Suprachoroidal Triamcinolone Acetonide and Intraocular Pressure:

Results of Phase 3 PEACHTREE Clinical Trial for Uveitis

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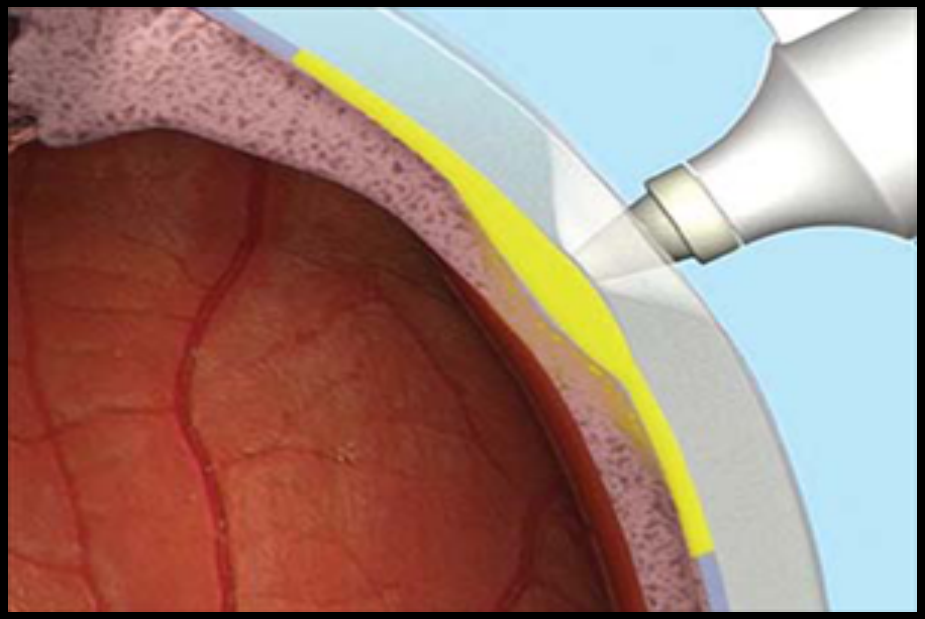
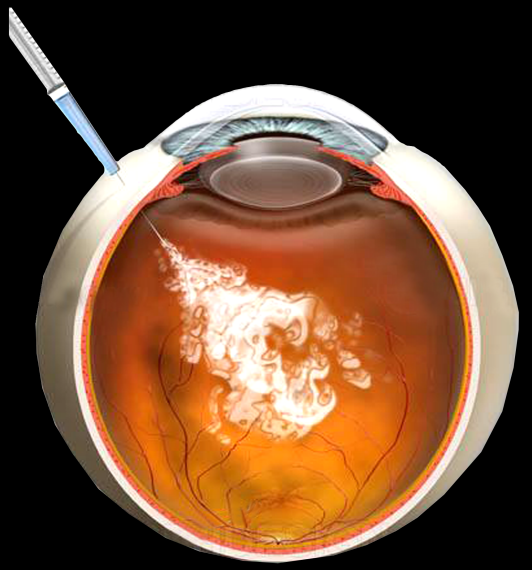
The Suprachoroidal Space: *Targeted Delivery*



Suprachoroidal (SCS)

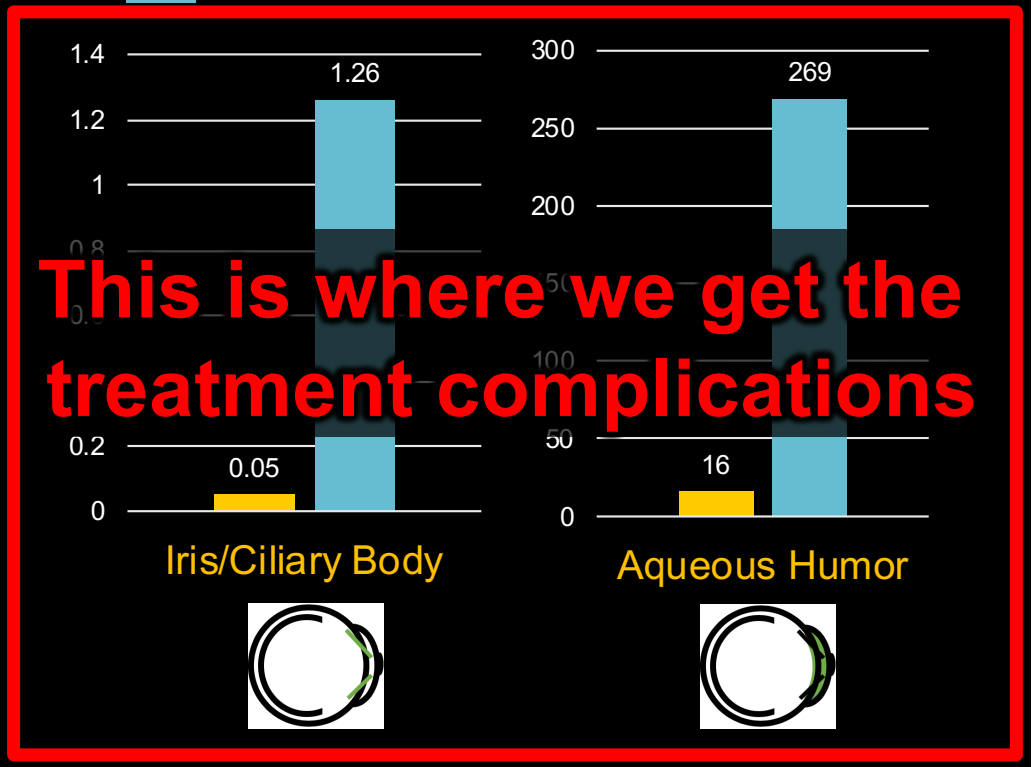


Intravitreal (IVT)

The Suprachoroidal Space: *Targeted Delivery*

Suprachoroidal (SCS) **Intravitreal (IVT)**

This is where we want the treatment effect



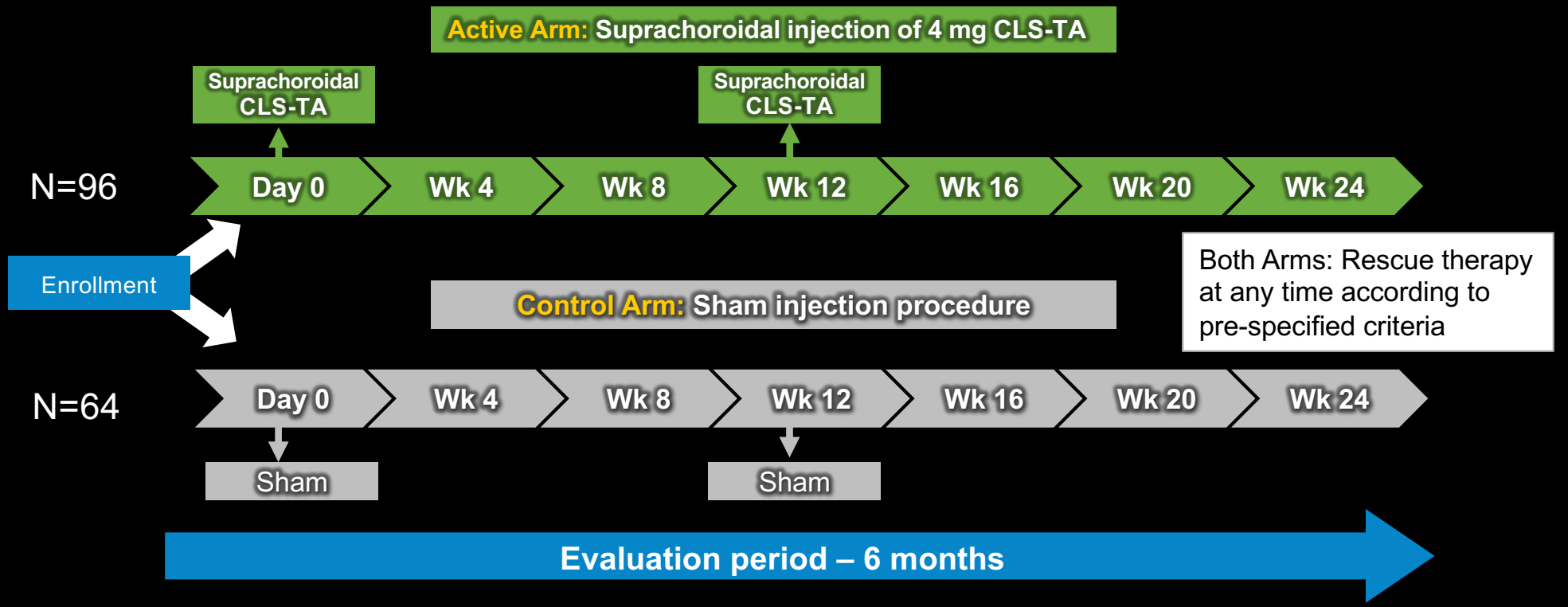
This is where we get the treatment complications

Scales of charts different – Note the relative differences

Edelhauser HF, et al. ARVO Annual Meeting. 2013.

PEACHTREE: Phase 3, Randomized, Controlled, Double-Masked, Multicenter Trial – Uveitic Macular Edema

Primary Endpoint: ***C****hange from baseline ≥15 letters in BCVA at Week 24*



Key Inclusion and Exclusion Criteria

Inclusion

- Macular edema with CFT ≥300 microns
- Noninfectious uveitis
- Any anatomic location: anterior, intermediate, posterior and panuveitis
- Visual acuity: 20/800 to 20/40 *(≥5 to ≤70 ETDRS letters)*

Exclusion

- Any active ocular disease or infection in the study eye other than uveitis
- IOP: >22 mmHg or uncontrolled glaucoma;
  could be on up to 2 IOP-lowering medications

ETDRS: Early Treatment Diabetic Retinopathy Study
IOP: intraocular pressure

Baseline Characteristics: *Similar Between Groups*

Characteristic	CLS-TA N=96	Control N=64	Overall N=160
Gender, n (%)			
Male	**42 (44 %)**	**30 (47 %)**	**72 (45 %)**
Female	**54 (56 %)**	**34 (53 %)**	**88 (55 %)**
Age, mean (SD)	**50 y/o (14)**	**50 y/o (15)**	**50 y/o (14)**
BCVA, (ETDRS letters)			
Mean (SD)	**55 (14)**	**54 (13)**	**54 (14)**
Median (range)	**57 (9 – 89)**	**54 (12-79)**	**56 (9-89)**
CST, (µm)			
Mean (SD)	**481 (153)**	**525 (158)**	**499 (156)**
Median (range)	**453 (256-857)**	**519 (274-971)**	**482 (256-971)**

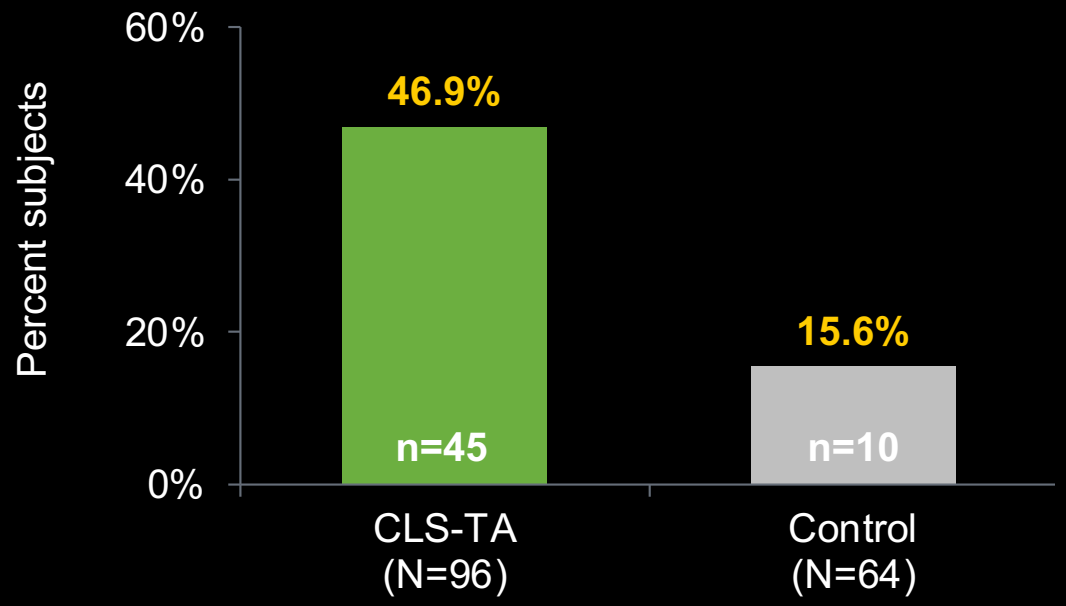
CST: central subfield thickness; ETDRS: Early Treatment Diabetic Retinopathy Study

Baseline Characteristics: *IOP and Glaucoma*

Characteristic	CLS-TA N=96 n (%)	Control N=64 n (%)
Any History Related to Glaucoma or IOP	**21** (22%)	**14** (22%)
Angle closure glaucoma	**0** (0%)	**1** (2%)
Glaucoma	**10 (**10%)	**4** (6%)
Glaucomatous optic disc atrophy	**1** (1%)	**0** (0%)
Intraocular pressure increased	**2** (2%)	0 (0%)
Ocular hypertension	**5** (5%)	**7** (11%)
Open Angle Glaucoma	**1** (1%)	**1** (2%)
Trabeculectomy	**1** (1%)	**0** (0%)
Uveitic glaucoma	1 (1%)	**1** (2%)
≥ 1 IOP lowering medication	**5** (5%)	**2** (3%)
Brimonidine Tartrate	**1** (1%)	**0** (0%)
Brimonidine Tartrate, Timolol Maleate	**1** (1%)	**0** (0%)
Dorzolamide Hyrdochloride, Timolol Maleate	**1** (1%)	**1** (2%)
Brimonidine Tartrate, Brinzolamide	**1** (1%)	**0** (0%)
Timolol	**2** (2%)	**1** (2%)

PEACHTREE: Met Primary Efficacy Endpoint

Primary Endpoint: Subjects gaining ≥15 BCVA letters from baseline



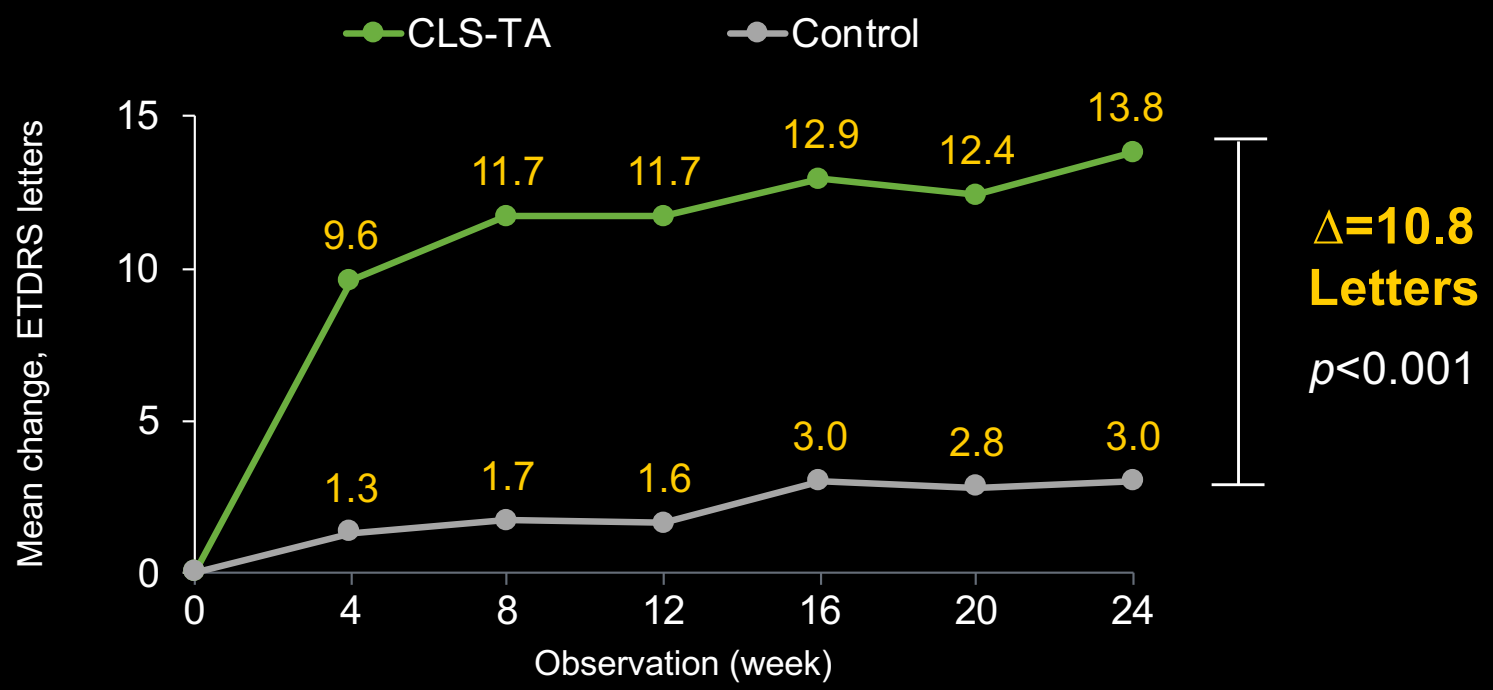
p<0.001

Intention-to-treat population; Last Observation Carried Forward imputation.
P-value based on Cochran-Mantel-Haenszel test

Mean Change in ***BCVA***

Improvement Observed as Early as Week 4 Through Week 24 in the CLS-TA Arm

Mean change from baseline in BCVA at each visit

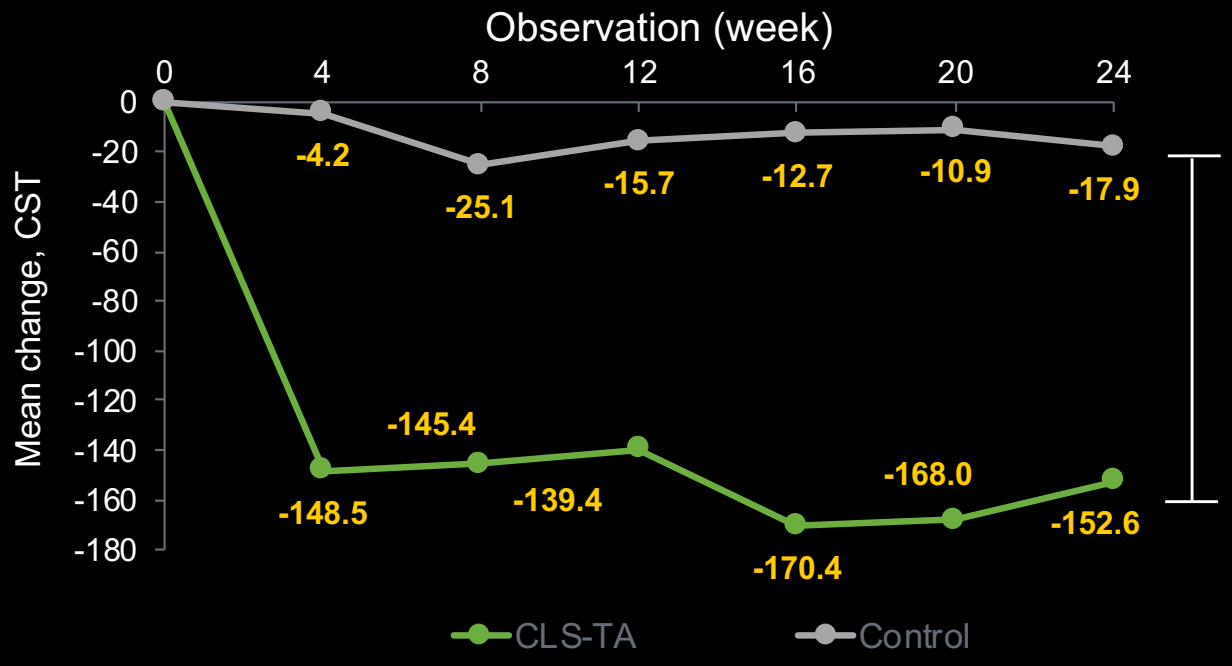


Intention-to-treat population; last observation carried forward imputation.
t-test. Differences between the CLS-TA and control arms were significant at each visit.

Mean Change in ***Central Subfield Thickness***

Improvement Observed as Early as Week 4 Through Week 24 in the CLS-TA Arm

Mean change from baseline at each visit in central subfield thickness (µm)

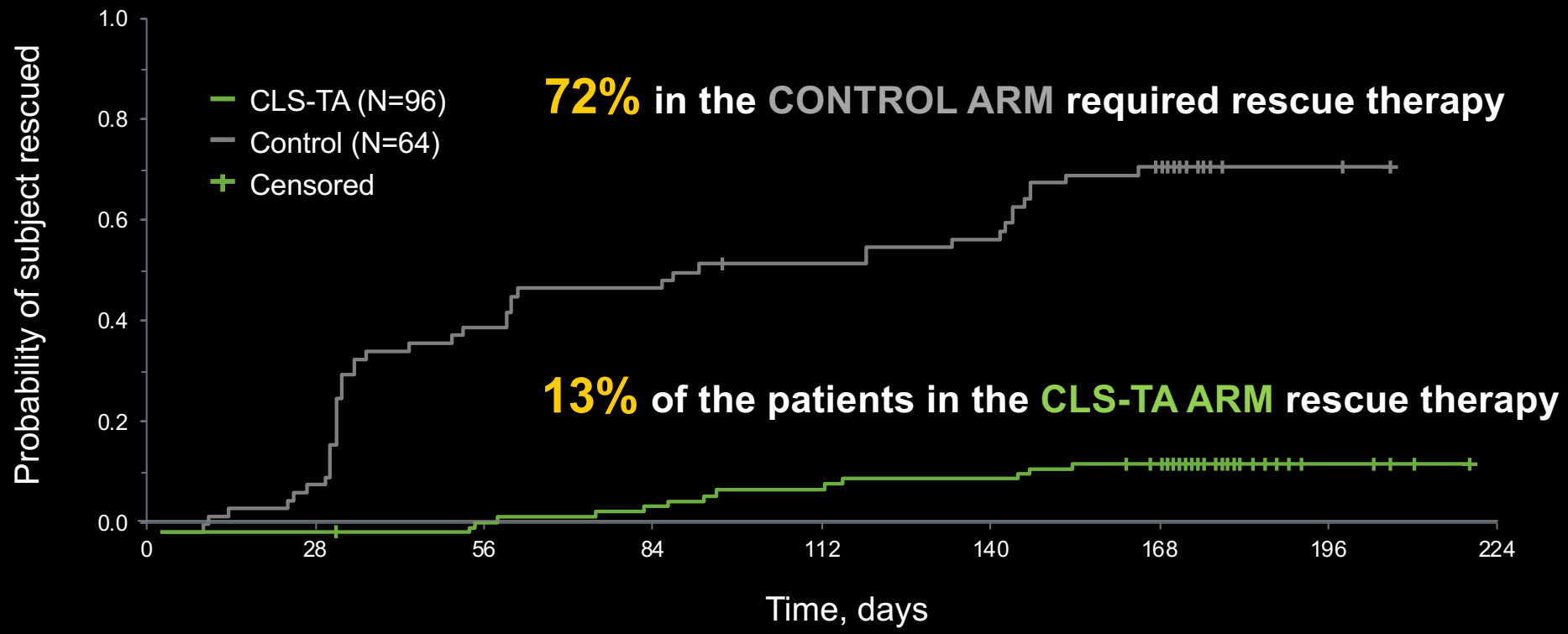


Δ=134.7 µm

p<0.001

Intention-to-treat population; last observation carried forward imputation.
BSL, baseline mean value; CST, central subfield retinal thickness.

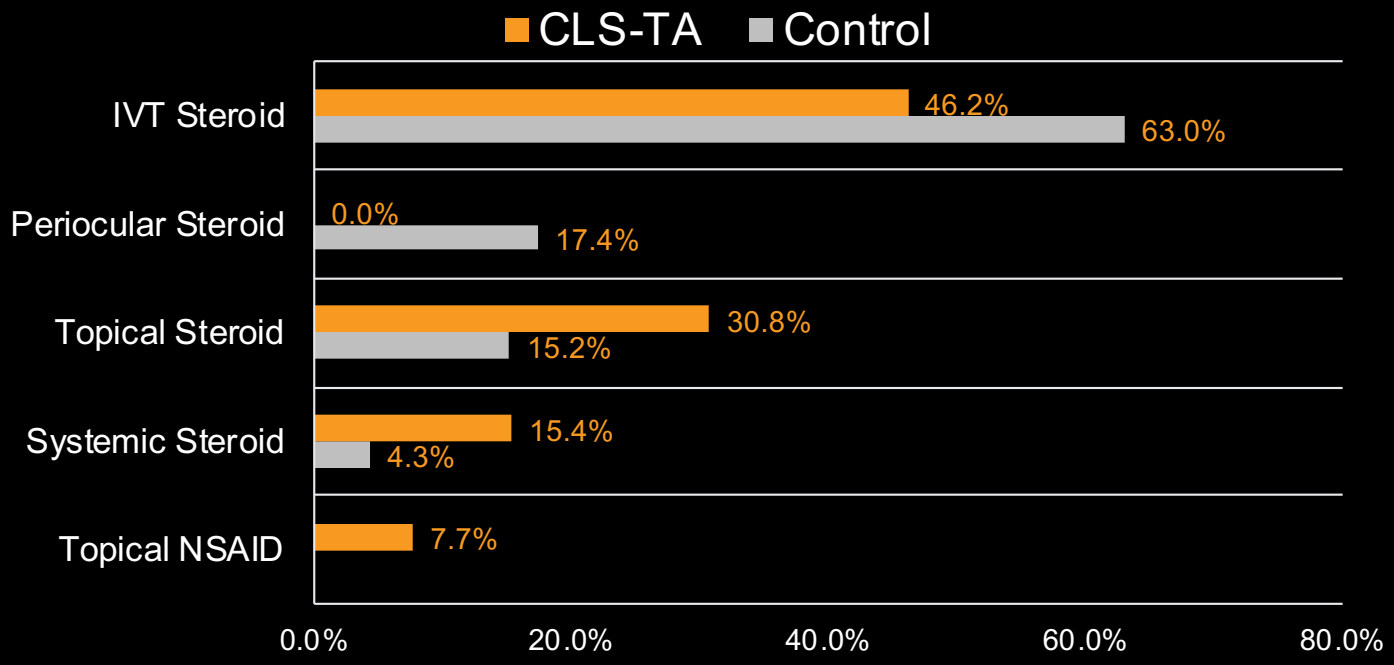
Kaplan–Meier Analysis: *Time to Rescue*



Intention-to-treat population

Rescue Therapy Rates: *CLS-TA (n=13) vs. Control (n=46)*

Most Targeted Medications Used Rates



*Rescue medications classified by most targeted type of therapy used during study, where:
Intravitreal Corticosteroid > Periocular corticosteroid > Topical Corticosteroid > Systemic Corticosteroid > Topical NSAID

Post-Hoc Analysis. Rescue medication used per investigator discretion.

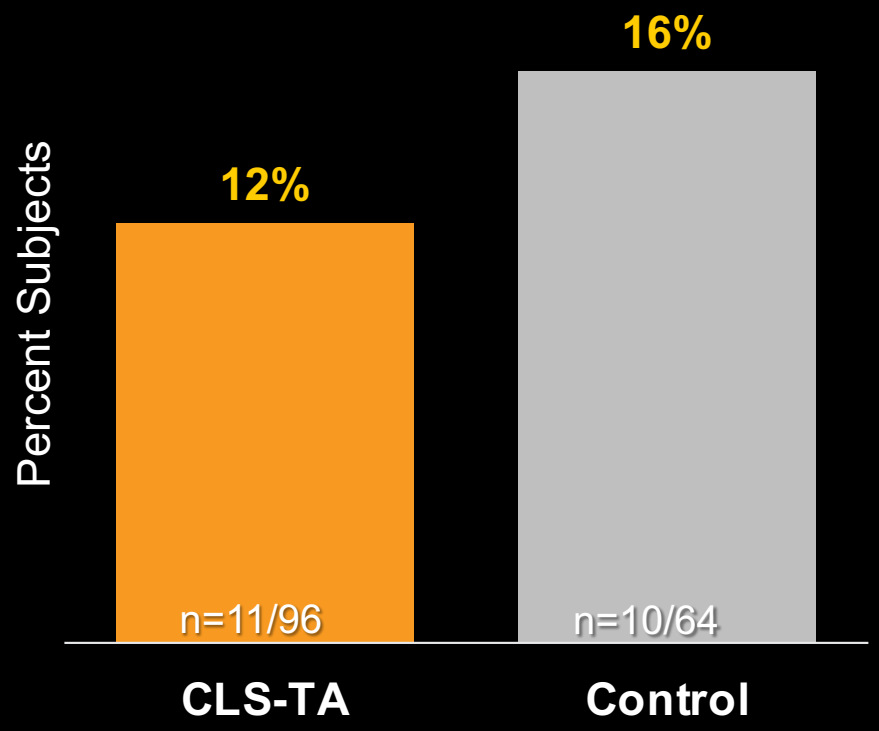
Safety

IOP-Related Adverse Events	CLS-TA 4.0 mg N = 96	Control N = 64
Elevated IOP adverse events	**11** (12%)	**10** (16%)
IOP elevation ≥10 mmHg change from baseline at any visit*	**9** (9%)	**7** (11%)
IOP elevation ≥30 mmHg at any post baseline visit*	**5** (5%)	**4** (6%)
Given additional IOP-lowering medication	**7** (7%)	**6** (9%)
Any surgical intervention for an elevated IOP Adverse Event	**0** (0%)	**0** (0%)

- **One serious ocular AE**
  - Retinal detachment 8 weeks after CLS-TA, in different quadrant
  - Determined to be unrelated to study drug by the Investigator
- **Cataract**: 7% (7/96) in the CLS-TA arm vs. 6% (4/64) in the sham arm

Safety population; includes subjects in the control group who received rescue medication
*Based on elevated intraocular pressure adverse reactions
**Continued for at least 30 days

Elevated IOP Adverse Events in PEACHTREE



- Why are IOP AEs higher in the control group?
  - 46/64 (72%) control patients received rescue therapy
  - All 10 patients with IOP AEs received intravitreal steroids as rescue therapy

"Elevated IOP" includes (a) increased IOP, (b) ocular hypertension, and (c) glaucoma.
AE, adverse event; IOP, intraocular pressure.

PEACHTREE: *Sub-Analysis of IOP*

Purpose: Characterize IOP in CLS-TA and control groups, in patients that were rescued vs. not rescued

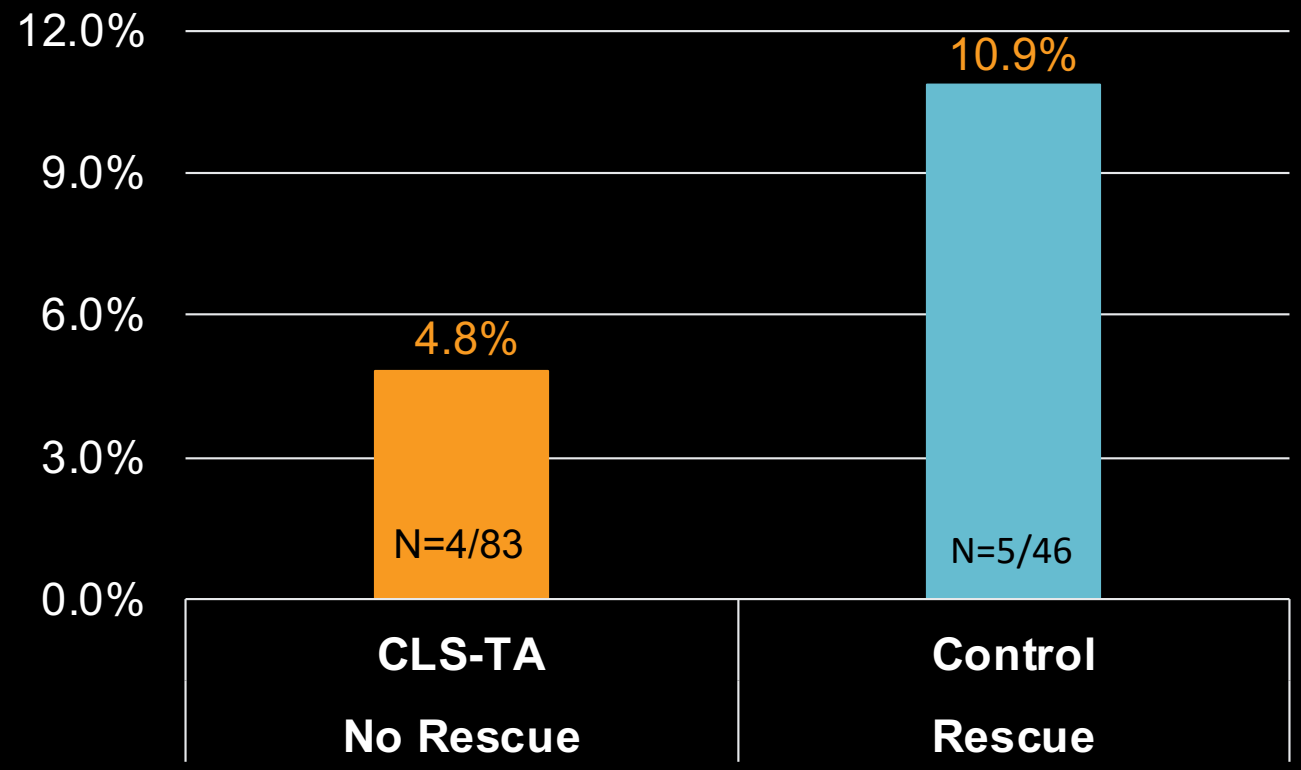
Method: Analyze IOP AEs for the clinically relevant endpoints of **≥30 mmHg IOP at any visit** and **≥1 IOP lowering medication**

Four (4) subgroups analyzed:

	Not Rescued	Rescued
CLS-TA	**N = 83/96 (87 %)**	**N = 13/96 (14 %)**
Control	**N = 18/64 (28 %)**	**N = 46/64 (72 %)**

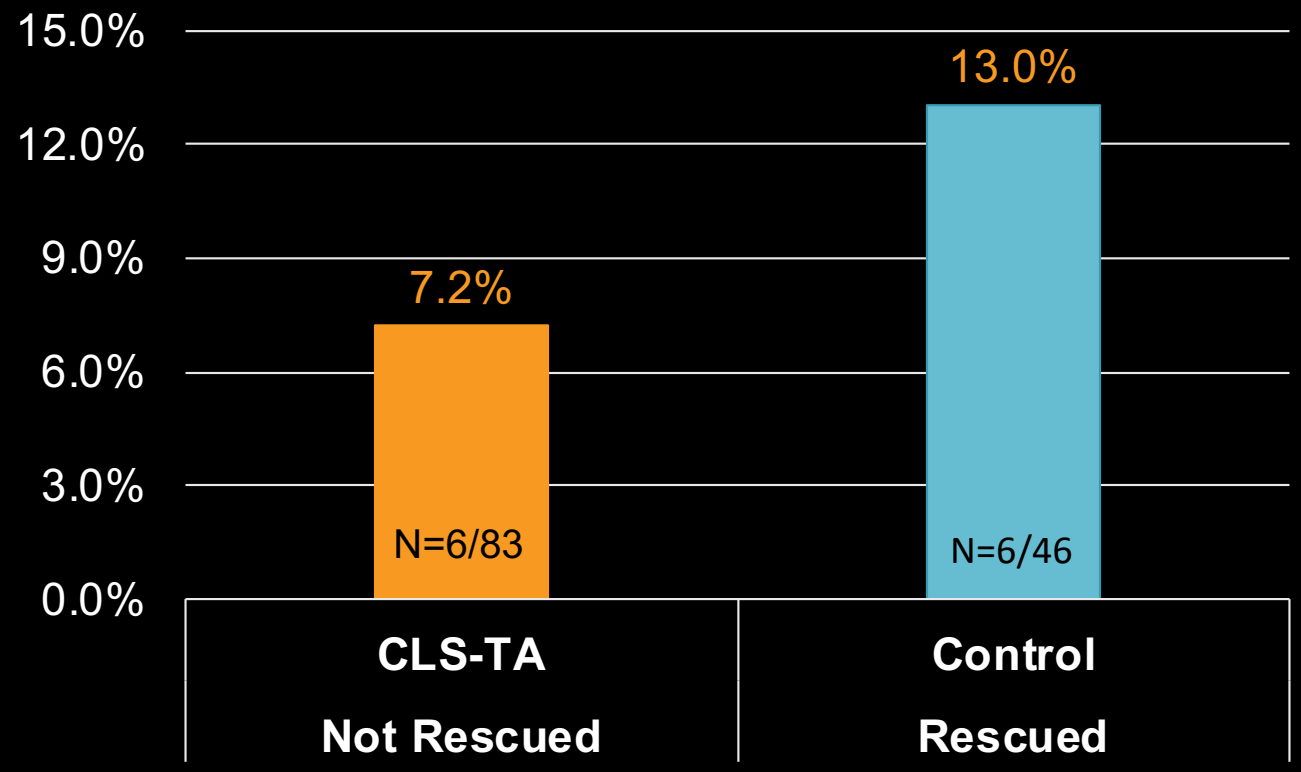
Sub-Analysis of IOP: ≥ 30 mmHg IOP at any visit through 24-wks

	Not Rescued	Rescued
CLS-TA	N = 83/96 (87 %)	N = 13/96 (14 %)
Control	N = 18/64 (28.%)	N = 46/64 (72 %)



Sub-Analysis of IOP: ≥ 1 IOP lowering meds* through 24-wks

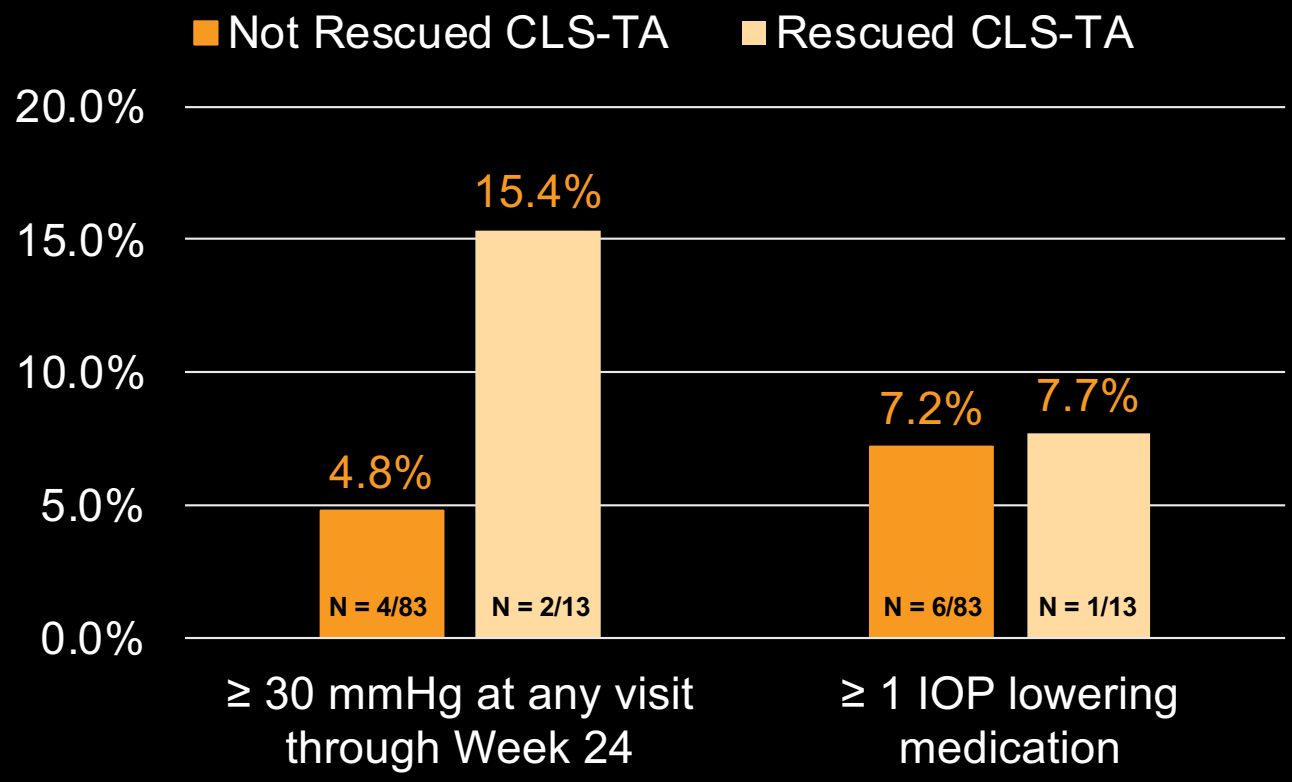
	Not Rescued	Rescued
CLS-TA	N = 83/96 (87 %)	N = 13/96 (14 %)
Control	N = 18/64 (28.%)	N = 46/64 (72 %)



*IOP lowering medications administered for 30 days or more

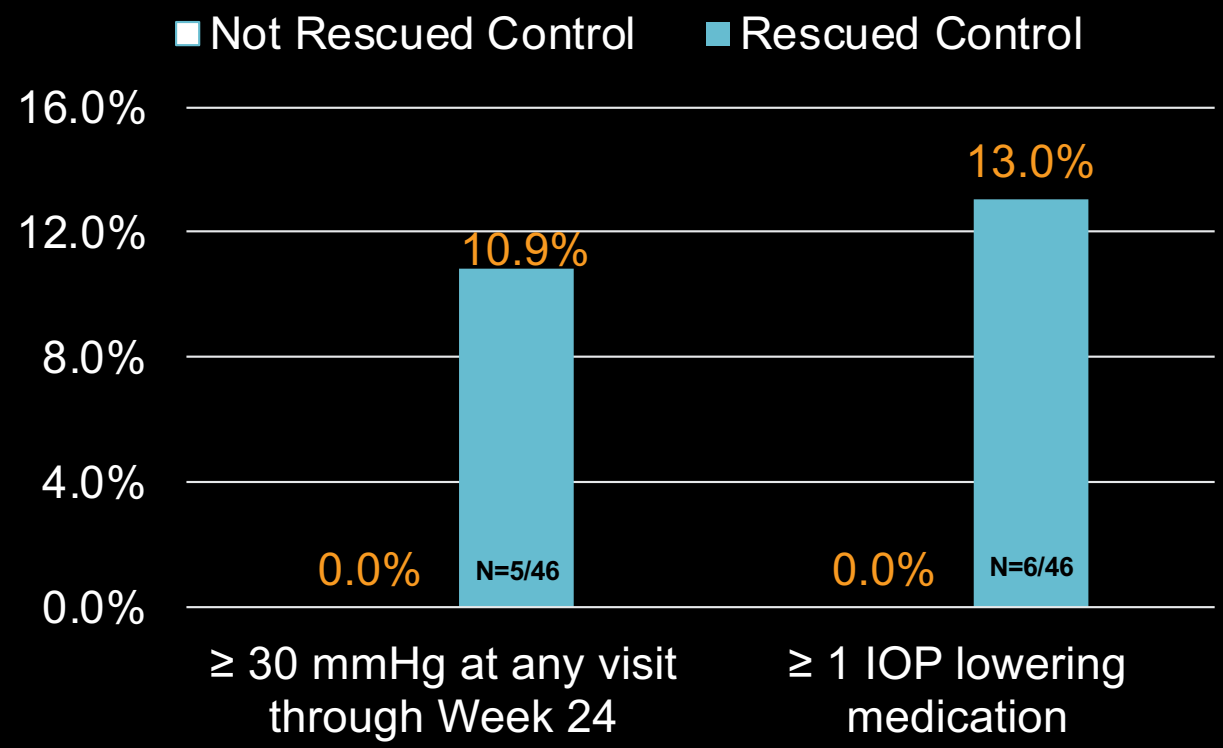
Sub-Analysis of IOP: **CLS-TA Patients** Not rescued (n=83) vs. Rescued (n=13)

	Not Rescued	Rescued
CLS-TA	n=83/96 (87%)	n=13/96 (14%)
Control	n=18/64 (28%)	n=46/64 (72%)

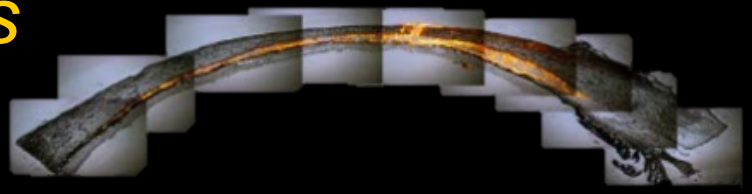


Sub-Analysis of IOP: **Control Patients** Not rescued (n=18) vs. Rescued (n=46)

	Not Rescued	Rescued
CLS-TA	N = 83/96 (87%)	N = 13/96 (14%)
Control	N = 18/64 (28%)	N = 46/64 (72%)



PEACHTREE: *Take Home Points*



Efficacy

- In patients with macular edema due to noninfectious uveitis, suprachoroidally injected CLS-TA significantly improved vision and macular edema

Safety

- No SAEs attributable to CLS-TA
- Low rates of elevated IOP and cataract
  - Patients rescued with intravitreal corticosteroid showed higher rates of IOP events

Limitations: small post-hoc subgroup analysis
Further study is warranted


Thank You