the IOP response, while also

TABLE. THE REGULATORY CLASSIFICATION OF MIGS DEVICES.

Class 1 Device
• Pathway: Device registration • The device has existing or reasonably foreseeable characteristics of commercially distributed devices within that generic type.
Class 2 Device
• Pathway: 510K • Data show substantial equivalence to a predicate device regarding safety and efficacy.
Class 3 Device
• Pathway: Premarket Authorization (PMA) • The US FDA requires these new devices undergo clinical trials; for MIGS implants, generally a 2-year clinical study.

Based on what we have learned from HORIZON, we can also have conversations with patients about how medications are affecting their daily lives and whether they have cost concerns, because we have data that show us a unique ability to reduce or eliminate drop burden by using a Hydrus device at the time of CS. Individualizing the approach to POAG while considering the impact on quality of life has long been held as the ideal in glaucoma management. Ultimately, these data from HORIZON show us that we are getting closer to that goal.

providing insights into the impact of MIGS on the clinical disease course relative to CS alone.

The findings from the study on their own demonstrate the benefits of this particular MIGS device. Yet, the fact that they come from a study which enrolled patients both in the United States and from outside the United States, and which was able to retain 80% of patients through 5 years, adds additional merit. We note, as well, that the demographics of the study population are similar to what the average US glaucoma specialist sees in clinical practice, making it that much easier to see our own patients in the data.[12]

WHAT IT ALL MEANS

Fundamentally, MIGS challenges the definition of a successful postoperative outcome in the sense that it asks clinicians to reconsider the goals, objectives, and endpoints of surgery. The safety data from major trials show us that MIGS devices are appropriate for use earlier in the disease continuum, thereby providing long-term, durable control of IOP, the only known modifiable risk factor in POAG.[9-11] Based on what we have learned from HORIZON, we can also have conversations with patients about how medications are affecting their daily lives and whether they have cost concerns, because we have data that show us a unique ability to reduce or eliminate drop burden by using a Hydrus device at the time of CS. Individualizing the approach to POAG while considering the impact on quality of life has long been held as the ideal in glaucoma management. Ultimately, these data from HORIZON show us that we are getting closer to that goal.

1. Saheb H, Ahmed II. Micro-invasive glaucoma surgery: current perspectives and future directions. *Curr Opin Ophthalmol*. 2012;23(2):96-104.
2. Johnson M. What controls aqueous humour outflow resistance? *Exp Eye Res*. 2006;82(4):545-557.
3. Goel M, Picciani RG, Lee RK, Bhattacharya SK. Aqueous humor dynamics: a review. *Open Ophthalmol J*. 2010;4:52-59.
4. HYDRUS Microstent [instructions for use]. Irvine, CA: Alcon Vision LLC; September 2021 (United States).
5. Pfeiffer N, Garcia-Feijoo J, Martinez-de-la-Casa JM, et al. A randomized trial of a schlemm's canal microstent with phacoemulsification for reducing intraocular pressure in open-angle glaucoma. *Ophthalmology*. 2015;122(7):1283-1293.
6. Gong H, Johnstone M, et al. Poster #115 American Glaucoma Society, New York 2012.
7. Allingham RR, de Kater AW, Ethier CR. Schlemm's canal and primary open angle glaucoma: correlation between Schlemm's canal dimensions and outflow facility. *Exp Eye Res*. 1996;62(1):101-109.
8. Vold S, Ahmed II, Craven ER, et al; CyPass Study Group. Two-Year COMPASS Trial Results: supraciliary microstenting with phacoemulsification in patients with open-angle glaucoma and cataracts. *Ophthalmology*. 2016;123(10):2103-2112.
9. Samuelson TW, Chang DF, Marquis R, et al; HORIZON Investigators. A schlemm canal microstent for intraocular pressure reduction in primary open-angle glaucoma and cataract: The HORIZON Study. *Ophthalmology*. 2019;126(1):29-37.
10. Ahmed IIK, Rhee DJ, Jones J, et al; HORIZON Investigators. Three-year findings of the HORIZON Trial: a schlemm canal microstent for pressure reduction in primary open-angle glaucoma and cataract. *Ophthalmology*. 2021;128(6):857-865.
11. Ahmed IIK, De Francesco T, Rhee D, et al; HORIZON Investigators. Long-term outcomes from the HORIZON Randomized Trial for a schlemm's canal microstent in combination cataract and glaucoma surgery. *Ophthalmology*. 2022;129(7):742-751.
12. Marketscope. 2021 Glaucoma Surgical Device Market Report: Global Analysis
for 2020 to 2026, July, 2021. Available at: https://www.market-scope.com/pages/reports/267/2021-glaucoma-surgical-device-market-report.

Key Data From HORIZON

Outcomes at 2 and 5 years.

BY I. PAUL SINGH, MD; BRIAN FLOWERS, MD; AND PRADEEP RAMULU, MD, PHD

BACKGROUND

The HORIZON trial was a phase 3 clinical trial conducted in two phases.[1] The first portion was designed as a 2-year pivotal study comparing Hydrus Microstent (Alcon LLC; Fort Worth, TX; USA) plus cataract surgery (CS) to CS alone. In the second phase, patients were studied for an additional 3 years for ongoing safety monitoring, as well as assessment of predefined efficacy endpoints. At a topline, the study met its primary endpoint: a statistically greater percentage of

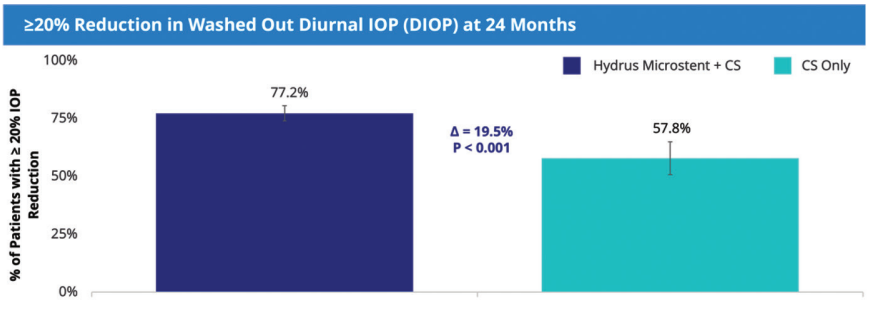

Figure 1. The primary endpoint after 2 years in the HORIZON trial.

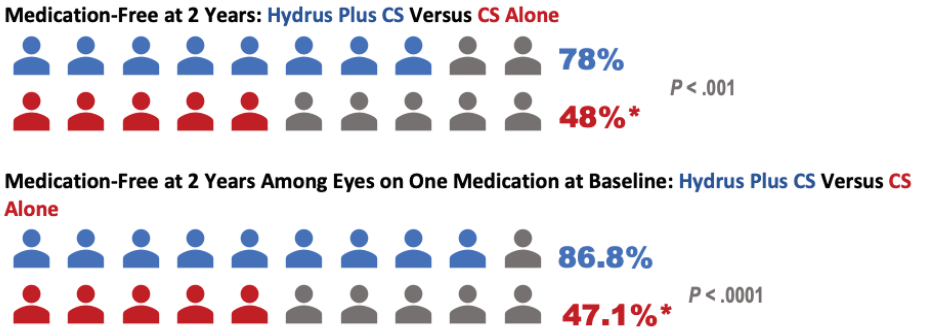

Figure 2. The difference in medication-free eyes throughout follow-up at 2 years in the HORIZON trial.

patients in the Hydrus plus CS group had 20% or greater reduction in washed-out diurnal IOP (DIOP) compared to the CS group; the secondary endpoint, change in washed-out DIOP, also favored the Hydrus plus CS group. Serious adverse events were similar between the two groups. Efficacy outcomes were confirmed after 5 years of follow-up, with a number of secondary endpoints showing significant and clinically meaningful benefits.

KEY FACTS, DEMOGRAPHICS, AND ENROLLMENT[1,2]

- HORIZON is the largest of the micro-invasive glaucoma surgery (MIGS) pivotal trials conducted to date, with 38 sites in nine countries. Approximately 40% of the Hydrus patient population came from outside the United States.
  - Groups were matched for baseline demographics.
  - Approximately 80% of enrollment was retained at 5 years.
- The study included subjects with mild to moderate primary open-angle glaucoma on one to four glaucoma medications.
- The subjects underwent CS and were randomized 2:1 to include either device placement (n = 369) or CS alone (n = 187).
- IOP and medication count, as well as safety, were assessed at months 1, 3, 6, 12, 18, and 24 postoperatively.

TWO-YEAR FINDINGS

Efficacy

- Primary endpoint (Figure 1).
- The difference in medication-free eyes throughout follow-up may reflect the clinical effect of device implantation (Figure 2).

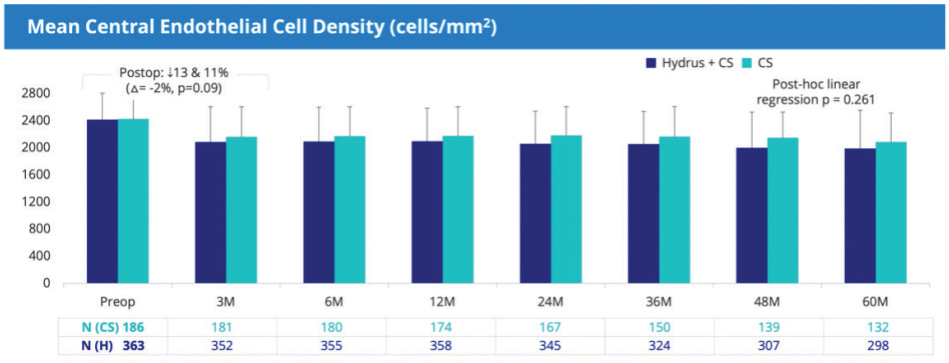

Figure 3. Mean central ECD between groups at 5 years.

Safety

- There was a low percentage of adverse events, overall.
- The rate of peripheral anterior synechiae (PAS) was greater in the Hydrus arm, but most were nonobstructive and did not affect the outcome.

FIVE-YEAR DATA[3]

Safety

- Primary safety outcomes:
  - There were no sight threatening adverse events related to the Hydrus Microstent.
  - The percent of subjects with reported serious adverse events was 3.5% in the Hydrus plus CS group (n = 13/369) and 4.3% in CS alone group (n = 8/187).
- Secondary safety outcomes:
  - No significant difference in safety outcomes from 2 to 5 years except for PAS:
- PAS was significantly higher at 5 years for Hydrus Microstent: 14.6% versus 3.7% (*P* = .0001).
- The majority of Hydrus Microstent eyes with PAS (8.7%) were not device obstructing.
- No difference in IOP control between Hydrus patients with and without PAS: 16.9± 3.3 mmHg versus 16.6± 3.5 mmHg (*P* = .49).
  - The baseline mean central endothelial cell density (ECD) was comparable between groups (*P* = .81).
- The between-group difference in mean central ECD was 2% at 3 months (11% CS, 13% Hydrus) which increased to 6% over 5 years (13% CS, 19% Hydrus), which was not significant.
- The 3-month postoperative decrease may be attributable to the additional manipulation when inserting the Hydrus Microstent (Figure 3).
- At 3 months, ≥ 30% endothelial cell loss (ECL) occurred in 17.3% in the Hydrus group and 9.4% in the CS group (difference = 7.9%).
- At the 5-year follow up, the proportion with ≥ 30% ECL increased from

17.3% at 3 months to 20.8% (P = .27) in the Hydrus group and from 9.4% at 3 months to 10.6% (P = .85) in the CS group.
- Logistic regression showed no difference in the rate of change of ≥ 30% ECL between the Hyrdus group compared to the CS group from 3 months to 5 years (P = .82).
- No eyes with ≥ 30% ECL in Hydrus Microstent or CS groups had associated clinical sequelae.

Secondary Effectiveness Outcomes[4]

- There was a > 50% reduction in the rate of secondary IOP lowering interventions with Hydrus plus CS versus CS alone (2.4% versus 5.3%).
  - The lower cumulative rate of secondary procedures (inclusive of nonincisional procedures) with Hydrus plus CS versus CS alone was 4.9% versus 7.5%.
- The change in diurnal IOP versus before surgery (mm Hg) in unmedicated patients was mean ± SD: -8.3 ± 3.8 in the Hydrus plus CS group versus -6.5 ± 4.0 in the CS group.
- Medication-free eyes were 66% in the Hydrus plus CS group versus 46% in the CS group.
  - Medication-free eyes + ≥ 20% IOP reduction resulted in 54.2% in the Hydrus plus CS group versus 32.8% in the CS group. ■

1. Samuelson TW, Chang DF, Marquis R, et al; HORIZON Investigators. A schlemm canal microstent for intraocular pressure reduction in primary open-angle glaucoma and cataract: The HORIZON Study. *Ophthalmology*. 2019;126(1):29-37.
2. Ahmed IIK, Rhee DJ, Jones J, et al; HORIZON Investigators. Three-year findings of the HORIZON Trial: a schlemm canal microstent for pressure reduction in primary open-angle glaucoma and cataract. *Ophthalmology*. 2021;128(6):857-865.
3. Ahmed IIK, De Francesco T, Rhee D, et al; HORIZON Investigators. Long-term outcomes from the HORIZON Randomized Trial for a schlemm's canal microstent in combination cataract and glaucoma surgery. *Ophthalmology*. 2022;129(7):742-751.
4. HYDRUS Microstent [instructions for use]. Irvine, CA: Alcon Vision LLC; September 2021 (United States).

Conclusion

BY I. PAUL SINGH, MD; BRIAN FLOWERS, MD; AND PRADEEP RAMULU, MD, PHD

When each of us sits with patients with primary open-angle glaucoma in the clinic, the actual data from a clinical trial are not an end in themselves, but a means to an end. We are focused on determining what course of action would be best for the individual in front of us, now and in the future. We want a plan to slow or prevent progression, but more so, we want to be able to share with patients that we are doing the best thing to help them save vision long-term. And so, while the detailed data from a clinical trial may not be part of our conversation, we nevertheless need to have confidence in what the data demonstrate and communicate these findings in ways that are meaningful to patients. The robustness of a study matters; whether the study population reflects real-world practice is important; the longevity of the data is important for a disease

In Their Own Words:

What Do You Take Away From the Evidence From HORIZON?

Pradeep Ramulu, MD, PhD: Everybody who has moderate or advanced disease once had mild disease. When I have a patient in front of me with mild primary open-angle glaucoma, I don't know if it will progress to moderate or severe, so why not use the device that has the 5-year pivotal data showing safety and efficacy? You could almost argue that you have an obligation to discuss Micro-Invasive Glaucoma Surgery (MIGS) options with patients who take medications for primary open-angle glaucoma and a visually significant cataract if they are eligible for the surgery. If you don't, there's a chance that patient will hear about it from a friend or family member, and you suddenly have a dissatisfied patient.

I. Paul Singh, MD: There are a lot of factors that influence our choice of MIGS option for each patient. In my view, the data from the HORIZON trial suggest that the Hydrus Microstent plus cataract surgery is an effective, profoundly IOP-lowering option available to us, and based on that, I am comfortable using it in appropriately selected patients regardless of glaucoma stage. The safety shows no significant difference in serious adverse events compared to cataract surgery. There was very little need for interventional surgery over time and in a post-hoc analysis, fewer postoperative IOP spikes[1] in these patients. If you feel comfortable and confident in this procedure and this stent, and you feel like it has the power you want, whether the IOP is mild or moderate, why not do it in either one of those populations of patients?

Brian Flowers, MD: When we sit with our patients, the options are often presented in a binary fashion. What we have learned from HORIZON and other studies forces us to rethink whether this is the case. There is mounting evidence that MIGS offers not only pressure control, but also less medication burden long-term with procedural interventions. It is difficult to know if this is based strictly on compliance or some other factors. Nevertheless, it's becoming difficult to ignore at this point.

1. Zebardast N, Zheng C, Jampel HD. Effect of a Schlemm's Canal Microstent on Early Postoperative Intraocular Pressure after Cataract Surgery: An Analysis of the HORIZON Randomized Controlled Trial. *Ophthalmology*. 2020 Oct;127(10):1303-1310.

that patients will live with for 15 to 20 years of their lifetime; and aspects of trial coordination that assure retention over time help us gauge the veracity of the data.

In the HORIZON trial, it was demonstrated that the Hydrus Microstent (Alcon LLC; Fort Worth, TX; USA) plus cataract surgery (CS) provided greater long-term IOP- and medication-lowering efficacy compared to CS alone with no additional safety risk. The individual primary and secondary endpoints followed over the planned 5-year study period reinforced that point. And if we learned nothing else from the study, that one conclusion alone would be significant.

Yet, what the data from HORIZON suggest is that Hydrus Microstent plus CS has a meaningful impact on patients' long-term disease course. Compared to CS alone, more patients in the Hydrus Microstent plus CS group achieved medication-free status, and fewer required an incisional secondary surgical intervention. Furthermore, among patients on one medication at the start of the study, the outcome for medication-free status was even more substantial.

Returning to how data such as those from HORIZON are useful when discussing treatment options with patients: certainly, the individual outcomes and data help guide evidence-based practices. The statistical analyses and the nuances of study design and methodology help us interpret the findings and their relatability to the real world. But when the conclusions from major clinical trials raise questions about the current status quo, we are challenged to change our thinking accordingly. Each of us has our own take on the most important thing we learned from reviewing HORIZON (see *In Their Own Words*…), yet we all agree that micro-invasive glaucoma surgery as a class, and the Hydrus Microstent in particular, has called on us to rethink the definition of a successful outcome. It has changed our approach to managing primary open-angle glaucoma. Because we have solid data from a well-executed trial, we can have confidence that offering patients surgical options earlier in the disease continuum compared to historical practice is viable, and we also do not have to wait and watch uncontrolled pressure because the safety profile is favorable enough to consider surgery even with controlled IOP (i.e., the context of concurrent cataract surgery).

So how do we use data from major clinical trials, and why are data important for real-world decision-making? Simply put, data help the clinician optimize the care of each individual patient based on the evidence. ■

I. PAUL SINGH, MD
- The Eye Centers of Racine & Kenosha, Racine and Kenosha, Wisconsin
- Member, *GT* Editorial Advisory Board
- ipsingh@amazingeye.com
- Financial disclosures: AbbVie/Allergan, Alcon, Glaukos, Nova Eye Medical, Sight Sciences

BRIAN FLOWERS, MD
- Glaucoma specialist and managing partner, Ophthalmology Associates, Fort Worth, Texas
- (817) 332-2020; bflowers@oafw2020.com
- Financial disclosures: Consultant (Alcon, EyeNovia, Glaukos, Iantrek, iStar, Ivantis, Santen, Sight Sciences); Research (Alcon, Aerie Pharmaceuticals, Glaukos, iStar, Ivantis, NiCox, Santen, Sight Sciences)

PRADEEP RAMULU, MD, PHD
- Chief, Glaucoma Division, and Professor of Ophthalmology, Johns Hopkins Wilmer Eye Institute, Baltimore
- pramulu@jhmi.edu
- Financial disclosures: Alcon, W.L. Gore, Heru Inc., Perfuse Therapeutics, NIH, Roche, Janssen