Variations in Intraocular Pressure Following Administration of Suprachoroidal Triamcinolone Acetonide Suspension (CLS-TA)

Results from the Phase 3 PEACHTREE Clinical Trial for Uveitic Macular Edema

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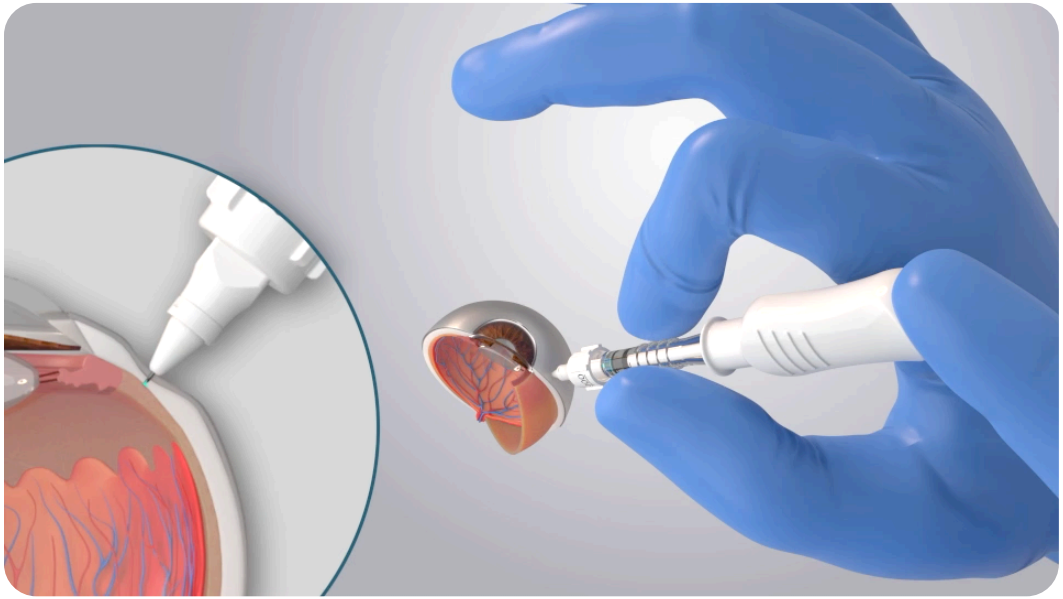
Disclosure

- Dr. Nguyen has served as advisor for Bayer,Clearside, Genentech/Roche, Regeneron, Santen
- Stanford University, the employer of Dr Nguyen, has received research funding from Genentech, Regeneron, and Santen, among others

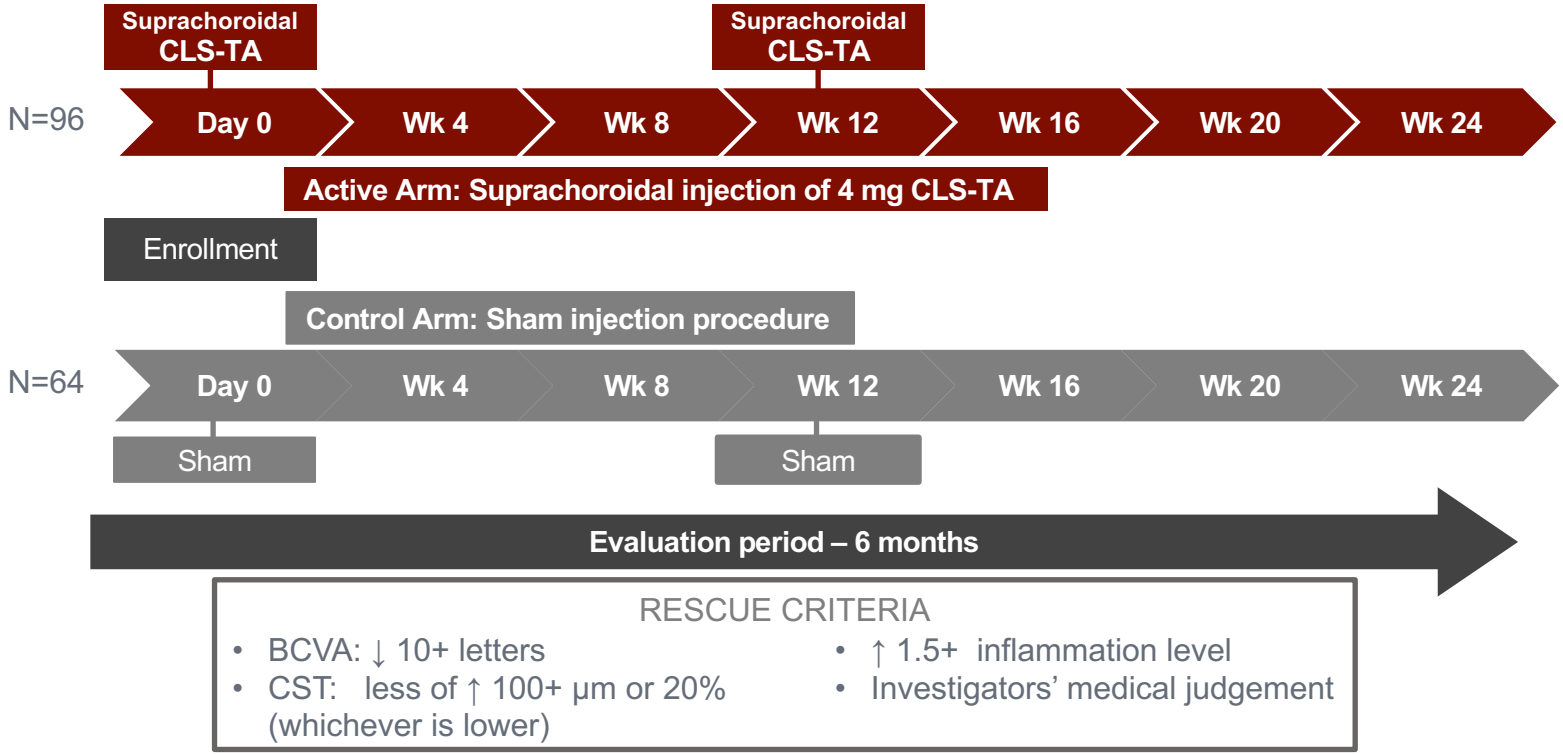
The Suprachoroidal Space

Targeted and Compartmentalized Delivery



PEACHTREE: Phase 3, Randomized, Controlled, Double-Masked, Multicenter Trial

Primary Endpoint: Proportion of patients with an improvement from baseline ≥15 letters in BCVA at Week 24



Key Inclusion and Exclusion Criteria

Inclusion

- Diagnosis of macular edema with central subfield thickness ≥300 microns
- Noninfectious uveitis of any associated diagnosis/etiology
- 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
- Intraocular pressure >22 mmHg or uncontrolled glaucoma; patients ≤22 mmHg could be on up to 2 IOP-lowering medications

Subjects could have active or controlled disease at enrollment

ETDRS: Early Treatment Diabetic Retinopathy Study
IOP: intraocular pressure

Baseline Subject Characteristics Similar Between Groups

Characteristic	CLS-TA N=96	Control N=64	Overall N=160
Gender, n (%)			
Male	42 (43.8)	30 (46.9)	72 (45.0)
Female	54 (56.3)	34 (53.1)	88 (55.0)
Age (years), mean (SD)	50.40 (14.18)	50.0 (15.08)	50.2 (14.5)
BCVA, study eye (ETDRS letters)			
Mean (SD)	54.7 (13.9)	53.5 (12.9)	54.2 (13.5)
Median (range)	57 (9 – 89)	54 (12-79)	56 (9-89)
CST, study eye (μm)			
Mean (SD)	480.9 (153.2)	525.4 (158.1)	498.7 (156.3)
Median (range)	453.0 (256-857)	518.5 (274-971)	481.5 (256-971)

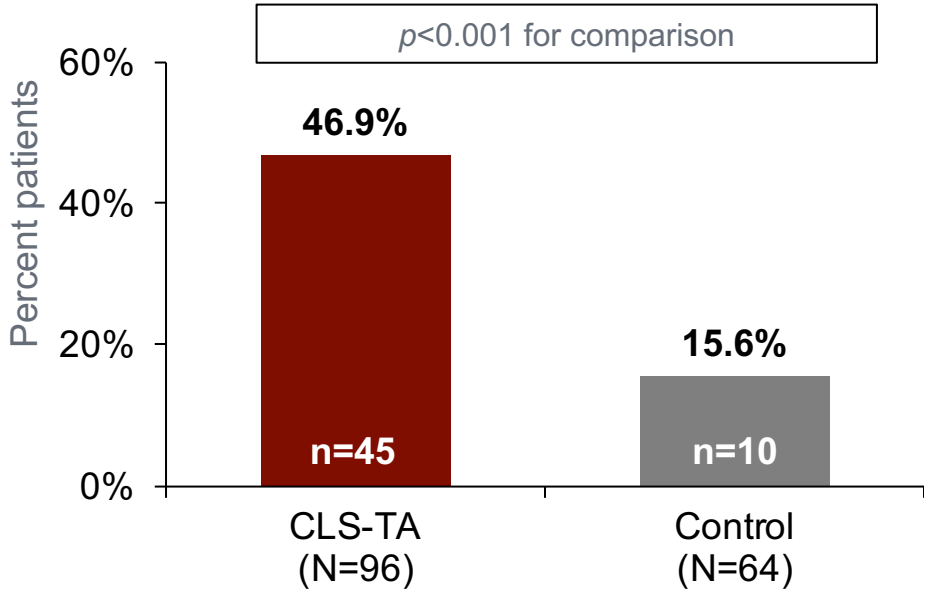
CST: central subfield thickness; ETDRS: Early Treatment Diabetic Retinopathy Study

Baseline Subject Characteristics: IOP and Glaucoma

Characteristic	CLS-TA N=96 n (%)	Control N=64 n (%)
Any Medical History Related to Glaucoma or IOP	21 (21.9)	14 (21.9)
Angle closure glaucoma	0 (0)	1 (1.6)
Glaucoma	10 (10.4)	4 (6.3)
Glaucomatous optic disc atrophy	1 (1.0)	0 (0)
Intraocular pressure increased	2 (2.1)	0 (0)
Ocular hypertension	5 (5.2)	7 (10.9)
Open Angle Glaucoma	1 (1.0)	1 (1.6)
Trabeculectomy	1 (1.0)	0 (0)
Uveitic glaucoma	1 (1.0)	1 (1.6)
≥ 1 IOP lowering medication	5 (5.2)	2 (3.1)

PEACHTREE: Met Primary Efficacy Endpoint

Primary Endpoint: Subjects gaining ≥15 BCVA letters from baseline at Week 24, %



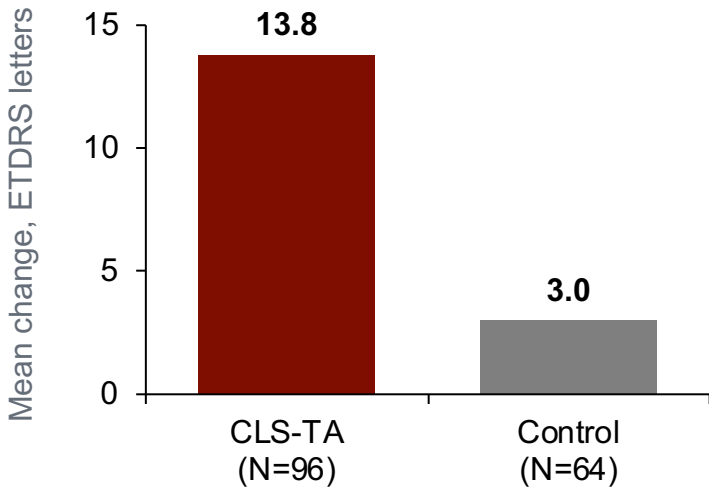
Intention-to-treat population; Last Observation Carried Forward imputation.
The p-value is based on a Cochran-Mantel-Haenszel test for general association between treatment and response with stratification by country.

Mean Change in BCVA

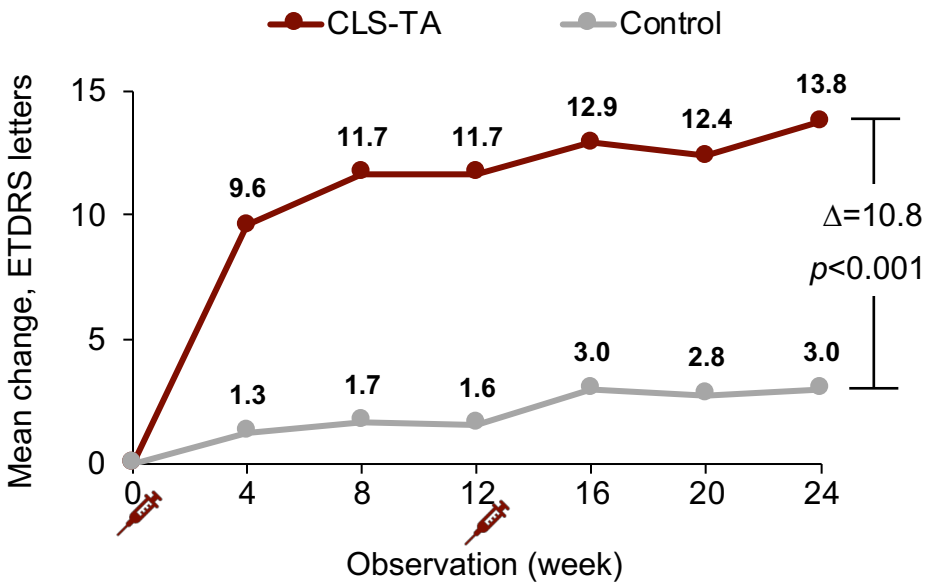
Improvement Observed as Early as Week 4 Through Week 24 in the CLS-TA Arm

Mean change from baseline in BCVA at Week 24

p<0.001 for comparison



Mean change from baseline in BCVA by visit



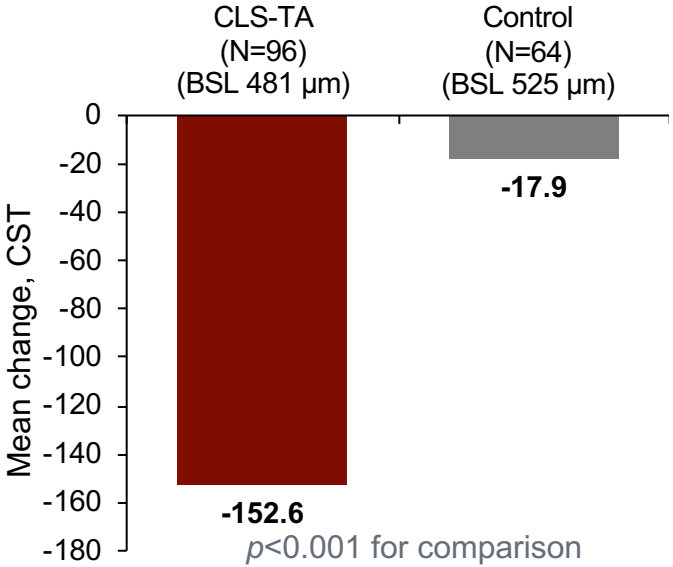
Intention-to-treat population; last observation carried forward imputation.
t-test. Differences between the CLS-TA and control arms were significant at each visit.
BCVA, best corrected visual acuity.

ANOVA with treatment, country and treatment-by-country interaction as fixed effects

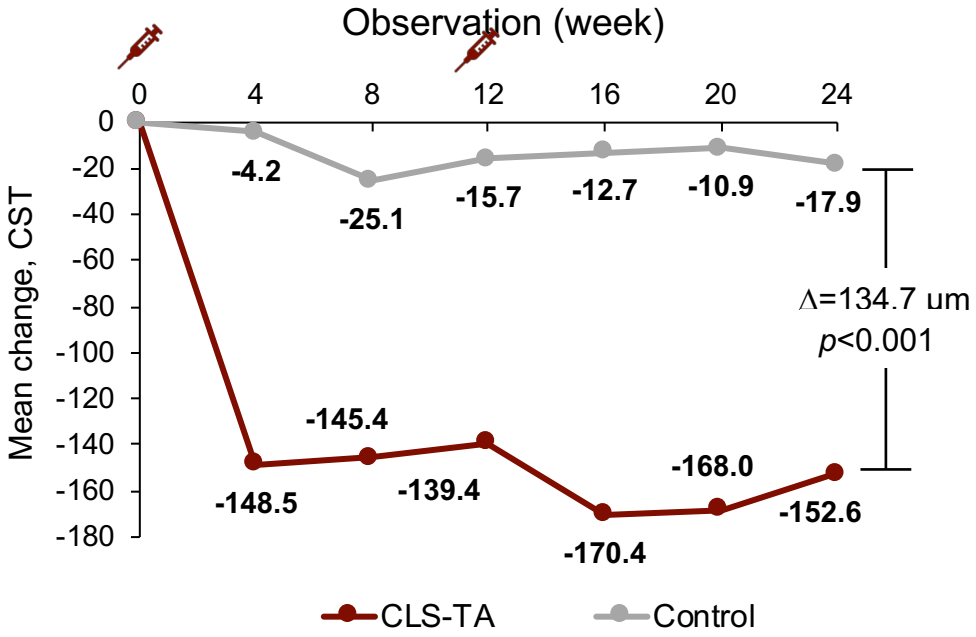
Mean Change in Central Subfield Thickness

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

Mean change from baseline at week 24 in central subfield thickness (µm)



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



Intention-to-treat population; last observation carried forward imputation.
ANOVA with treatment, country and treatment-by-country interaction as fixed effects
BSL, baseline mean value; CST, central subfield retinal thickness.

Safety

IOP-Related Events	CLS-TA 4.0 mg N = 96	Control N = 64
Elevated IOP adverse events	11 (11.5%)	10 (15.6%)
IOP elevation ≥10 mmHg change from baseline at any visit*	9 (9.4%)	7 (10.9%)
IOP elevation ≥30 mmHg absolute reading at any post baseline visit*	5 (5.2%)	4 (6.3%)
Given any additional IOP-lowering medication	7 (7.3%)	6 (9.4%)
Any surgical intervention for an elevated IOP Adverse Event	0	0

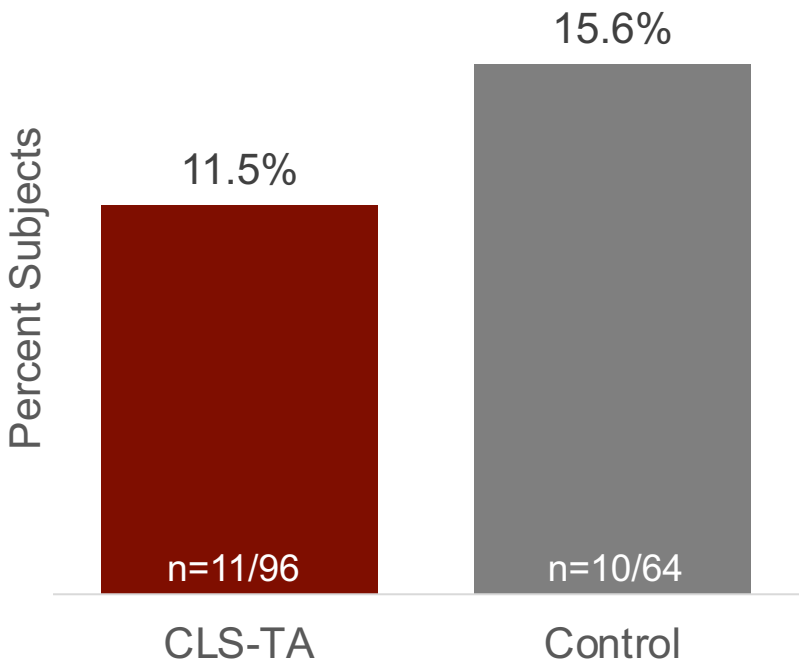
One serious ocular AE

- Retinal detachment 8 weeks after CLS-TA, in different quadrant
- Determined to be unrelated to study drug by the Investigator

Cataract: 7.3% (7/96) in the CLS-TA arm vs. 6.3% (4/64) in the sham arm

Safety population; includes patients in the control group who received rescue medication
*Based on elevated intraocular pressure adverse reactions

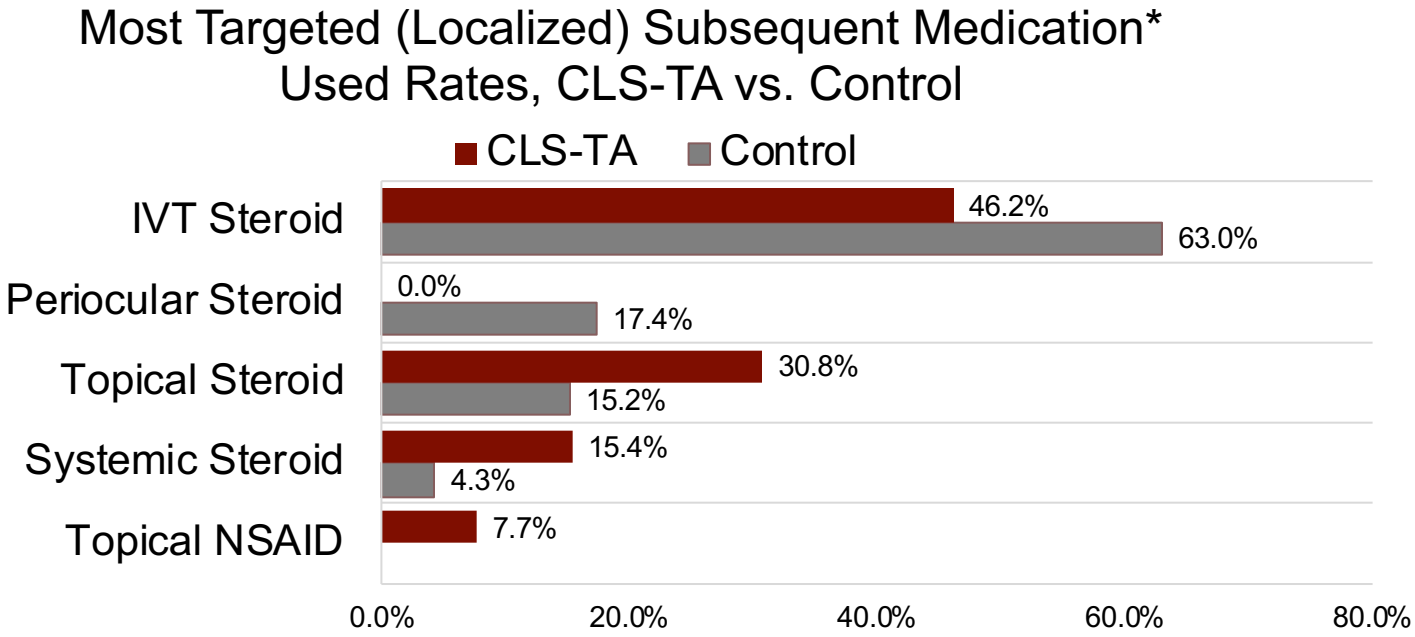
Elevated IOP Adverse Events in PEACHTREE



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

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

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



*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.

Sub-Analysis of IOP in PEACHTREE

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

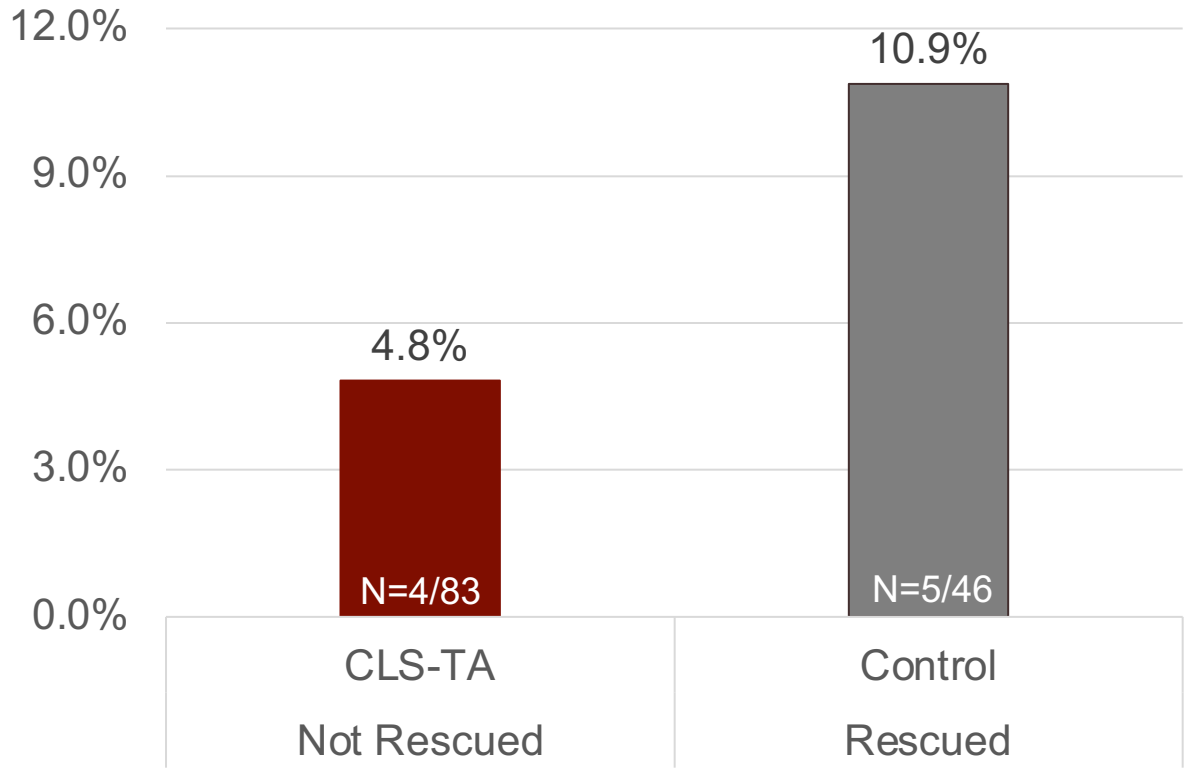
Method: Analyze IOP AEs for the clinically relevant endpoints of **≥30 mmHg IOP at any visit** and **≥1 IOP lowering medication**

Four (4) subgroups analyzed:

	Not Rescued	**Rescued**
CLS-TA	n=83/96 (86.5%)	n=13/96 (13.5%)
Control	n=18/64 (28.1%)	n=46/64 (71.9%)

≥ 30 mmHg IOP at any visit through 24-weeks

	Not Rescued	Rescued
CLS-TA	n=83/96 (86.5%)	n=13/96 (13.5%)
Control	n=18/64 (28.1%)	n=46/64 (71.8%)



≥ 1 IOP lowering medication* through 24-weeks

	Not Rescued	Rescued
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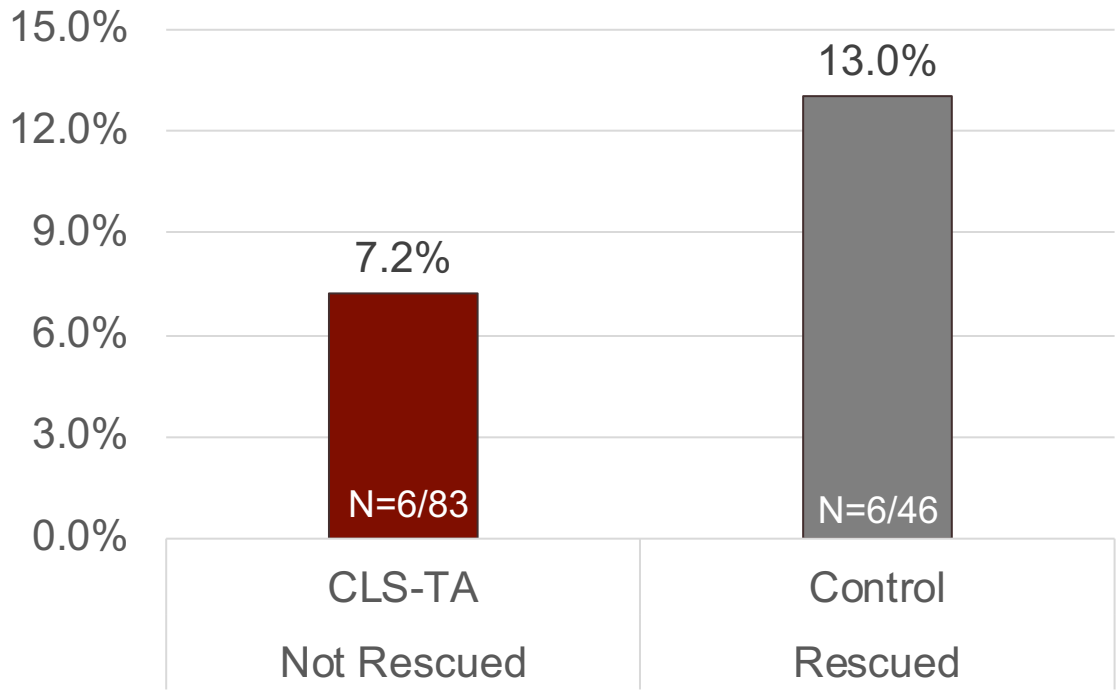
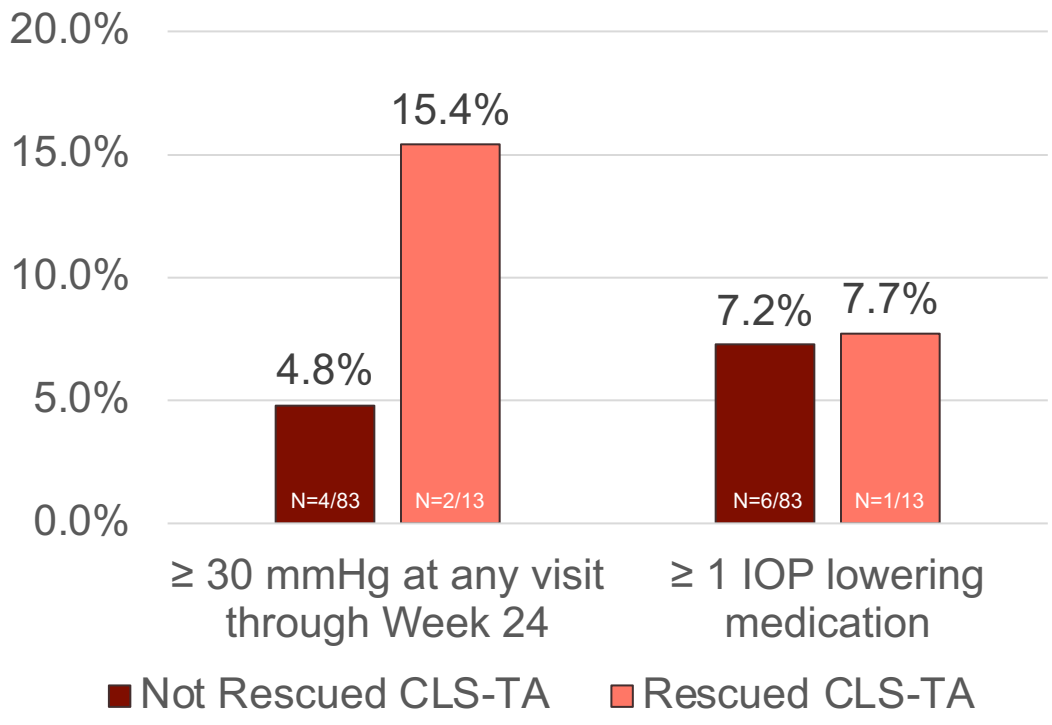


*IOP lowering medications administered for 30 days or more

IOP Rates
CLS-TA patients not rescued (n=83) vs rescued (n=13)

	Not Rescued	Rescued
CLS-TA	n=83/96 (86.5%)	n=13/96 (13.5%)
Control	n=18/64 (28.1%)	n=46/64 (71.8%)



IOP Rates:
Control patients not rescued (n=18) vs rescued (n=46)

	Not Rescued	Rescued
CLS-TA	n=83/96 (86.5%)	n=13/96 (13.5%)
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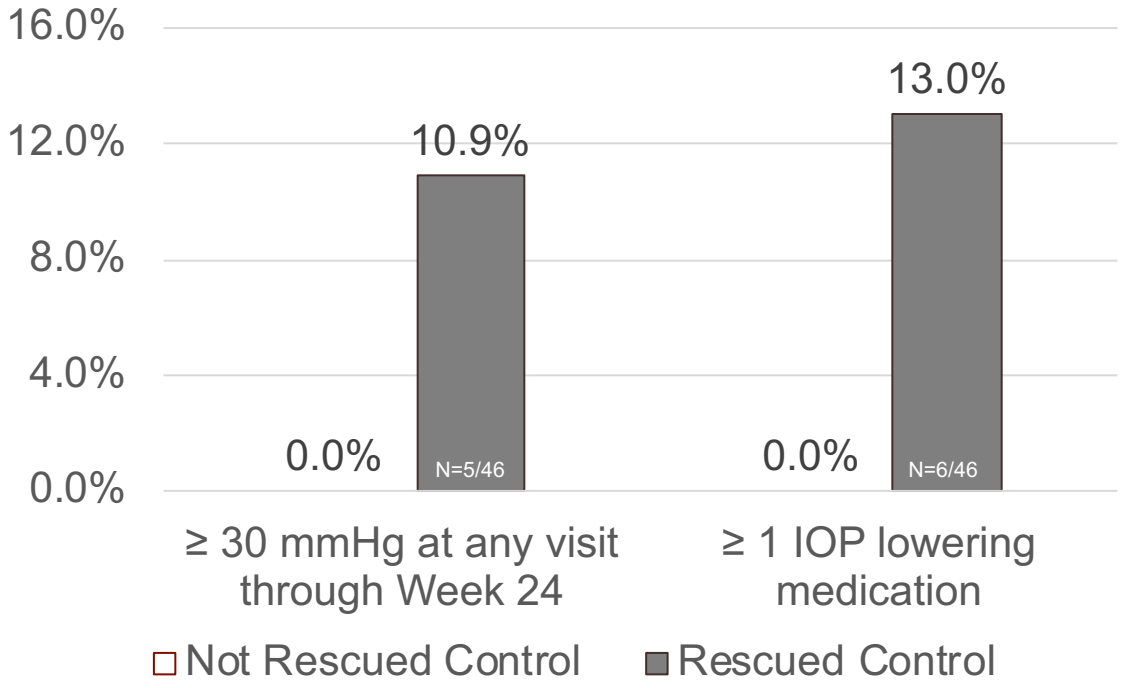

PEACHTREE Study
Take Home Points

Efficacy

- Primary endpoint was met, with ~47% of patients gaining ≥15 ETDRS letters
- **Suprachoroidally injected CLS-TA significantly improved vision and macular edema in noninfectious uveitis at all anatomical locations**

Safety

- No SAEs attributable to CLS-TA
- **Low rates of elevated IOP and cataract**
- Cataract rate was similar to that in the control arm
- No surgical intervention for an elevated IOP adverse event