Selection of Effectiveness Endpoints and Targets: What Do We Need to Show?

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- **Abbott Medical Optics: P,S;**
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- **FDA C**

Sources:

- Implantable Glaucoma Devices
  - American National Standard for Ophthalmics 2013
- World Glaucoma Association
  - Guidelines on Design and Reporting of Glaucoma Surgical Trials 2009
- Clinical and Surgical Experience

Refractory vs Non-Refractory

- Refractory glaucoma has been traditionally treated with Trabs and Tubes

- Surgery for non-refractory glaucoma, traditionally treated with drops and laser, has introduced new questions for industry, MDs and the FDA

Efficacy Endpoint Concepts from the MIGS Experience

- "Washout Period":
  - Necessary because the modest IOP lowering with MIGS devices could be augmented or masked by topical medications
  - Before the baseline visit
  - Before or at the visit window for assessing the primary endpoint

- Limiting surgeon/center bias:
  - Set minimum and maximum numbers for both study & control devices

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- There is little debate over what we need to show. We need to show sustained IOP lowering that is significant.

- The major question is not “what” it is “when” and “for how long” and “in what % of patients”.

Extended Follow Up for MIGS

- The ANSI Endpoints Document recommends twenty-four months of follow-up for safety/efficacy endpoints
- However, shorter study durations may be justified and longer study durations may be necessary based upon the risk analysis or emergent safety issues
- Risk analysis is a major factor in determining study duration but we don't have great insight into risk-benefit analyses for MIGS

When it comes to risk, are all MIGS equal?

- The current recommendations (ANSI) appear at first glance to treat all devices equally regardless of method of implantation, location of implantation and historical perspective available (ie, already approved devices in the same space).

From the clinician's perspective:

- Each anatomical space is unique
  - Risk profile of Schlemm's Canal vs Suprachoroidal
  - Full thickness procedures (blebs) might present more risk than others

- Historical data can drive decision making for study duration
  - Have other devices been approved that occupy the same anatomical space?
  - Are there any patterns in the first 12 months of data that present a red flag?
  - Can we perform a risk benefit analysis based on one year results if the safety profile proves clear and the efficacy is measurable?

- Is there room to adopt guidance set forth by "The Least Burdensome Provisions of the FDA Modernization Act (2002)" that advocates for using post-marketing information to ensure timely public access to beneficial new products?

How many patients need to benefit to justify using a device that has a negligible downside in those where it does not work?

- The efficacy & benefit post MIGS device implantation can be masked when concentrating on statistical means

- A discussion of means (especially when the downside of implantation is minimal) disregards a significant subset of patients that had more robust IOP lowering

We need to maximize our efforts to decrease uncertainty:

- More uncertainty = less funding = less innovation = lost opportunities for novel and advanced treatments = Fewer options to enhance outcomes for glaucoma patients

- There are significant deficits in how clinicians define glaucoma, stage disease and measure “significant”

- If the experts can’t agree, why would we expect the FDA to take definitive actions on endpoints?

Suggested Steps

- Professional organizations can provide guidance for “risk-benefit” analyses in each MIGS space (input from MDs, FDA & Industry)

- Use the risk-benefit analyses to help dictate duration of pivotal trials. How much do we really learn about safety after 1 year? If the answer is minimal, then MIGS device efficacy can likely be measured at 1 year and allow for quicker access to newer technologies

Suggested Steps

- Maximize the use of post-marketing information (Registries) to expedite approval of devices that have a low risk profile and fill a large unmet need for patients with mild to moderate POAG (the majority of our glaucoma patients)

- Push for less concentration on statistical means and more discussion about the upside for some patients with little to no downside for all patients

- The final document(s) can serve as a regulatory guide for MIGS devices and support innovation by addressing uncertainties

Thank You