The potential for treatment of noninfectious uveitis using a suprachoroidal approach

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Acknowledgments

- Phase 1/ 2 and Phase 2 uveitis trial investigators

Suprachoroidal injection in development

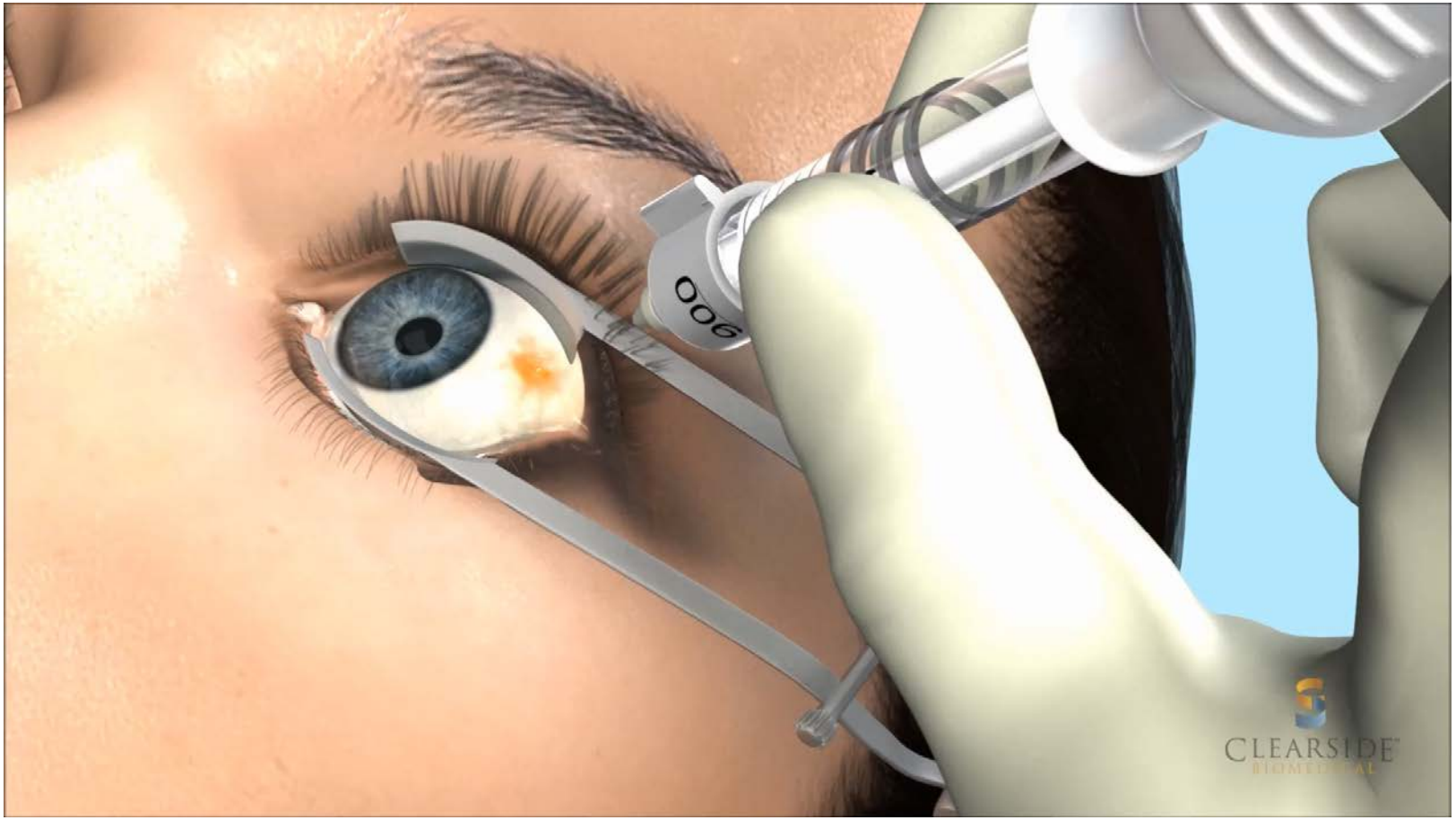
- **Potentially useful approach for the treatment of ocular conditions**

- **Novel technique**
  - 30G needle (approximately 1000 micron in length)
  - Proprietary microinjector syringe

- **Proposed benefits**
  - High bio-availability in target tissues[1]
  - Sparing anterior segment might result in fewer ocular side effects[2]
  - Potential for longer duration[2]

1. Gilger et al Invest Ophthalomol Vis Sci. 2013;54:173-178. Treatment of acute posterior uveitis in a porcine model by injection of triamcinolone acetonide into the suprachoroidal space using microneedles
2. Noronha G. Using suprachoroidal administration as an approach to treat noninfectious uveitis – from concept through clinical data. ISOPT 2015 Clinical Conference proceedings. Published March 2016

Precise access to posterior areas of the eye via suprachoroidal injection



Rationale for the suprachoroidal approach

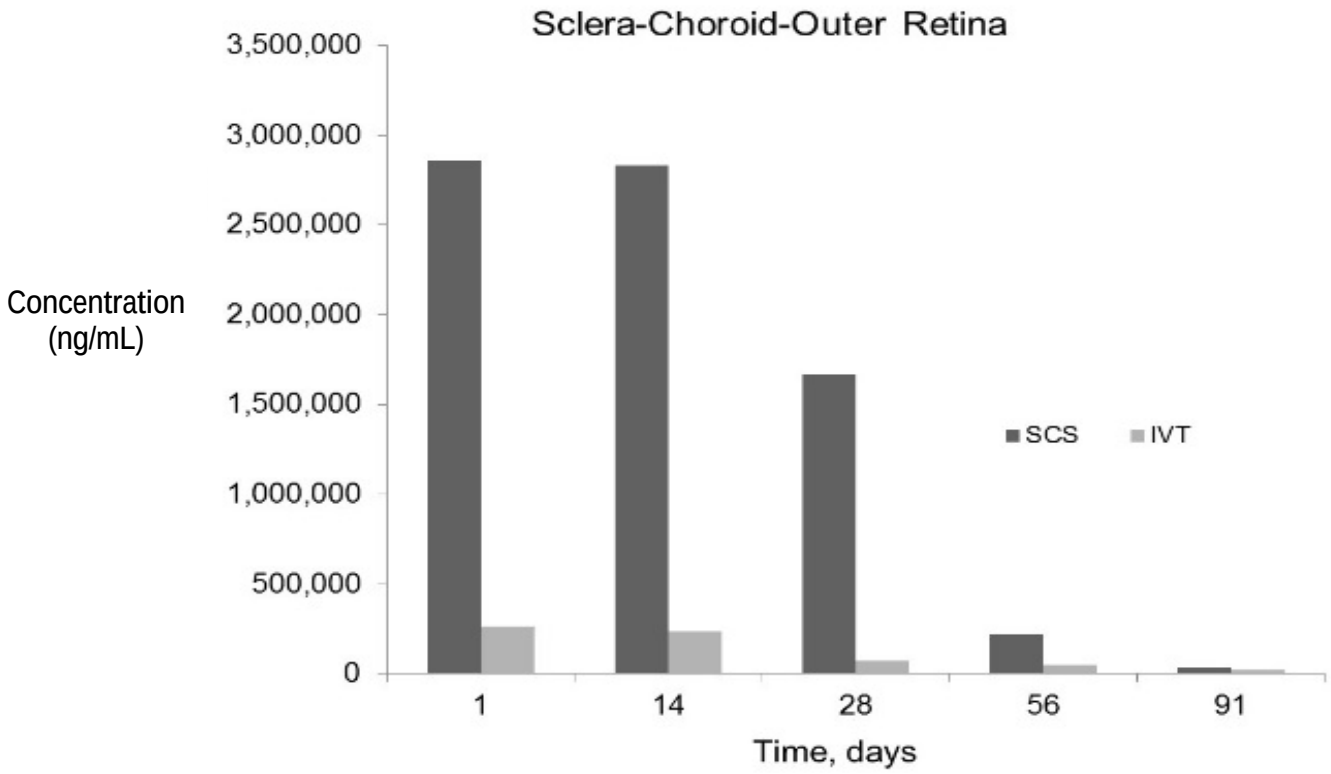
- **Preclinical data showing potential**
  - Ocular distribution study showing high amounts of drug in the choroid and retina compared to intravitreal injection in a rabbit PK model
  - Same study showing relative sparing of the anterior segment including lens

- **Early clinical efforts**
  - Phase 1/ 2 and Phase 2 data showing robust efficacy
  - Both clinical trials showing no increases in IOP

- **Injection approach/personal experiences**

Preclinical rabbit model: 3 month study of ocular distribution following injection of TA

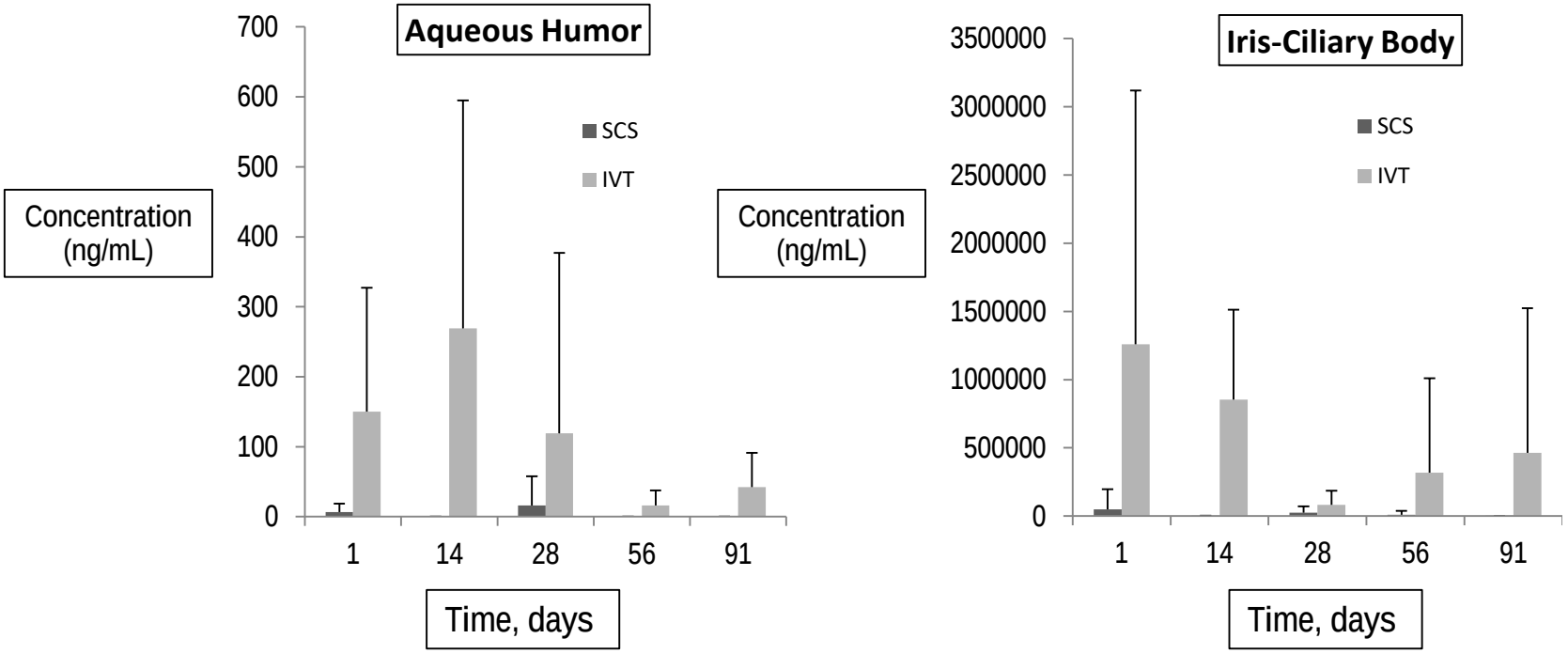
Administration of TA to the eye using **suprachoroidal injection provided high amounts of drug in the choroid and the retina, *compared to* that seen from intravitreal dosing**



There is over 10X the amount of TA remaining the choroid and retina following suprachoroidal injection compared to intravitreal

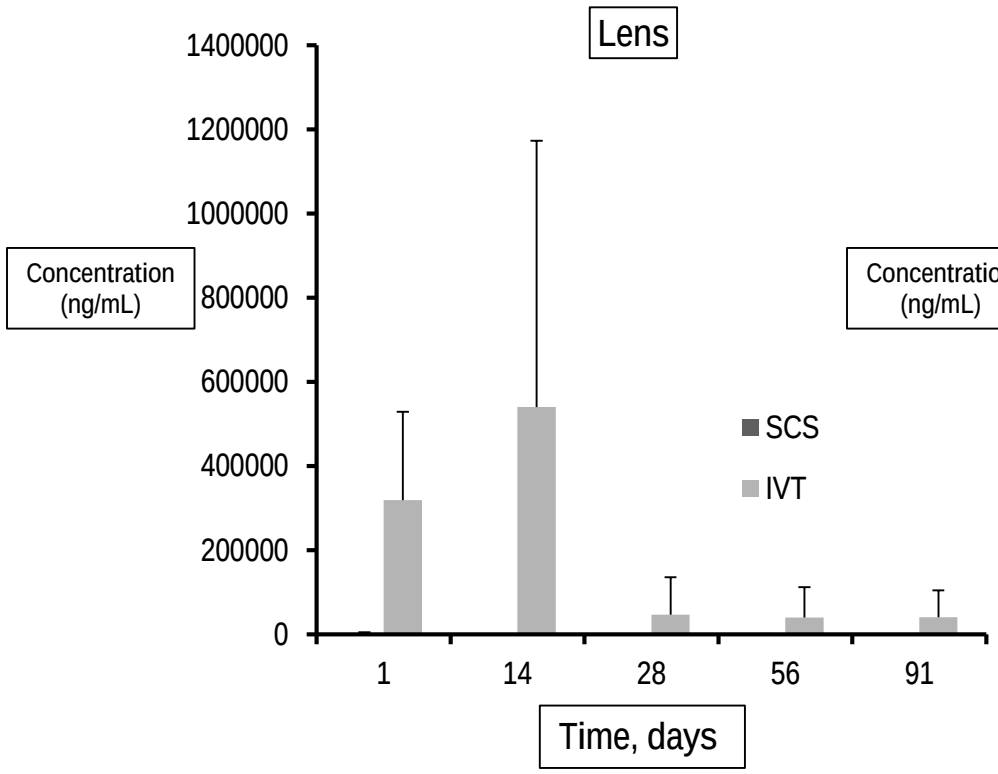
Same experiment: evaluation of anterior areas of the eye

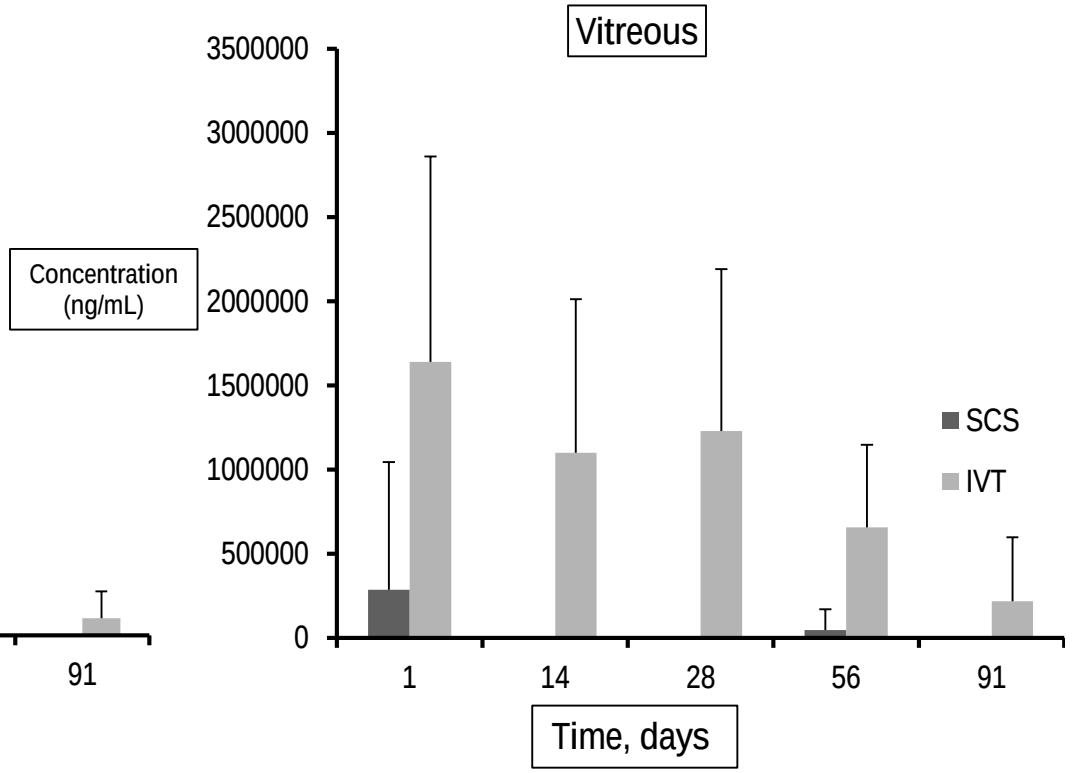
The anterior segment is relatively spared following suprachoroidal dosing when compared to intravitreal dosing



TA levels in the lens and in the vitreous

Low amounts of drug are found in the lens and the vitreous following suprachoroidal dosing





Patient experience

- Easier than previous shots
  - STK, Ozurdex
  - Same comfort for most for intravitreal injection with a 30 gauge needle
  - Few with “pressure” sensation
- Rapid vision improvement
- All but one patient would do it again

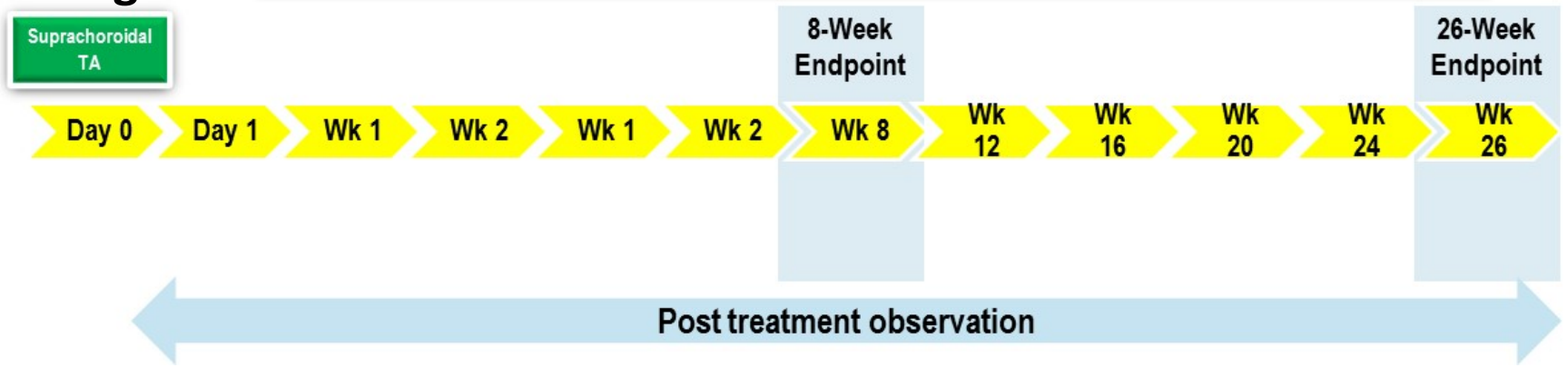
Efficacy/injection procedure

- Seems to act just as rapidly as an intraocular steroid shot
- Long duration of action. Some patients have not had a return of macular edema
- No patients with cataract nor glaucoma thus far
- Theoretically no chance of endophthalmitis/retinal tears
- Injection technique is as easy and rapid as intraocular anti-VEGF injection
  - no resistance
  - Key to stay perpendicular

Phase 1/2 study in patients with noninfectious uveitis

Study design

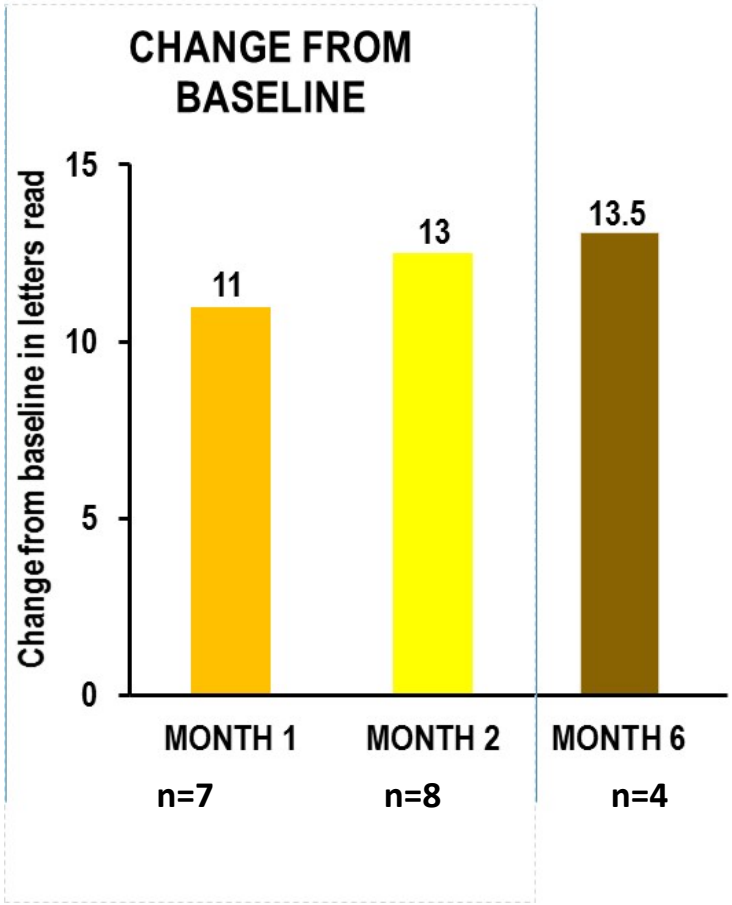
Single suprachoroidal injection of TA; patients were followed for 6 months

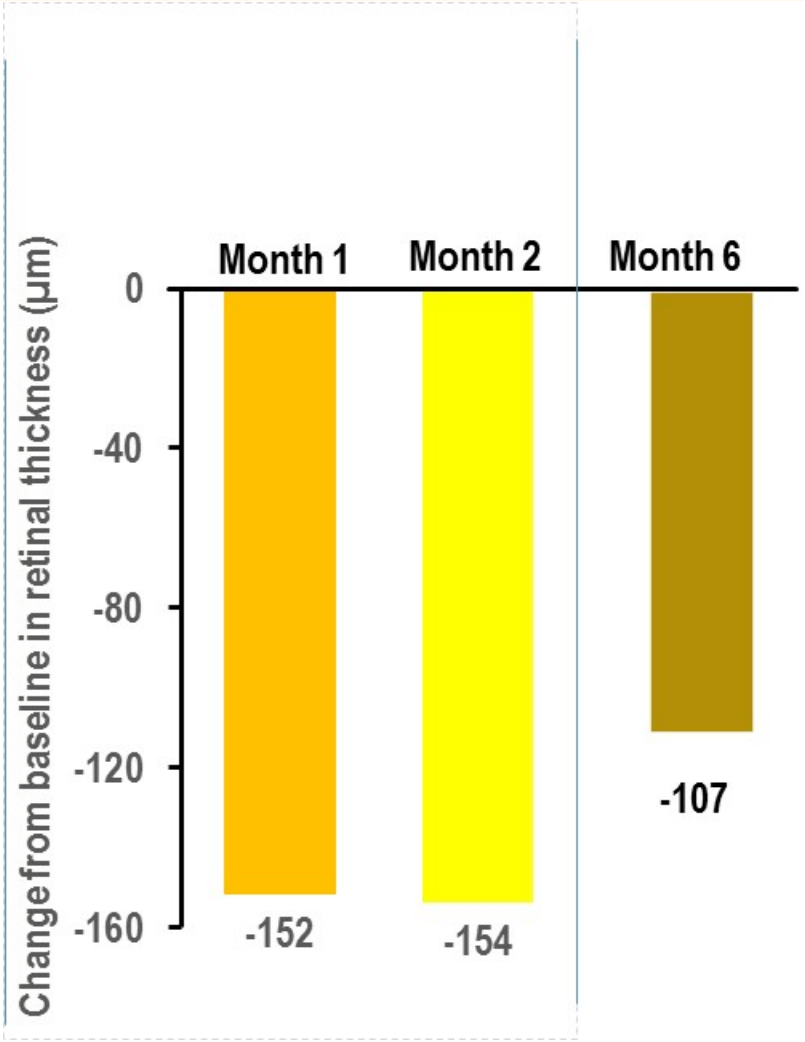


Open label, multi-center study

- Patients with noninfectious uveitis, and
  - Vitreous haze ≥1.5 or macular edema >310 µm on SD-OCT
  - BCVA in each eye +1.0 logMAR or better (20/200 Snellen equivalent) by ETDRS
- Single suprachoroidal injection of TA to one (study) eye
  - Patients were observed for 26 weeks post treatment
  - 8 subjects received a single unilateral suprachoroidal injection of TA and followed for 26 wks

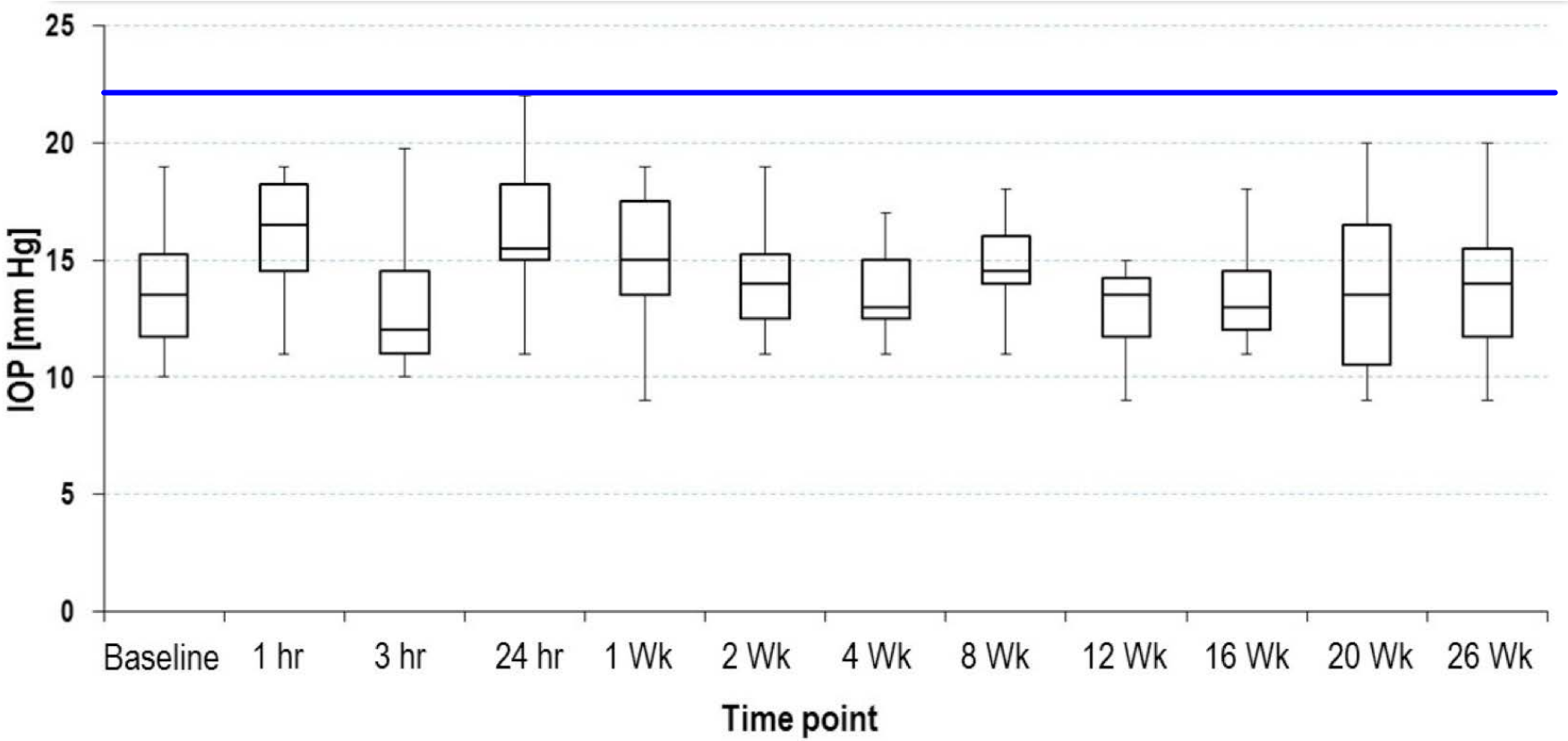
Phase 1/2 study – efficacy; changes from baseline





Phase 1/2 Study – Changes in IOP from baseline

No increases in IOP were observed; no one received IOP lowering medication;

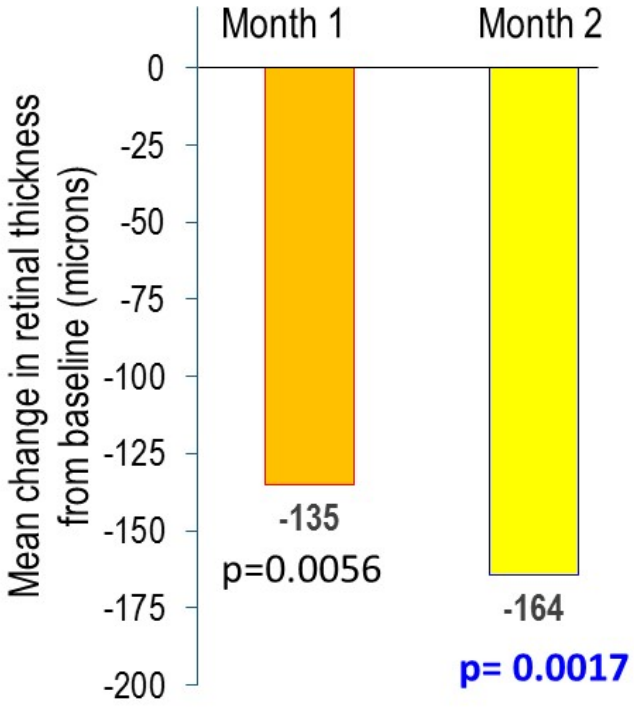


Phase 2: controlled, masked, randomized study met primary endpoint

- **To be eligible for the study, non-infectious uveitis patients needed to have ME >310 µm**
  All uveitis disease etiologies and all geographic locations of uveitis were allowed

Single suprachoroidal injection of CLS-TA (4 mg; 100 µL) to the study eye
Patients were followed for 2 months – Steve Yeh presented data this morning

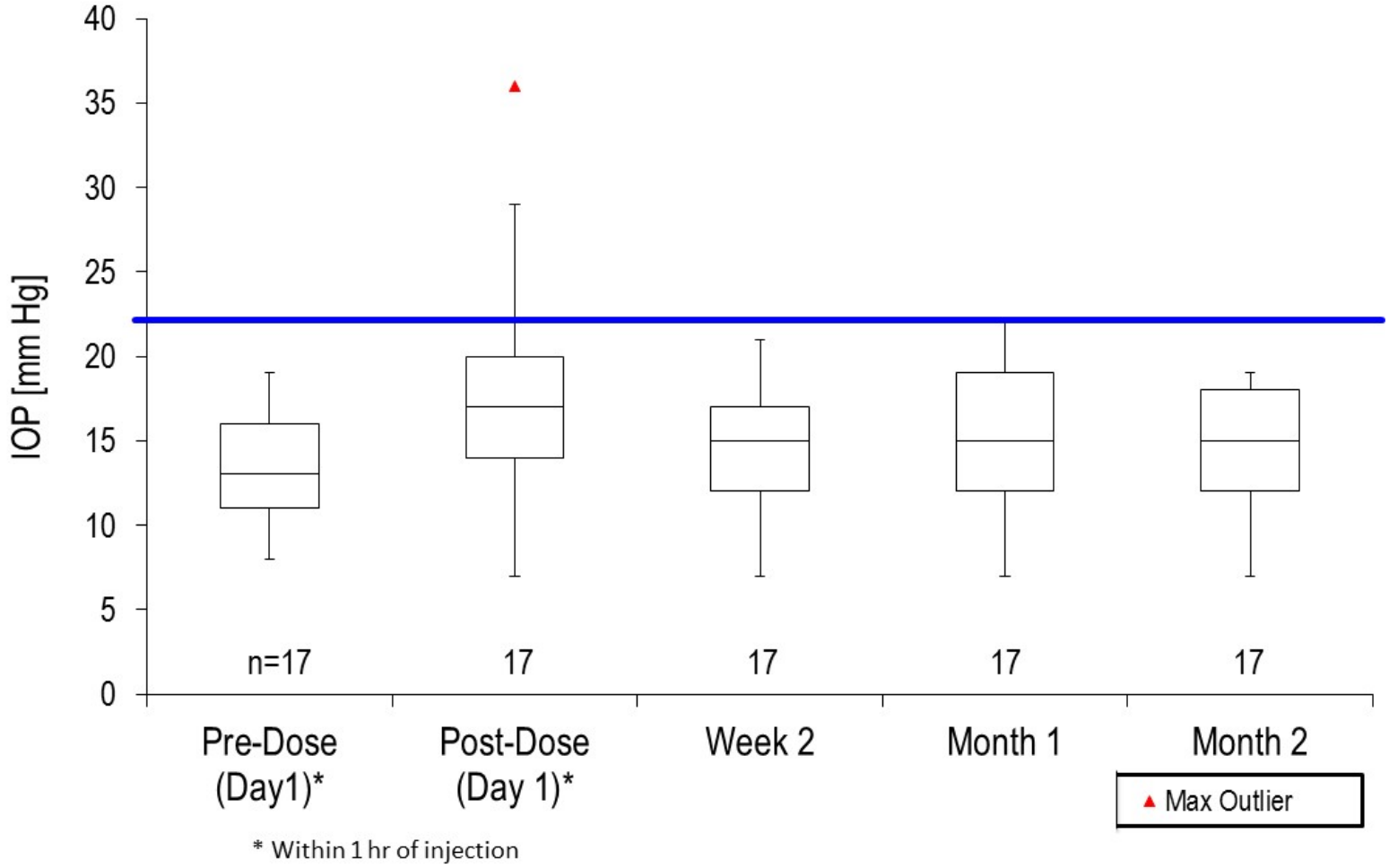
Intent-to-treat (ITT) population: 4.0 mg dose N=16



Visit	Central subfield thickness (CST)	4.0 mg
Month 1	≥ 20% reduction in CST	9
	CST <310 microns	9
Month 2	≥ 20% reduction in CST	11
	CST <310 microns	9

Phase 2: IOP changes

No patient showed steroid related increases in IOP in either trial
No IOP lowering medication was required or used



Suprachoroidal treatment for ocular diseases…

In my view, the injection of TA via suprachoroidal injection is well tolerated in uveitis patient

- **Potential for safety advantages:**
  - **No IOP increases attributable to steroid in both completed studies in uveitis patients**
- **Efficacy advantages:**
  - Significant improvements in anatomy by OCT
  - Significant improvements in BCVA
  - **Improvements in other signs of uveitis: anterior chamber cells, flare and vitreous haze**

Suprachoroidal injection based treatments are still in development

Safety, applicability across diseases, other types of pharmacological treatments including biologicals and genes, other advantages or disadvantages, other unknowns

Clinical and nonclinical data taken together support the development of suprachoroidally injected CLS-TA for the treatment of [macular edema due to] noninfectious uveitis