A Description of a Non-interventional Study Design Based Upon Data Extracted from an EHR-based Registry to Assess Long-term Real World Outcomes with Ophthalmic Devices

- Flora Lum M.D., presenting author
- Stephen Lane M.D., Alvin Relucio M.D.

Financial disclosures:

Flora Lum is an employee of AAO. Stephen Lane and Alvin Relucio are employees of Alcon.

Additional disclosure - The study methodology outlined in this Poster was intended for the CyPass® MicroStent that is no longer available in the market. Nevertheless, the following study design shows how big data (e.g. AAO IRIS® Registry) can potentially provide real-world evidence for medical devices approved for use.

Brand names have been replaced with generic terms.

Planned Study Objective

To illustrate how BIG DATA from EHR-based registries can potentially provide long-term REAL-WORLD effectiveness and safety data on FDA-approved ophthalmic devices using a MIGS device as an example

AAO IRIS® Registry

IRIS - Intelligent Research In Sight

- Electronic Health Record (EHR)-based
- Only specialty-sponsored comprehensive registry in the U.S.
- Centralized data repository and reporting
- Can validate quality of care and identify opportunities for improvement

IRIS® Registry (September 2018)	
Sites enrolled	3,147
Ophthalmologists	9,291
Optometrists	3,572
Other (NPs, PAs)	232
Patients enrolled	51.81 million
Glaucoma procedures (2013-17)	660,336
Cataract procedures (2013-17)	5,308,290
Patients with glaucoma diagnosis (2013-17)	3,084,874

https://www.aao.org/iris-registry

AAO IRIS® Registry and Verana Health

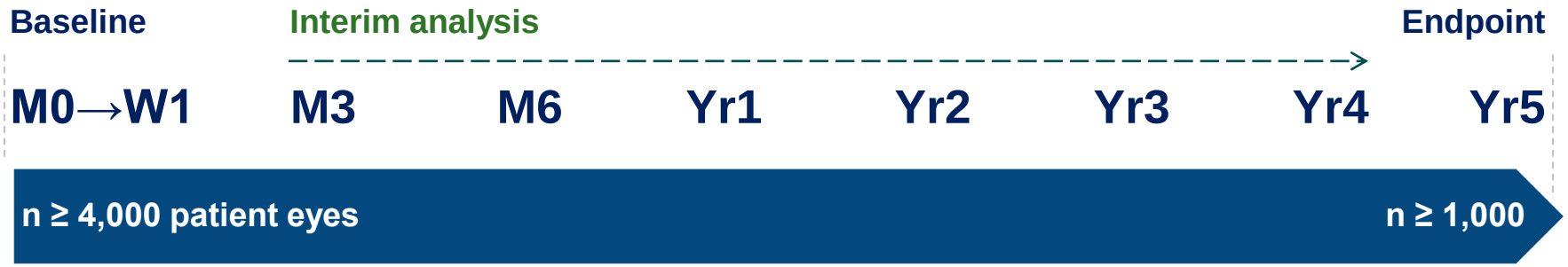
- Collaboration agreement between AAO and Verana

- Verana's capabilities:
  - Led by health care and technology veterans
  - Deploys IT resources to respond quickly to big data needs
  - Builds new analytic applications and user interfaces
  - Markets to pharmaceutical companies, manufacturers, health systems, payers
  - Supports the vision of the IRIS® Registry and the mission of the AAO

https://www.aao.org/newsroom/news-releases/detail/academy-digisight-collaboration-news-release
https://www.veranahealth.com

Example Study Design

- Post-marketing, non-interventional, descriptive, registry-based case series
- Data from ≥4,000 eyes (to ensure ≥1,000 eyes with 5 year follow-up) entered in IRIS® Registry and implanted with an approved ophthalmic medical device
- Only one eye per patient included
  - To ensure that only one eye per patient is included, Alcon will ask AAO-Verana Health to NOT include a patient more than once



Baseline: IOP, BCVA, Refraction, Medications, C/D, VF, Past surgeries (baseline and 1 week peri-operatively)
Month 3: IOP, BCVA, Refraction, Medications, AEs, SAEs, Sx_2
Month 6: IOP, BCVA, Refraction, VF, Medications, AEs, SAEs, Sx_2
Years 1-5: IOP, BCVA, Refraction, C/D, VF, Medications, AEs, SAEs, Sx_2

AE, adverse event; BCVA, best corrected visual acuity; C/D, cup to disk ratio; IOP, intraocular pressure; SAE, serious adverse event; Sx_2, secondary surgeries; VF, visual field; W1, week 1

Example of a Patient Population

Inclusion criteria

- Eyes diagnosed with OAG
- Patients ≥18 years of age at diagnosis date
- Eyes implanted with medical device (device specific CPT code)

Exclusion criteria

- Eyes diagnosed with:
  - angle-closure, traumatic, malignant, uveitic and/or neovascular glaucoma
  - other specified glaucoma
  - unspecified glaucoma
  - discernable abnormalities of the anterior chamber angle
- Contralateral eye already included in the study
- Eyes with surgery to control IOP prior to device implantation

Example Sample Size Calculation and Study Endpoints

- **Sample Size Calculation**
  - To ensure ≥1,000 patient eyes 5 years after the procedure, ≥4,000 eyes should be enrolled
- **Effectiveness Endpoints**
  - Mean IOP (mmHg) at each visit and mean change in IOP from baseline
  - Proportion of eyes with ≥20% reduction in IOP from the visit immediately prior to device implantation
  - Proportion of eyes with IOP >6 mmHg and <18 mmHg at each visit
  - Mean VA at each visit and mean change in VA from baseline
- **Safety Endpoints**
  - Ocular and non-ocular AEs and SAEs measured at each post-implantation visit
  - Procedural and device related AEs and SAEs at each visit

Example Statistical Analysis Plan

Descriptive statistics for all endpoints:

- **Frequency, proportion and distribution** (mean, standard deviation, median, range and interquartile range [IQR])

Analyses stratified by variables of interest:

- Patients **with and without concomitant** use of anti-glaucoma agents at date of device implantation
- Patients satisfying inclusion criteria. but with glaucoma indications other than POAG

Data from the IRIS® Registry: Mean IOP and Mean Change in IOP

Characteristics	Statistic	Mean IOP	Mean Change in IOP from baseline
Baseline (visit prior to device implantation)	n	878	
	Mean (SD)	18.84 (5.77)	
	Median	18	
Day 1 after implantation	n	1,187	693
	Mean (SD)	12.85 (6.11)	5.73 (7.53)
	Median	12	6
Day 7 after implantation	n	1,065	631
	Mean (SD)	12.47 (5.41)	6.44 (7)
	Median	12	6
Day 30 after implantation	n	634	370
	Mean (SD)	14.5 (6.47)	4.08 (7.43)
	Median	14	4

Analysis by Verana Health; data sourced from American Academy of Ophthalmology IRIS® Registry September, 2018

Data from the IRIS® Registry: Proportions of Eyes with ≥20% Decrease in IOP from Baseline

Characteristics	No. with ≥20% decrease in IOP from baseline	No. with IOP measured at that time and at baseline	Proportion with ≥20% decrease
Day 1 after implantation	438	693	63.20
Day 7 after implantation	414	631	65.61
Day 30 after implantation	202	370	54.59

Data from the IRIS® Registry: Eyes Having IOP >6 mmHg and <18 mmHg

Characteristics	No. with IOP >6 mmHg and <18 mmHg	No. with IOP measured at that time	Proportion with IOP >6 mmHg and <18 mmHg
Baseline (visit prior to device implantation)	485	878	55.24
Day 1 after implantation	916	1187	77.17
Day 7 after implantation	871	1065	81.78
Day 30 after implantation	468	634	73.82

Analysis by Verana Health; data sourced from American Academy of Ophthalmology IRIS® Registry September, 2018

Data from the IRIS® Registry: Mean VA and Mean Change in VA

Characteristics	Statistic	Mean VA (logMAR)	Mean Change of VA from baseline
Baseline (visit prior to device implantation)	n	923	
	Mean (SD)	0.32 (0.36)	
	Median	0.3	
Day 1 after implantation	n	717	422
	Mean (SD)	0.36 (0.46)	-0.03 (0.45)
	Median	0.3	0
Day 7 after implantation	n	815	465
	Mean (SD)	0.21 (0.32)	0.12 (0.33)
	Median	0.1	0.08
Day 30 after implantation	n	508	292
	Mean (SD)	0.17 (0.27)	0.14 (0.31)
	Median	0.1	0.12

Analysis by Verana Health; data sourced from American Academy of Ophthalmology IRIS® Registry September, 2018

Conclusion

This example of a study plan shows that evidence gaps between well-controlled clinical trials and real-world clinical practice ***MAY*** be bridged using BIG DATA from EHR-based registries like IRIS®

This example of a study plan illustrates how BIG DATA from EHR-based registries ***MAY*** provide long-term effectiveness and safety data on FDA-approved ophthalmic devices relevant to everyday clinical usage and practice