Suprachoroidal Triamcinolone Acetonide with & without Intravitreal Aflibercept for DME: Results of the 6 Month Prospective Phase 1/2 Hulk trial

Blanton Eye Institute

Charles C. Wykoff MD PhD
Rahul N. Khurana MD

Retina Consultants Houston

Disclosures

- Financial
  - Consultant - Allergan, Alimera, Bayer, Clearside, DORC, Genentech, ONL Therapeutics, Regeneron
  - Speaker - Allergan, Regeneron
  - Research Support – Acucela, Alcon/Novartis, Alimera, Allergan, Apellis, Clearside, DORC, DRCR.Net, Genentech/Roche, Iconic, Ophthotech, Santen, Regeneron/Bayer, Thrombogenics, Tyrogenex

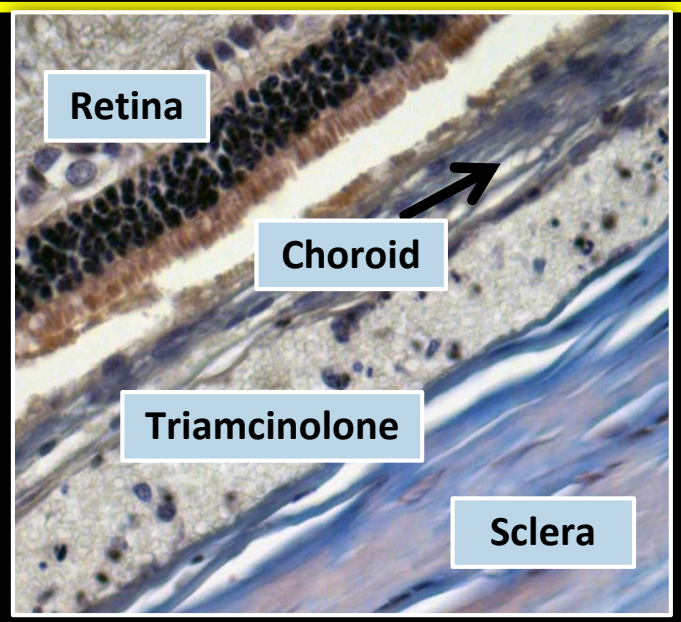
- Human Subjects
  - This study is Institutional Review Board approved

- Funding: Investigator Initiated Trial
  - Grant from Clearside Biomedical
  - CCW had total control & is fully responsible for study design, data collection & analysis

Suprachoroidal Delivery of Corticosteroids

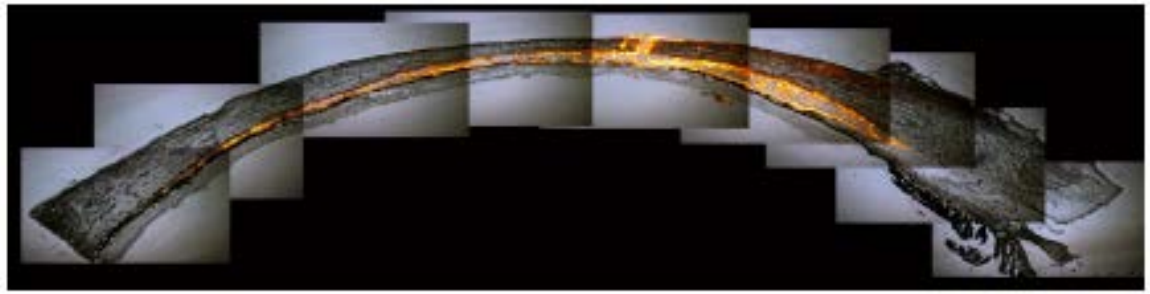
- Maximize drug levels in retina
- Minimize drug levels in AC
- Potential to
  - Reduce cataract acceleration
  - Reduce incidence of increased IOP

Triamcinolone acetonide (TA) s/p suprachoroidal injection in a rabbit eye



Olsen *AJO* 2006
Patel *IOVS* 2012

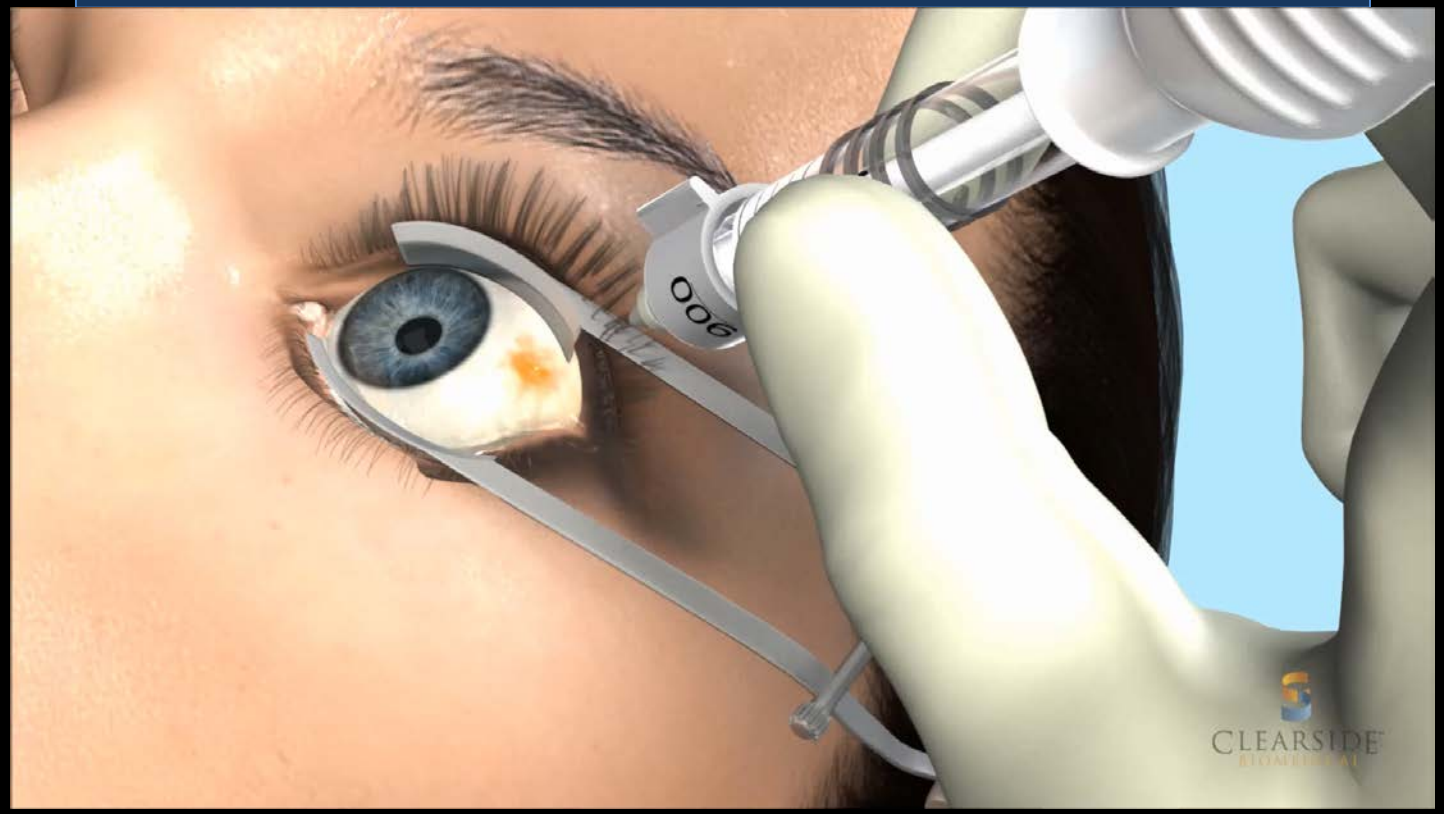
Fluorescent particles s/p suprachoroidal injection in a pig eye



Microneedle

Specifically for Suprachoroidal Delivery of Preservative Free Triamcinolone Acetonide (CLS-TA)

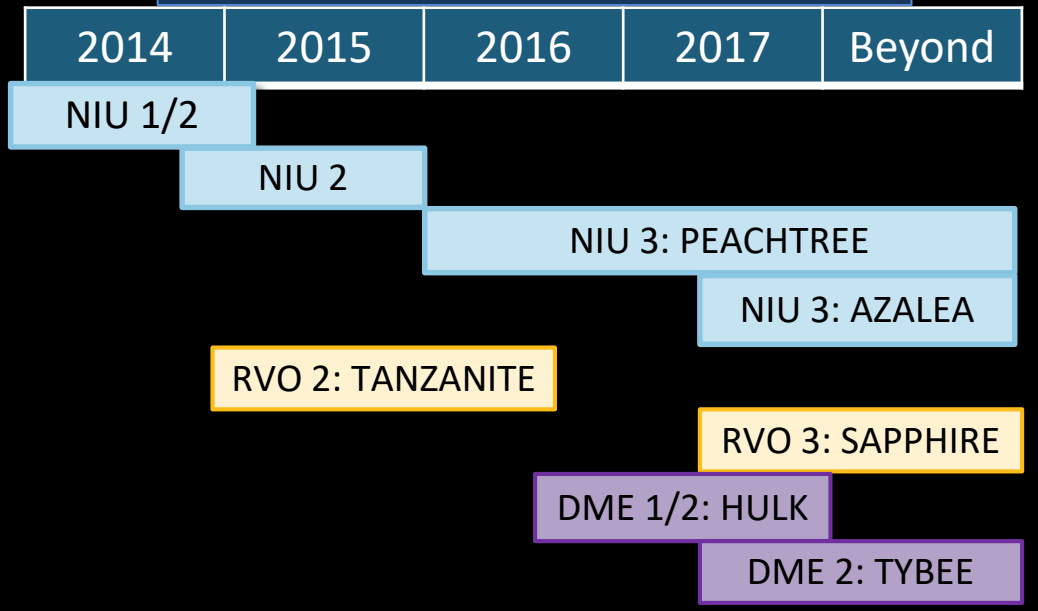
Illustration of CLS-TA Suprachoroidal Delivery



Goldstein *TVST* 2016

CLS-TA: Non-preserved, terminally sterilized, aqueous suspension of triamcinolone acetonide administered as a single injection of 4 mg in 0.1mL

Clinical Trials



Campochiaro PA, Wykoff CC, Brown DM, Boyer DS, Barakat M, Taraborelli D, Noronha G. Suprachoroidal Triamcinolone Acetonide for Retinal Vein Occlusion: Results of the Tanzanite Study. *Ophthalmology Retina*. E-Pub 09/28/2017

Objective: To evaluate the safety & efficacy of 4 mg suprachoroidal triamcinolone acetonide injectable suspension (CLS-TA) alone or in conjunction with 2 mg of intravitreal aflibercept for DME

Locations

Retina Consultants of Houston, Houston, TX

Northern California Retina Vitreous Associates, Mountain View, CA

HULK

Month (N=20)	0	1	2	3	4	5	6
Tx Naïve	CLS-TA + Intravitreal Aflibercept	Visit Without Treatment	CLS-TA PRN	CLS-TA PRN	CLS-TA PRN	CLS-TA PRN	Visit Without Treatment
Previous Tx	CLS-TA	Visit Without Treatment	CLS-TA PRN	CLS-TA PRN	CLS-TA PRN	CLS-TA PRN	Visit Without Treatment

PRN CLS-TA Re-Treatment*

CRT > 320 µm & not improved at least 20% from prior 2 visits

Endpoints

- Mean change BCVA, CRT & IOP
- Number of CLS-TA injections
- Incidence of adverse events

CLS-TA

CLS-TA PRN

CLS-TA + Intravitreal Aflibercept

Visit Without Treatment

*And loss ≥ 10 ETDRS letters from either prior 2 visits due to DME

Tx Naïve = Treatment Naïve (no prior treatment for DME within 1 year). **Previously Tx** = Previous DME Treatment (Washout: 3 months for anti-VEGF and 6 months for intraocular steroids.

ClinicalTrials.gov NCT02949024

Baseline Demographics & Characteristics

	ALL (n=20)	Tx Naïve (n=10)	Previous Tx (n=10)
Gender (% Female)	40% (8/20)	40% (4/10)	40% (4/10)
Mean Age (range)	63 (46-73)	62 (48-71)	63 (46-73)
DM Duration (range), years	12.5 (2-25)	11.7 (3-25)	13.2 (3-25)
Mean HbA1c (range)	7.5 (5.9-11.1)	7.9 (6.1-11.1)	7.2 (5.9-8.9)
HTN (%)	90% (18/20)	100% (10/10)	80% (8/10)
Mean BCVA (range), letters	67.2 (52-83)	67.2 (52-83)	67.2 (54-81)
Snellen Equivalent	20/50 (20/100-20/25)	20/50 (20/100-20/25)	20/50 (20/80-20/25)
CRT (range)	447 (328/691)	442 (337/638)	473 (328/691)
IOP (range)	13.8 (9/22)	14.2 (11/22)	13.3 (9/17)
Mean Number prior DME Treatments (Median)*	12.15 (3.5)	1.4 (0)	23.0 (12.5)

DM = diabetes mellitus. HTN = hypertension. BCVA = best corrected visual acuity. CRT = central retinal thickness.
IOP = Intraocular Pressure. DME = diabetic macular edema. *Includes anti-VEGF, corticosteroids, and laser

HULK

6-Month Results

Treatment Experience			
	Scheduled Visits Performed	**Scheduled Visits Missed**	**Patients Retained**
Total (n=20)	132	3.7%	19
Tx naïve (n=10)	66	5.7%	10
Previous Tx (n=10)	66	1.5%	9*

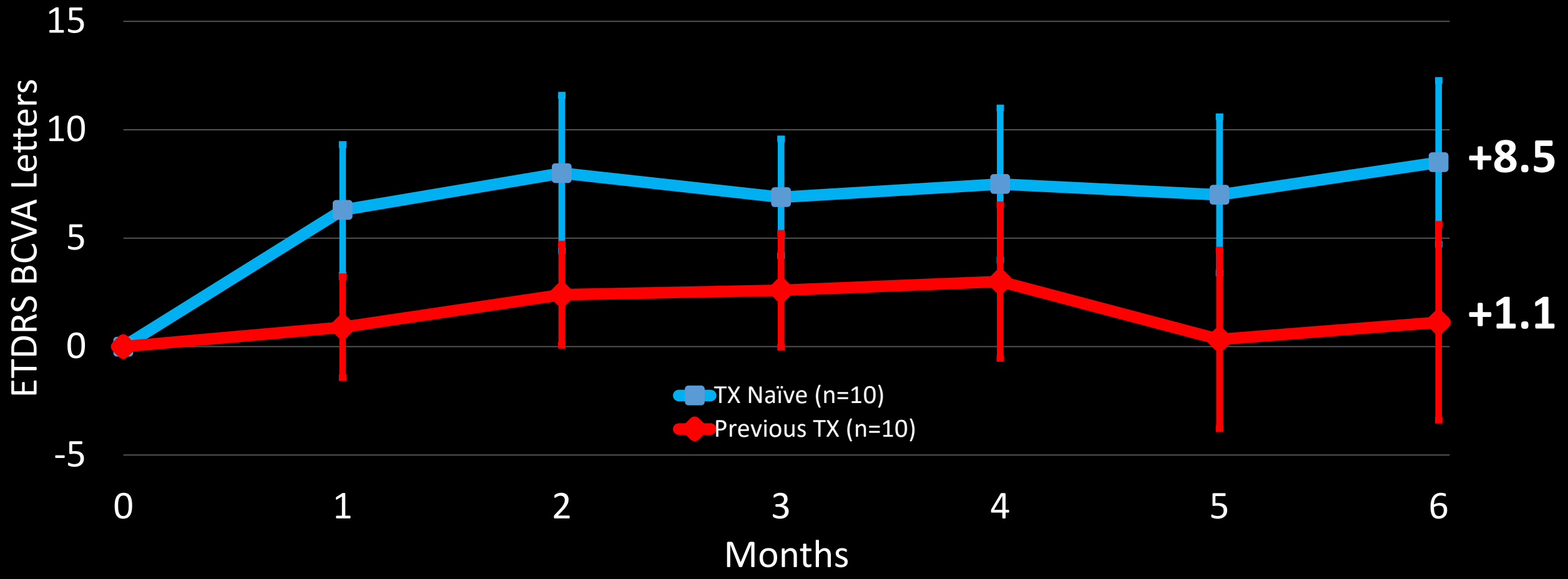
* 1 patient lost to follow-up out at M4

Mean Change in BCVA (all patients)

ETDRS = early treatment diabetic retinopathy study. BCVA = best corrected visual acuity

Δ BCVA 6 Months	Mean (SE)
All Patients (n=20)	5.2 (± 3.0)

Mean Change in VA (by arm)



ETDRS = early treatment diabetic retinopathy study. BCVA = best corrected visual acuity

Δ BCVA 6 Months	Mean (SE)
Tx Naïve	8.5 (± 3.8)
Previous Tx	1.1 (± 4.5)

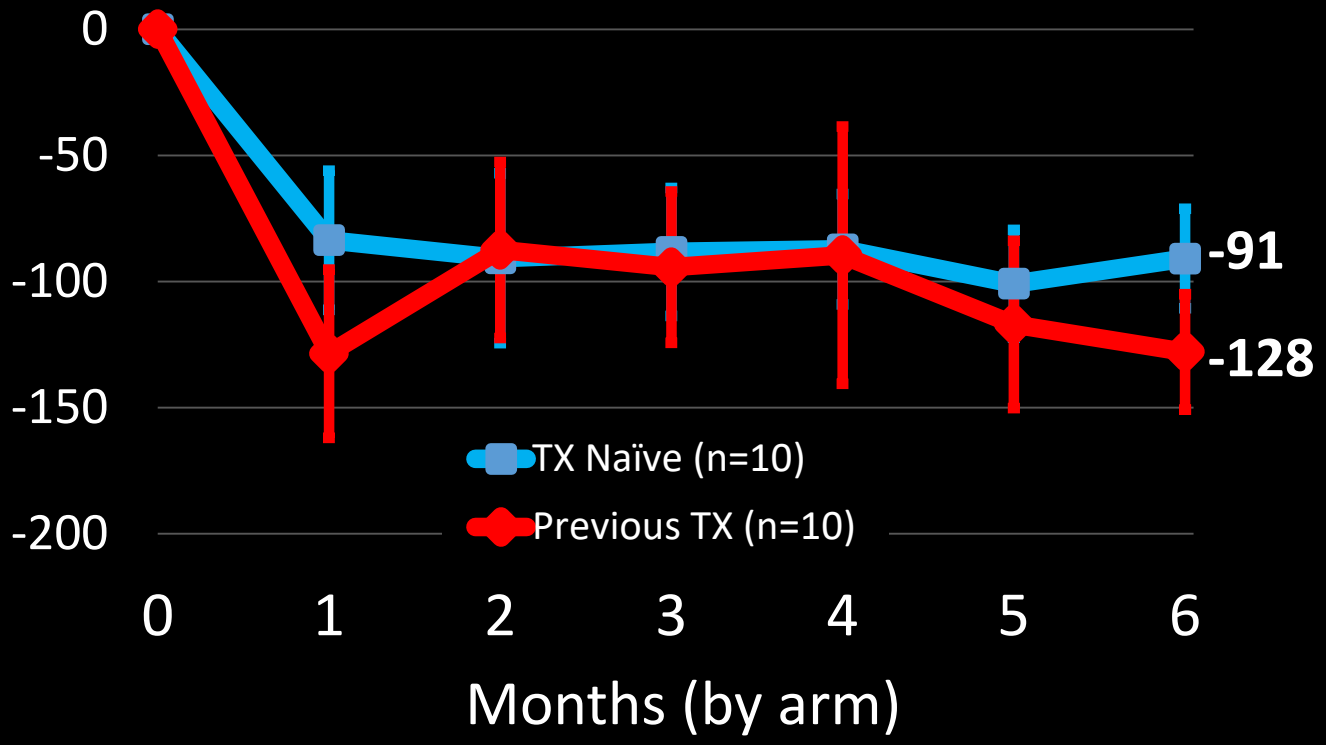
Mean Central Retinal Thickness (all patients)

CRT = central retinal thickness

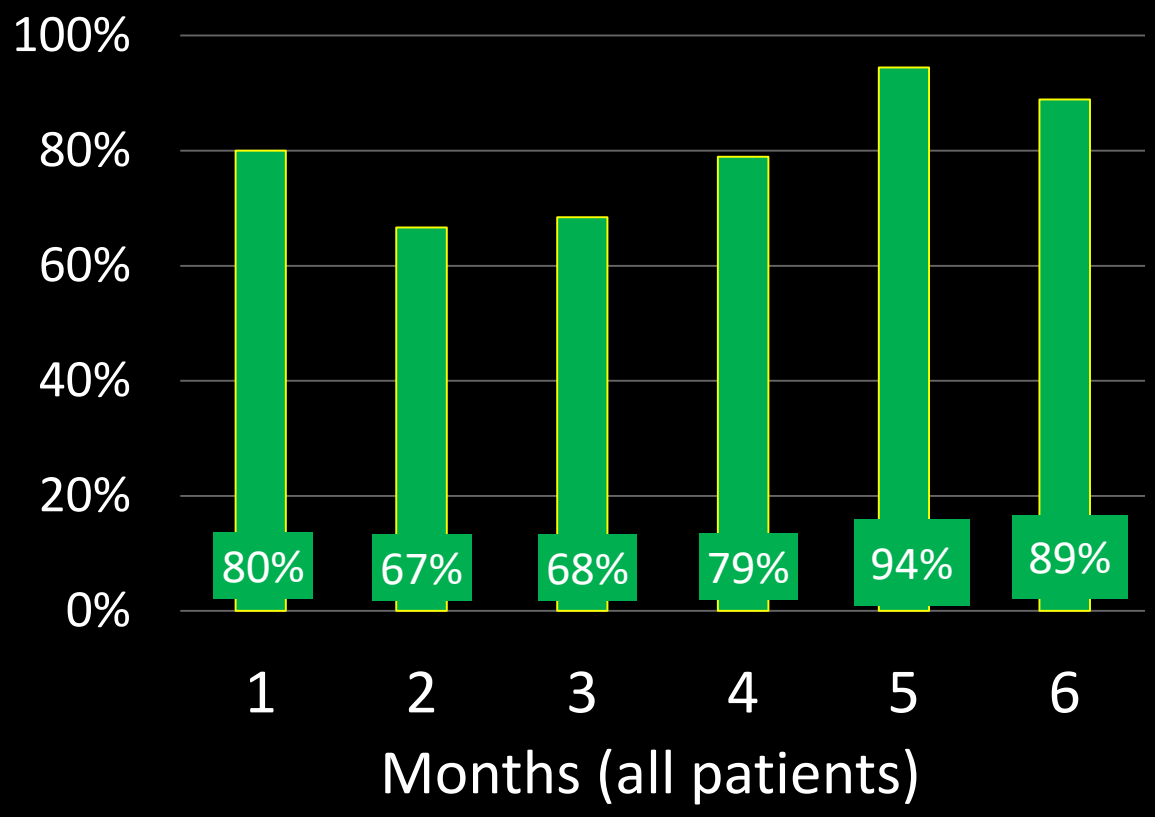
CRT Month 6 (µm)	Mean (SE)
All Patients (n=20)	348 (± 15)

Anatomic Outcomes

Mean Change (µm) CRT

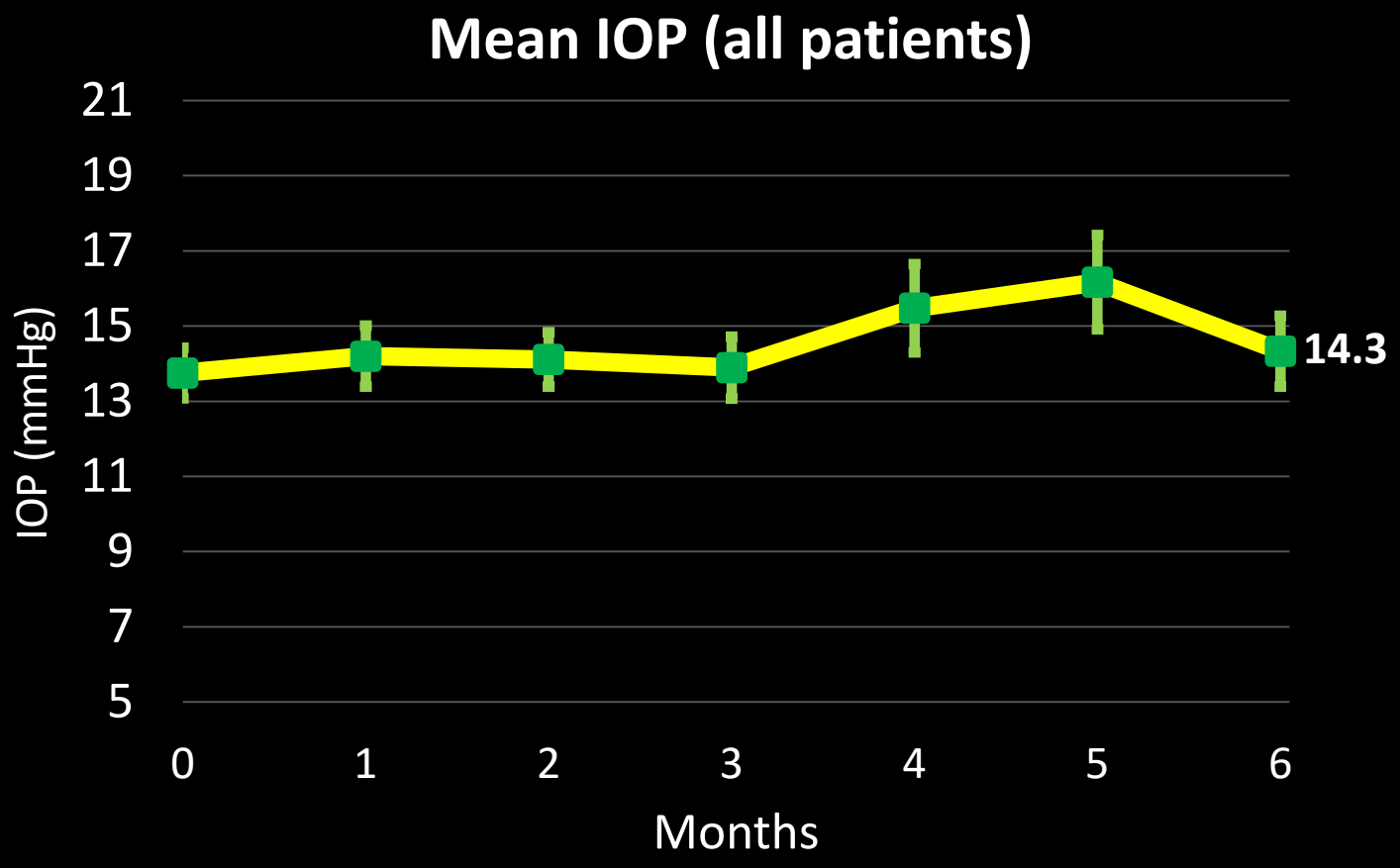


Patients Achieving > 50% Reduction in Excess CRT



CRT = Central retinal thickness. Excess CRT = CRT > 320 µm, the retreatment threshold

Intraocular Pressure



M6 All Patients		14.2 mmHg (± 0.9 SE)
Δ BL to M6 Tx Naïve		-0.3 mmHg (± 0.8 SE)
Δ BL to M6 Previously Tx		0.9 mmHg (± 2.1 SE)
Started Topical IOP Lowering Medication		3 patients (15%)
>10 mmHg Rise	**All patients**	2 patients (10%)
	Tx Naïve	0 patients
	Previously Tx	2 patients (20%)

M6 = Month 6. BL = Baseline. IOP = Intraocular Pressure

CLS-TA PRN Re-Treatment Experience

	Mean (Range) CLS-TA Injections	CLS-TA Re-Treatments				
		Possible #	Administered #	Administered %	Received 0 %	Received 1 %
Tx Naïve (N=10)	2.6 (1-5)	36	16	44%	40%	20%
Previous Tx (N=10)	3.3 (1.5)	38	23	61%	10%	30%
ALL (N=20)	**3.0 (1-5)**	**74**	**39**	**53%**	**25%**	**25%**

Adverse Events

No Serious Ocular or Systemic Adverse Events

Systemic Adverse Events	Frequency
Headache	3
Upper respiratory infection	2
Worsening hypercholesterolemia	1
Continuous lower back pain	1
Right foot ulcers and right foot pain	1
Right foot pain due to cut	1
Worsening hypertension	1
Worsening neuropathy	1

Ocular Adverse Events	Frequency
Subconjunctival hemorrhage	5
Worsening of cataract	3
Increased IOP	2
Ocular irritation	1
Triamcinolone in the vitreous	1
Iritis	1
Epiretinal membrane	1
Ocular pain	1
Dry eyes	1
Cataract surgery	1

IOP = intraocular pressure

Limitations

- Sample size: 20 patients
- Limited follow-up: 6 months
- Variable disease management prior to enrollment
- Different treatment exposure in 2 arms

Summary

6-Month Phase I/II Trial

- Demonstrated VA benefit for the entire population (+5.2 letters) & greater benefit for Tx naïve eyes (+8.5) vs previously Tx eyes (+1.1)
- All eyes demonstrated anatomic improvement with CLS-TA; over 65% showed >50% reduction in excess CRT at all timepoints through 6 months
- Multiple suprachoroidal CLS-TA injections were well tolerated with a low incidence of IOP elevation
  - 10% of patients experienced an IOP rise > 10 mmHg

THANK YOU

HULK Study Group

Charles C. Wykoff MD, PhD, Rahul N. Khurana, MD, Shaun I.R. Lampen, BS, William C. Ou, BS, David M. Brown, MD, Matthew S. Benz, MD, J. Luigi Borrillo, MD, Louis K. Chang, MD, PhD, Eric Chen, MD, Richard H. Fish, MD, Rosa Y. Kim, MD, James C. Major Jr, MD, PhD, Ronan E. O'Malley, MD, James D. Palmer, MD, Amy C. Schefler, MD, Ankoor R. Shah, MD, Sushma K. Vance, MD, Tien P. Wong, MD, Christopher R. Henry MD.