Suprachoroidal Delivery of CLS-TA for Uveitic Macular Edema: Results of the Phase 3 PEACHTREE Trial

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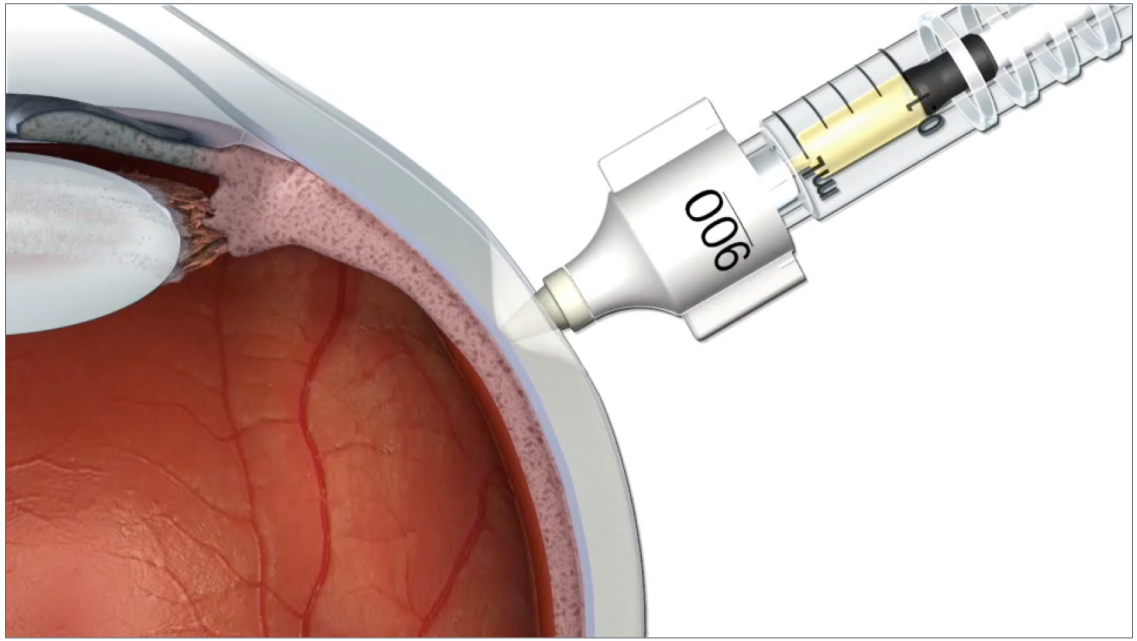
PEACHTREE
CLS1001-301

Suprachoroidal Injection for Posterior Segment Disease



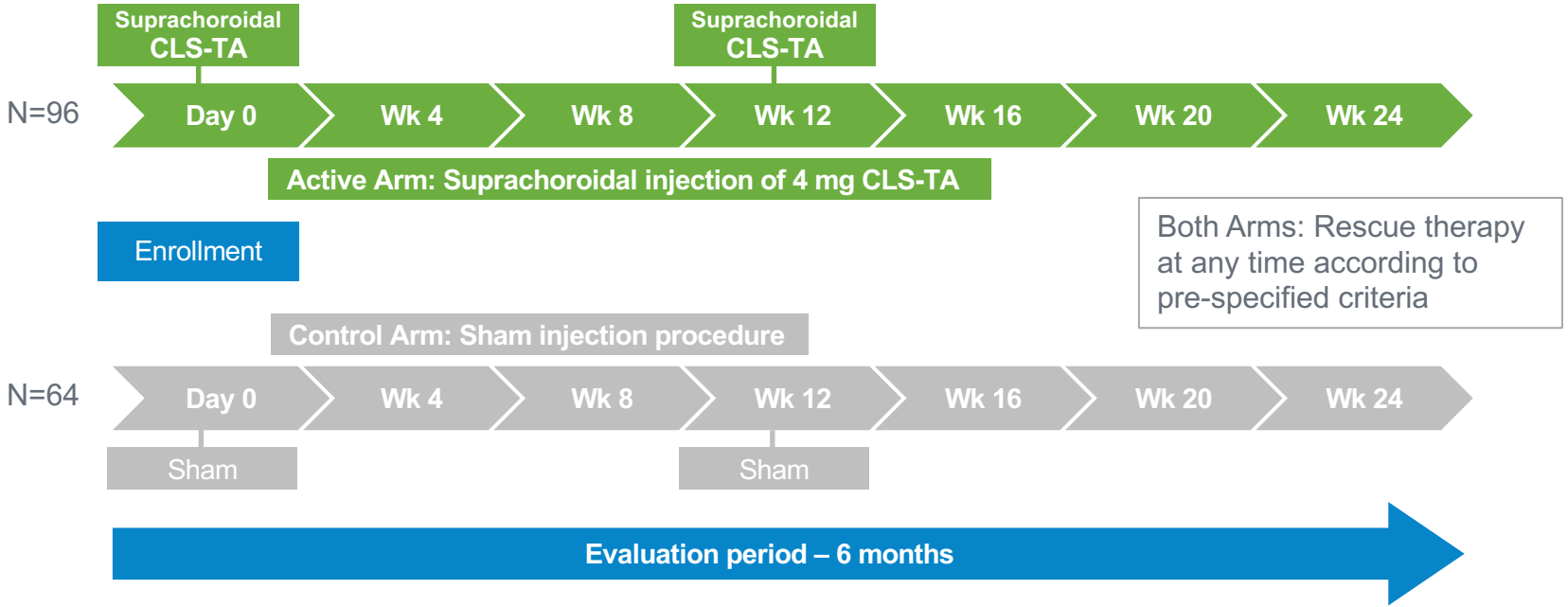
Animal model data for suprachoroidal vs. intravitreal injection of TA show:

- Higher amounts of drug in the choroid, RPE cells, and retina
- Lower exposure to the anterior segment

A potentially useful ocular distribution of drug for the treatment of uveitic macular edema

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

Visual acuity primary endpoint



Key Inclusion and Exclusion Criteria

Inclusion

- **Diagnosis of macular edema** with central subfield thickness ≥300 microns
- Noninfectious uveitis of any associated diagnosis/etiology
- 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
- More than 2 IOP-lowering medications

Subjects could have active or controlled disease at enrollment

ETDRS: Early Treatment Diabetic Retinopathy Study
IOP: intraocular pressure

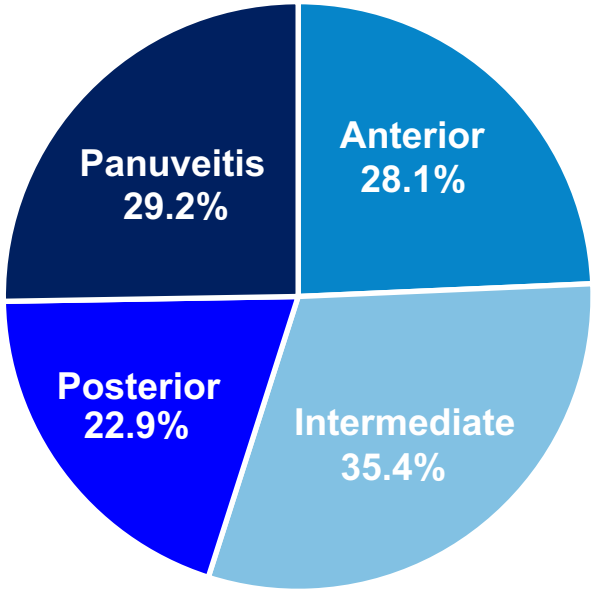
Baseline Subject Characteristics Were Similar Between Treatment Groups

Characteristic	CLS-TA n=96	Control n=64
Gender, n (%)		
Male	42 (43.8)	30 (46.9)
Female	54 (56.3)	34 (53.1)
Age (years), mean (SD)	50.4 (14.2)	50.0 (15.1)
BCVA, study eye (ETDRS letters)		
Mean (SD)	54.7 (13.9)	53.5 (12.9)
Median (range)	57 (9-89)	54 (12-79)
CST, study eye (μm)		
Mean (SD)	480.9 (153.2)	525.4 (158.1)
Median (range)	453 (256-857)	518 (274-971)

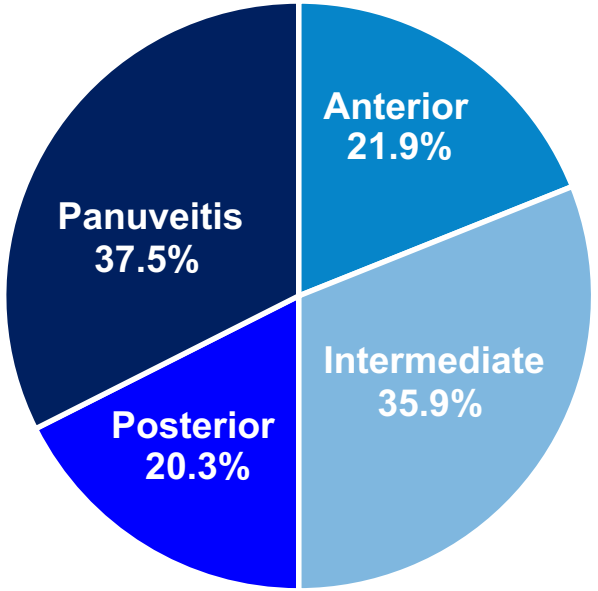
CST: central subfield thickness; ETDRS: Early Treatment Diabetic Retinopathy Study

All Anatomic Subtypes Were Enrolled

CLS-TA (N=96)



Control (N=64)

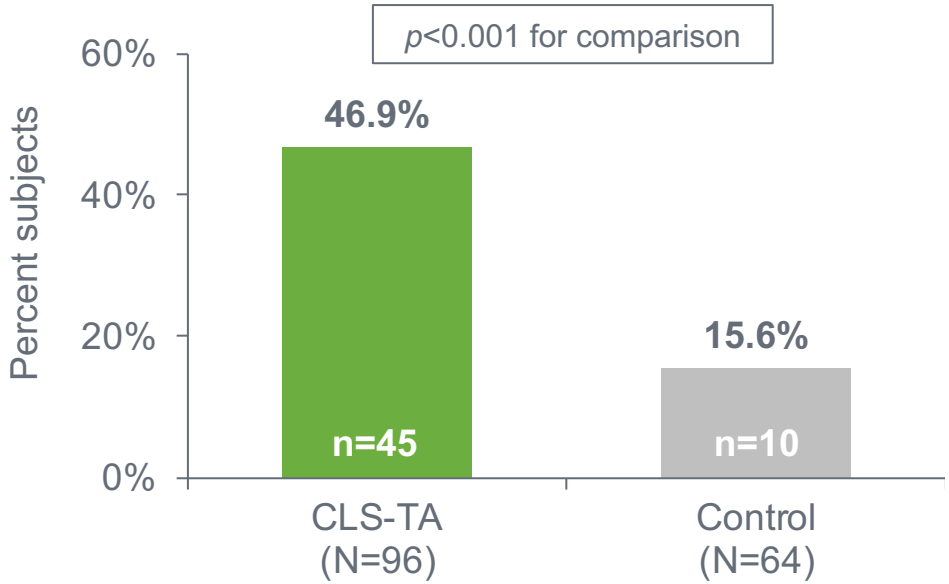


Distribution of Uveitis Diagnosis Was Similar Between Treatment Groups

Characteristic	CLS-TA (N=96) n (%)	Control (N=64) n (%)
Idiopathic	69 (71.9)	44 (68.8)
Pars planitis	7 (7.3)	4 (6.3)
Sarcoidosis	4 (4.2)	5 (7.8)
HLA-B27 related	4 (4.2)	1 (1.6)
Other	3 (3.1)	1 (1.6)
Juvenile idiopathic arthritis	2 (2.1)	1 (1.6)
Vogt-Koyanagi-Harada syndrome	1 (1.0)	2 (3.1)
Reactive arthritis	2 (2.1)	0
Birdshot retinochoroidopathy	2 (2.1)	0
Behçet's syndrome	1 (1.0)	0

PEACHTREE Met Its Primary Efficacy Endpoint

Subjects gaining ≥15 ETDRS letters from baseline, %

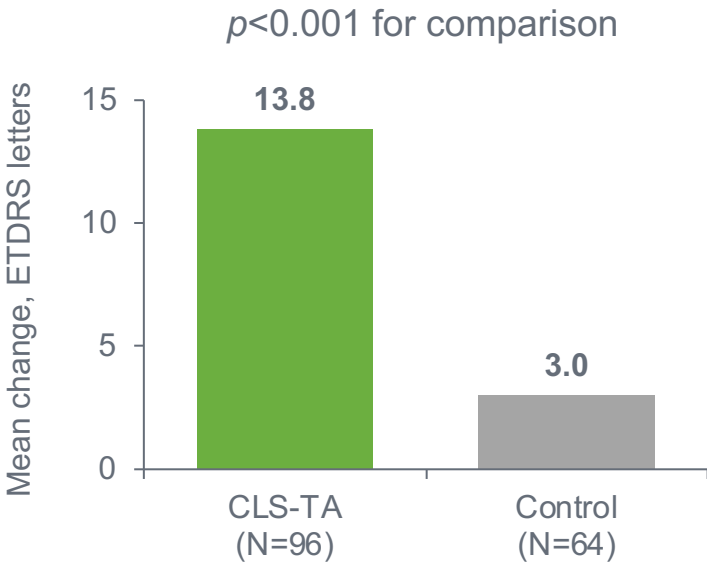


Intention-to-treat population; LOCF imputation.
The p-value is based on a Cochran-Mantel-Haenszel test for general association between treatment and response with stratification by country.
ETDRS, Early treatment diabetic retinopathy study; LOCF, last observation carried forward.

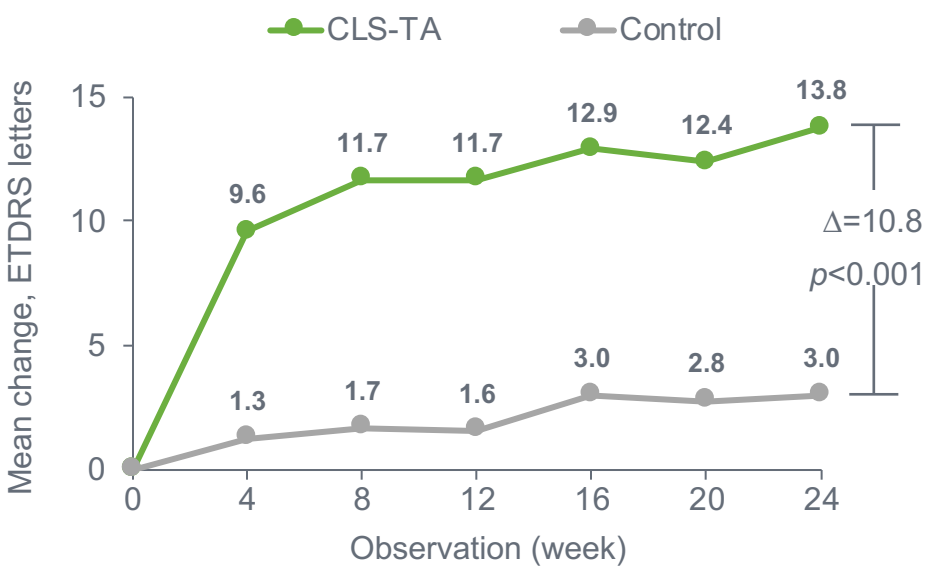
Mean Change in BCVA

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

Mean change at week 24 from baseline in BCVA in ETDRS letters read



Mean change at each visit from baseline in BCVA in ETDRS letters read

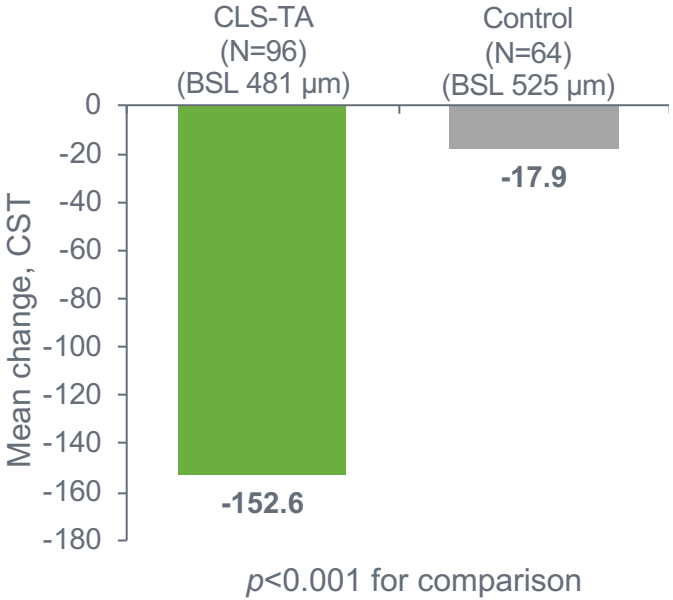


Intention-to-treat population; last observation carried forward imputation.
t-test. Differences between the CLS-TA and control arms were significant at each visit.
BCVA, best corrected visual acuity.

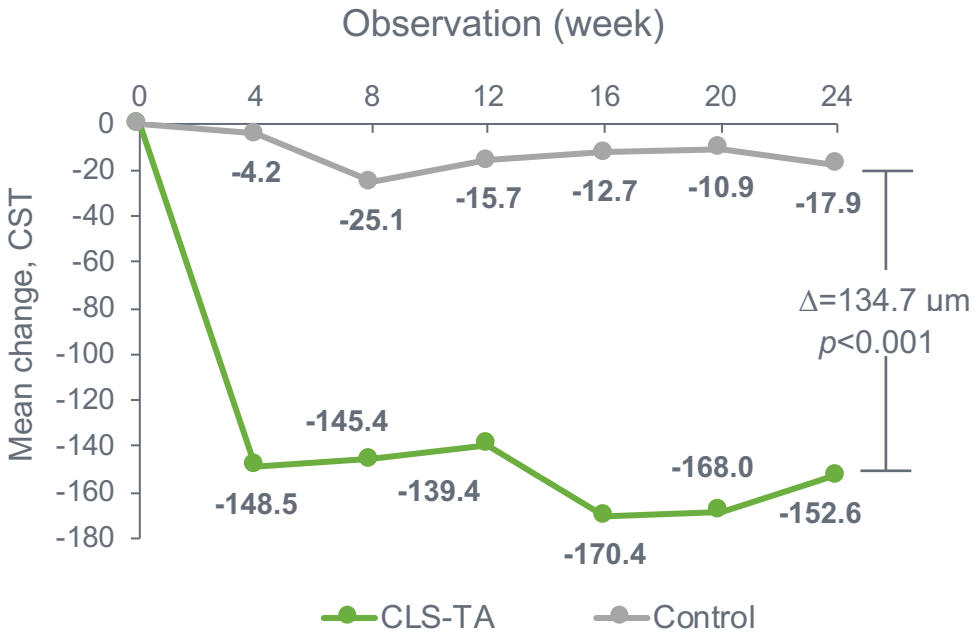
Mean Change in Central Subfield Thickness

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

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



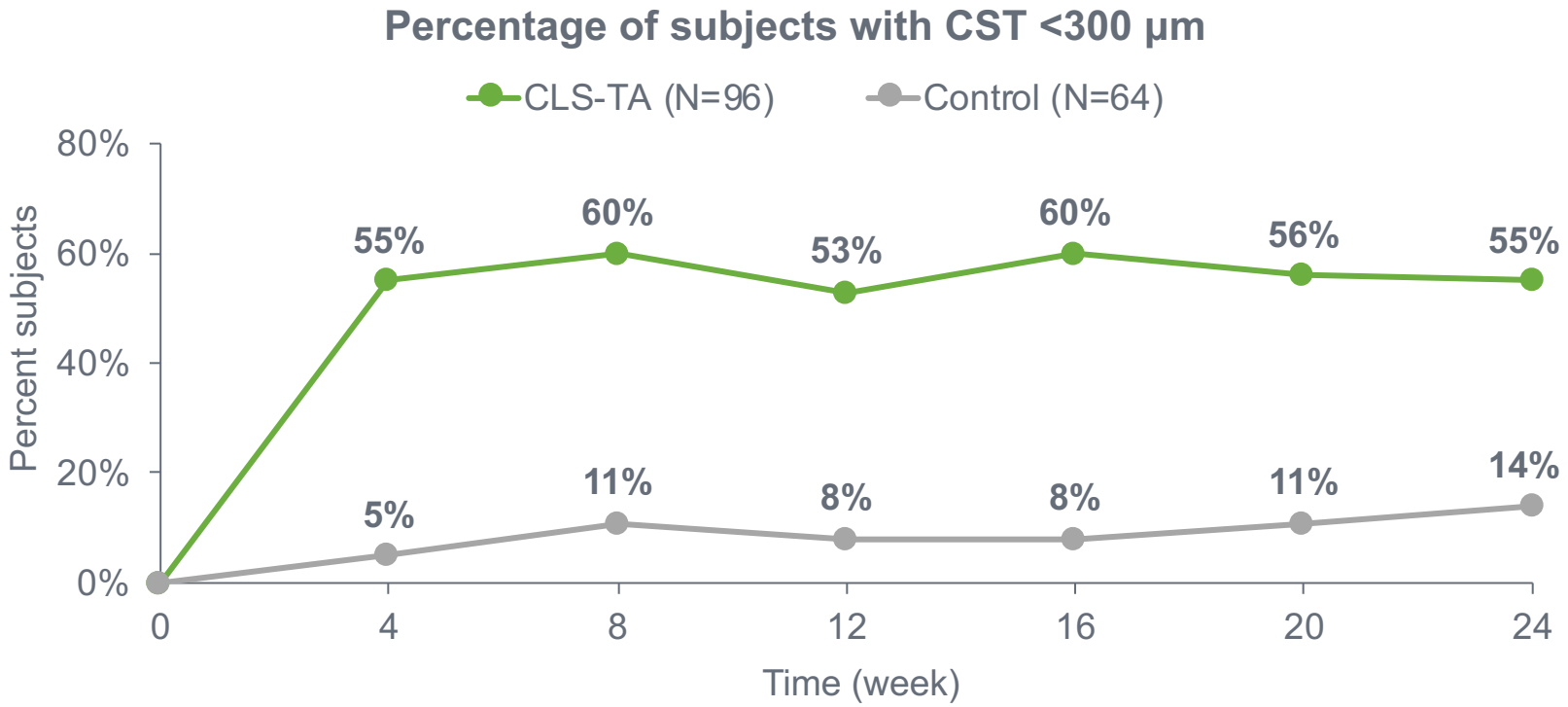
Mean change at each visit from baseline in central subfield thickness (µm)



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

Resolution of Macular Edema, CST <300 µm

Additional resolution in CLS-TA group at Week 4, Maintained through Week 24



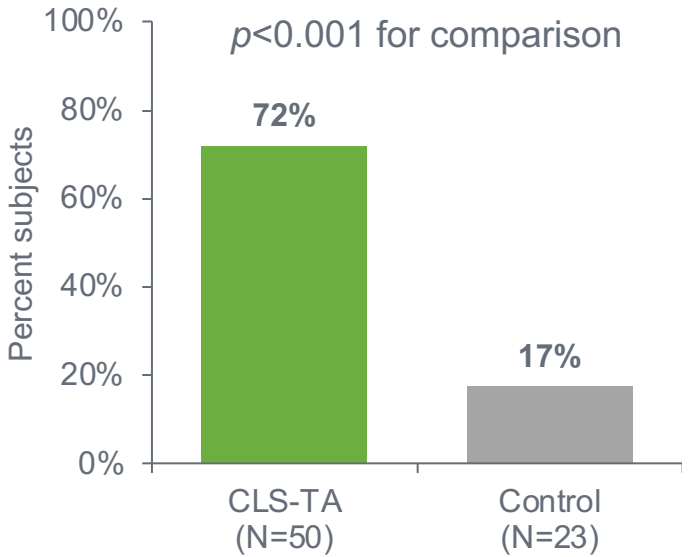
Intention-to-treat population; last observation carried forward imputation.
Less than 300 microns by SD-OCT
CST, central subfield retinal thickness.

Signs of Inflammation

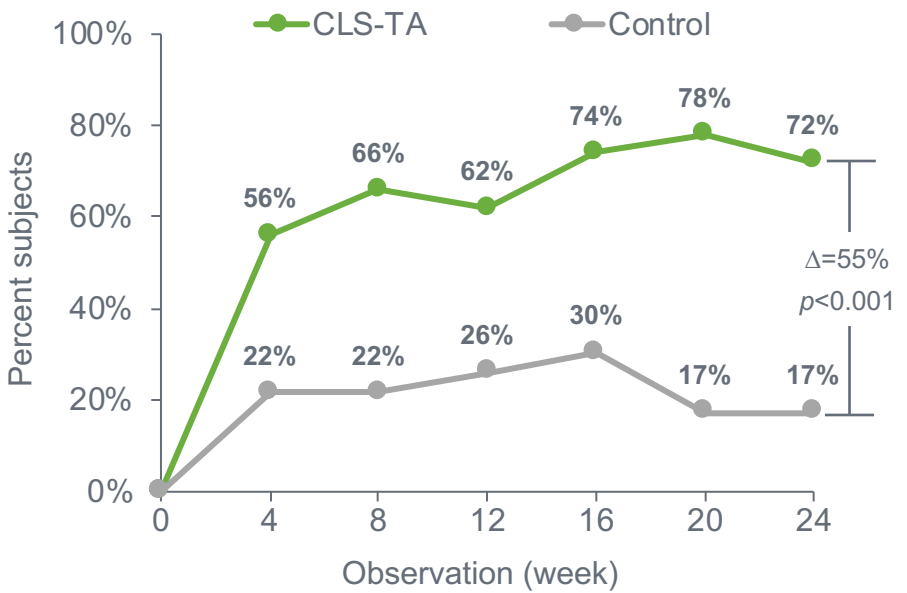
Resolution of Anterior Chamber Cells

In Subjects With Anterior Chamber Cells at Baseline

Percentage of subjects with resolution at week 24



Percentage of subjects with resolution at each visit from baseline

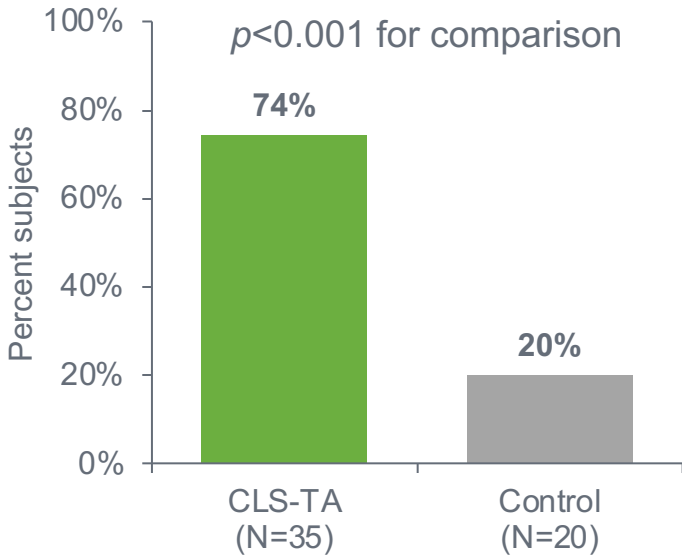


Intention-to-treat population; last observation carried forward imputation. The p-value is based on a Cochran-Mantel-Haenszel chi-square test for general association stratified by pooled country. Differences between the CLS-TA and control arms were significant at each visit.

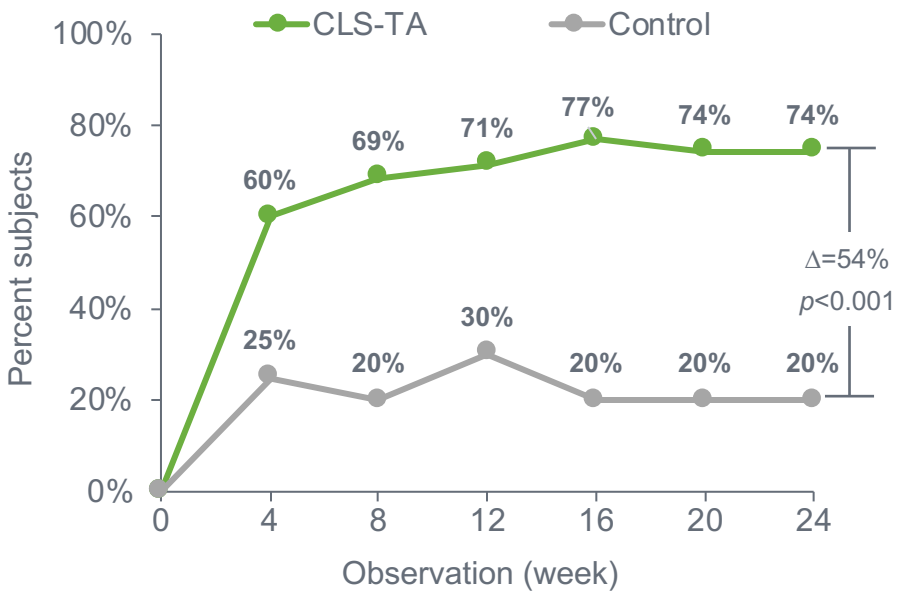
Resolution of Anterior Chamber Flare

In Subjects With Anterior Chamber Flare at Baseline

Percentage of subjects with resolution at week 24



Percentage of subjects with resolution at each visit from baseline

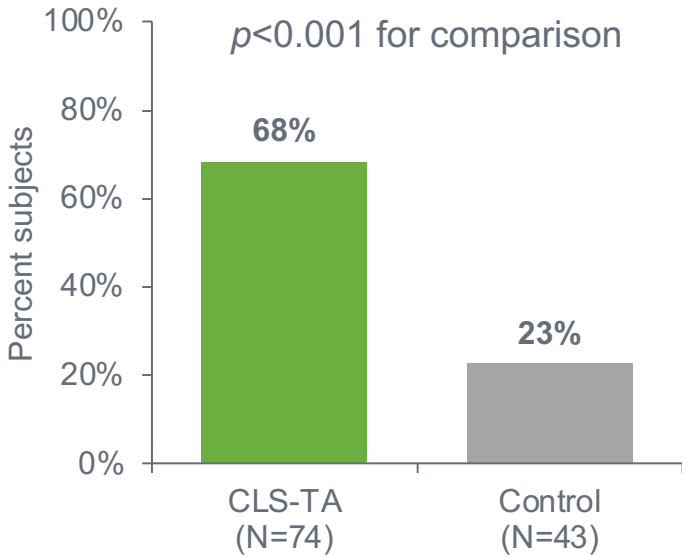


Intention-to-treat population; last observation carried forward imputation. The p-value is based on a Cochran-Mantel-Haenszel chi-square test for general association stratified by pooled country. Differences between the CLS-TA and control arms were significant at each visit from week 8.

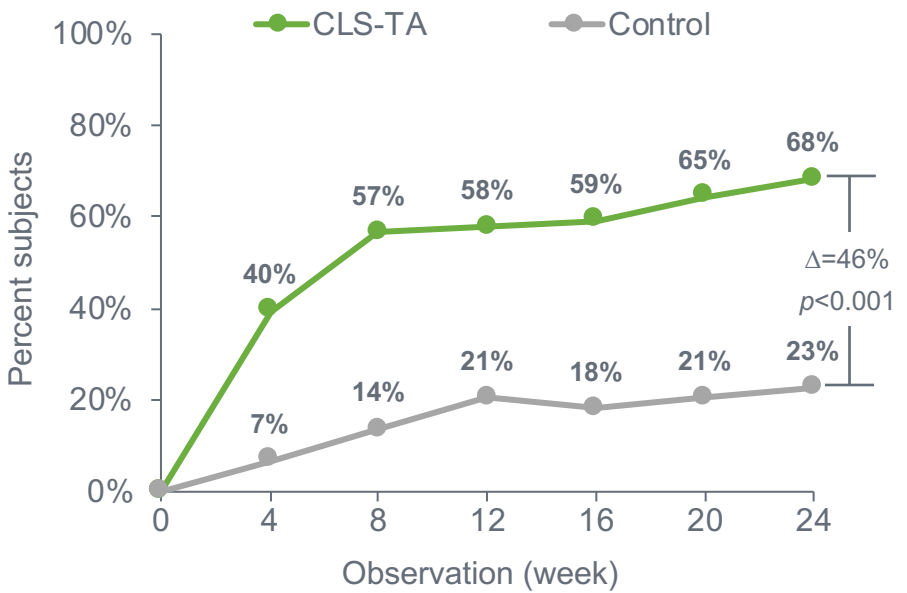
Resolution of Vitreous Haze

In Subjects With Vitreous Haze at Baseline

Percentage of subjects with resolution at week 24

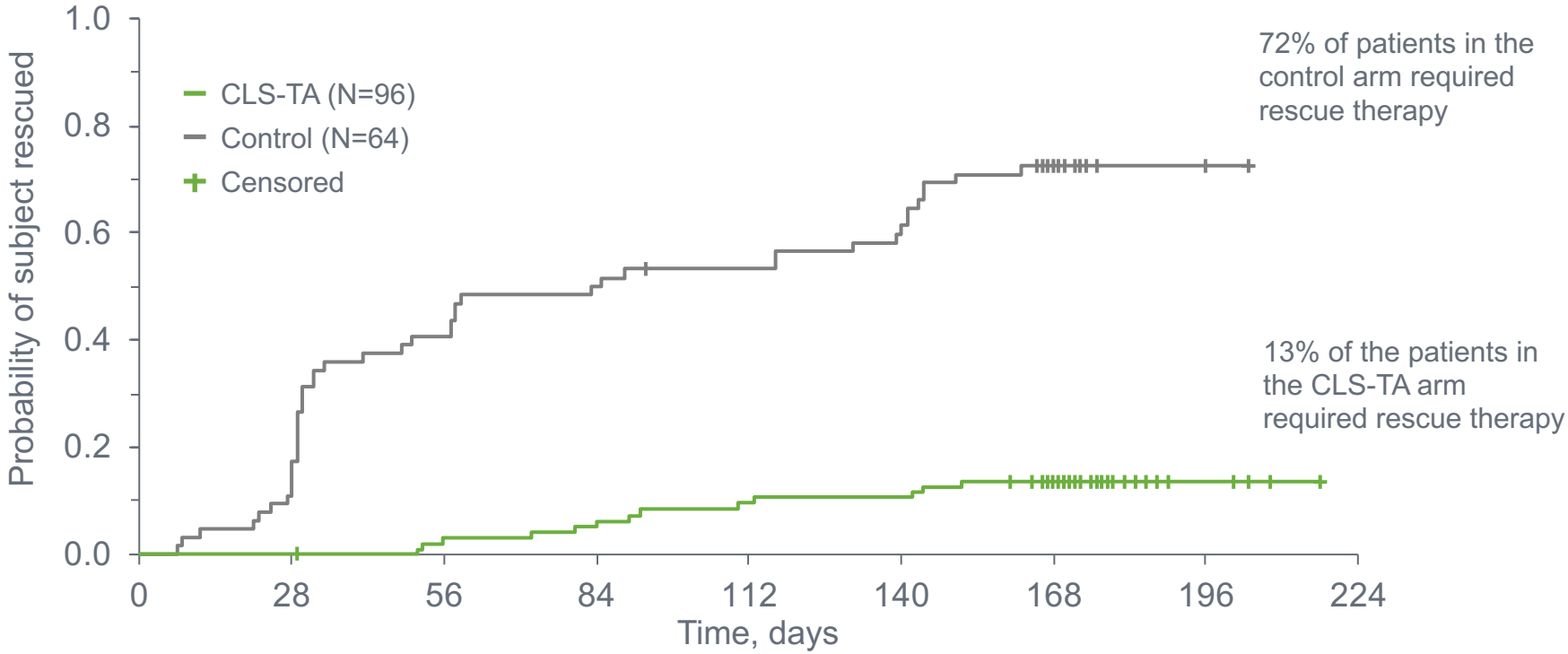


Percentage of subjects with resolution at each visit from baseline



Intention-to-treat population; last observation carried forward imputation. The p-value is based on a Cochran-Mantel-Haenszel chi-square test for general association stratified by pooled country. Differences between the CLS-TA and control arms were significant at each visit.

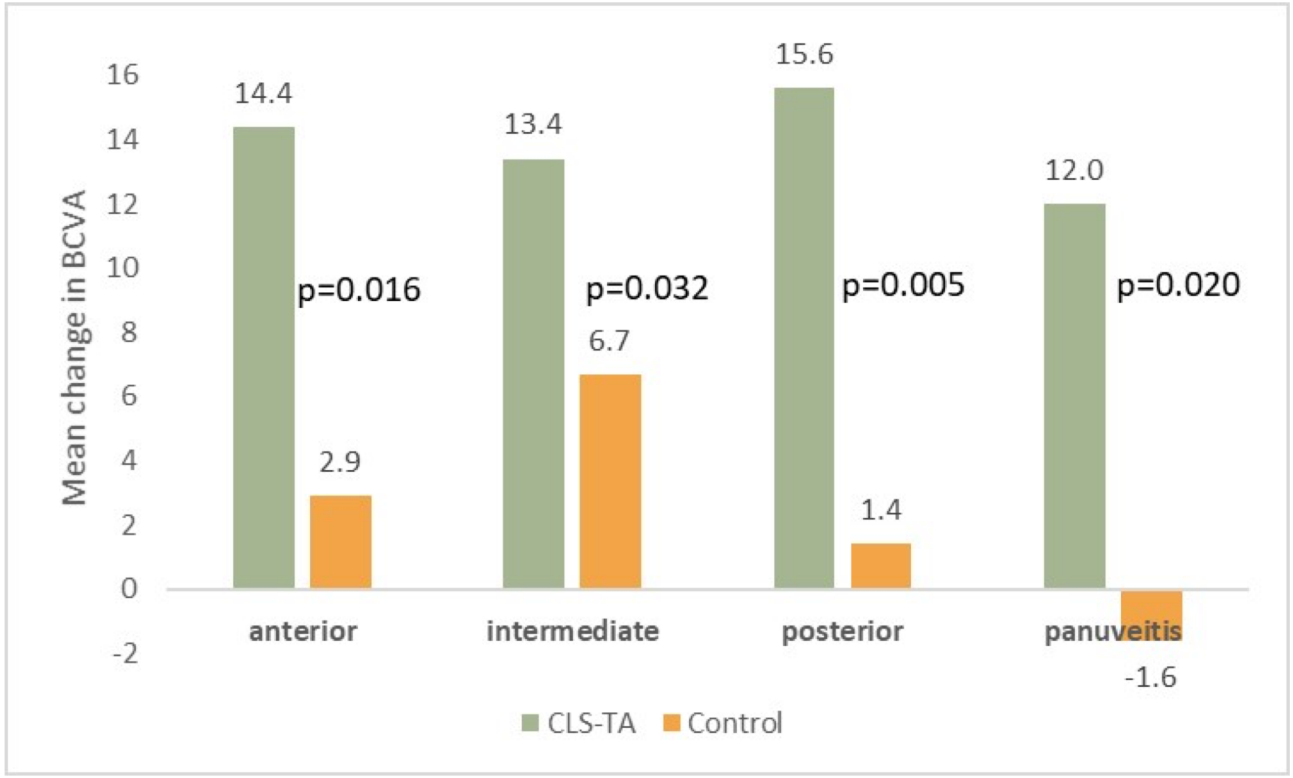
Kaplan–Meier Analysis: Time to Rescue



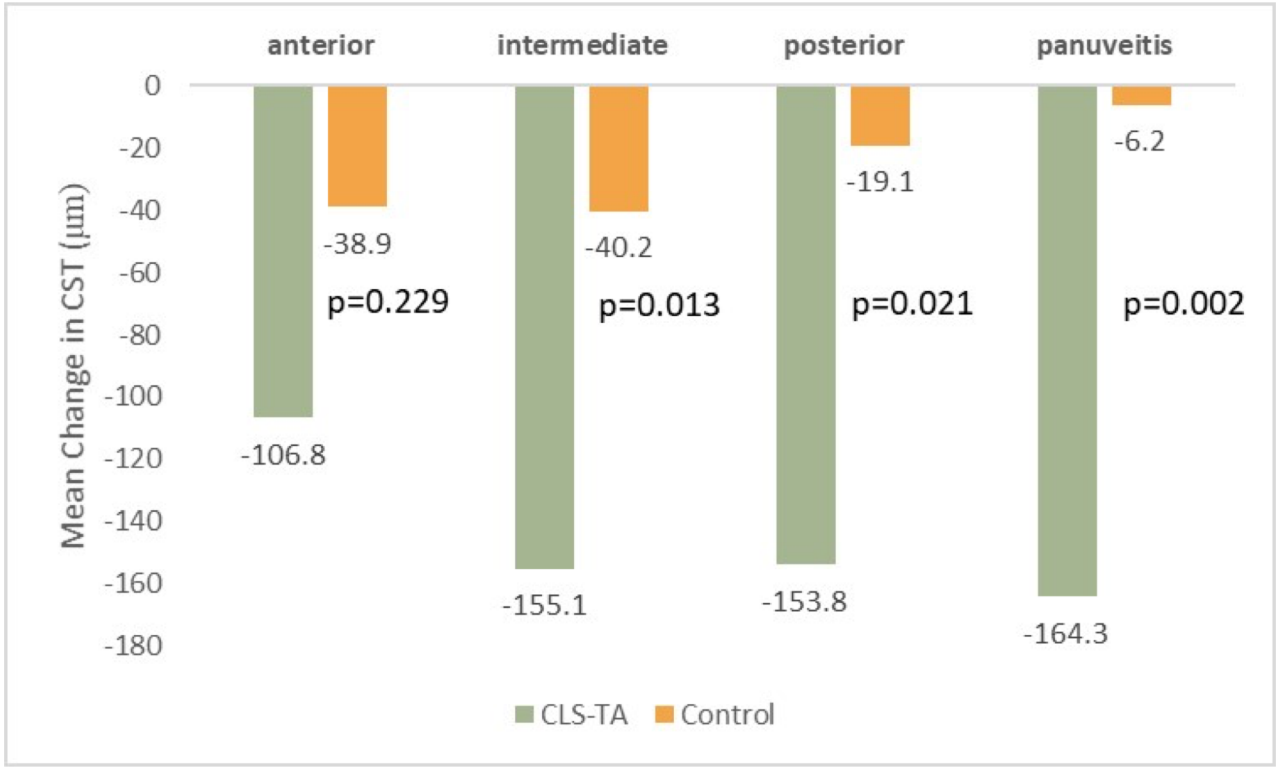
Intention-to-treat population

Anatomic location of uveitis

Anatomic location of uveitis



Anatomic location of uveitis



Safety

Safety

Serious AEs

- Three serious AEs, all in CLS-TA arm: none considered treatment-related
  - Two nonocular serious AEs (sialoadenitis, lumbar vertebral fracture)
  - One ocular serious AE (retinal detachment approximately 8 weeks after injection)

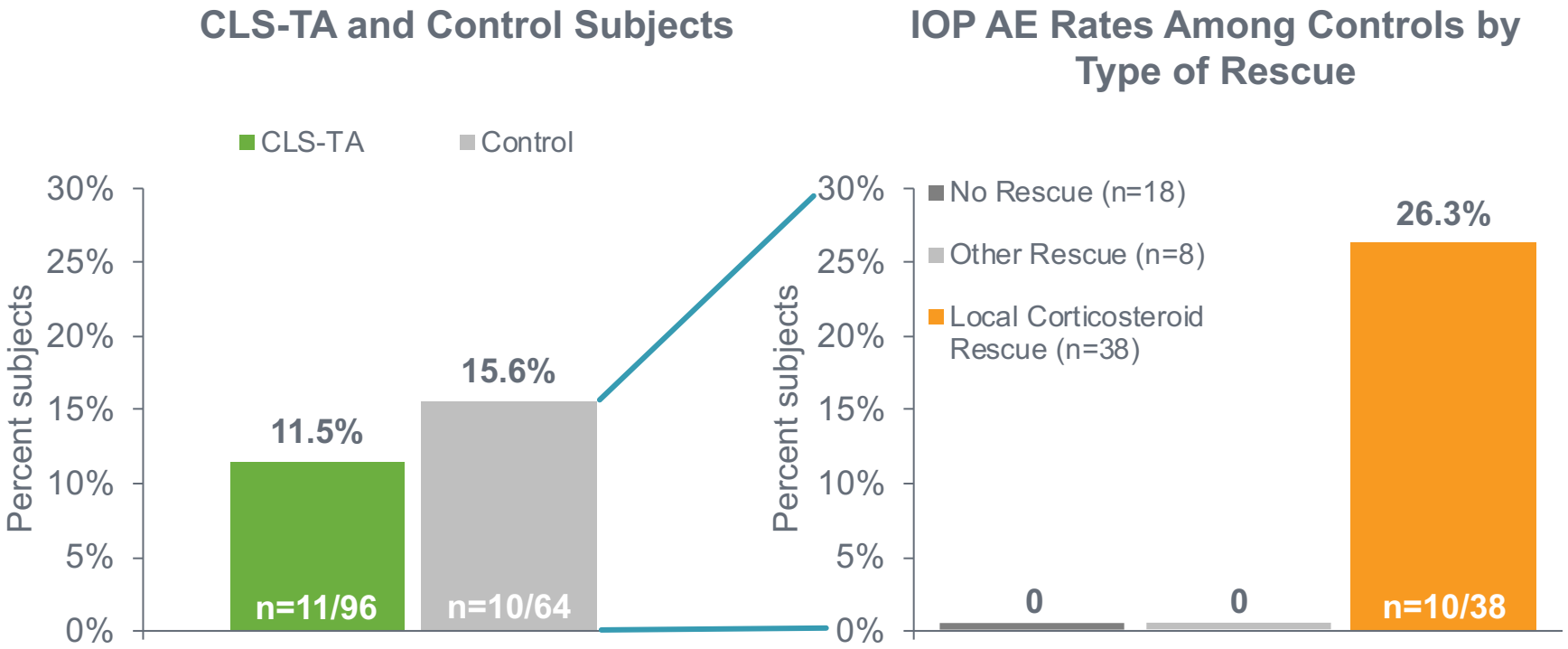
Ocular AEs in Study Eye	CLS-TA 4.0 mg N=96 n (%)	Control N=64 n (%)
Number of subjects with ≥1 ocular AEs	49 (51.0)	37 (57.8)
Treatment-related ocular AEs	29 (30.2)	8 (12.5)

Most Frequent AEs

- AEs occurring in >5% subjects in the CLS-TA arm were: elevated IOP (11.5%), eye pain (12.5%), cataract (7.3%)

AEs, adverse events.

Elevated IOP Adverse Events



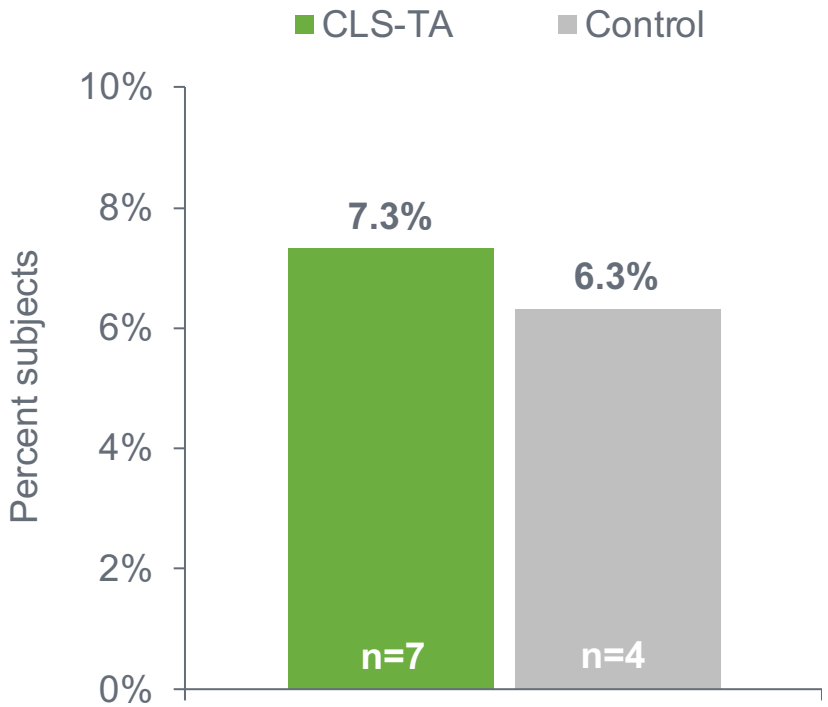
"Elevated IOP" includes (a) increased IOP, (b) ocular hypertension, and (c) glaucoma.
AE, adverse event; IOP, intraocular pressure.

Summary of AEs of Elevated IOP*

IOP-related Outcome	CLS-TA 4.0 mg N=96 n (%)	Control N=64 n (%)
IOP elevation ≥10 mmHg above baseline at any visit	9 (9.4)	8 (12.5)
≥30 mmHg at any visit	5 (5.2)	4 (6.3)
Given IOP lowering meds	10 (10.4)	9 (14.1)
Any surgical intervention for an elevated IOP AE	0	0
All AEs of elevated IOP	11 (11.5)	10 (15.6)

*"Elevated IOP" includes the preferred terms (a) IOP increased, (b) ocular hypertension, and (c) glaucoma.

Cataract Adverse Events



- New or worsening cataracts occurred with similar frequency in the CLS-TA and control groups
- No cataract-related surgeries in this trial

"Cataract" includes (a) cataract, (b) subcapsular cataract, and (c) nuclear cataract.

Case example

46 year old AA male with panuveitis OS

Baseline vision: 20/15 OD, 20/40 OS

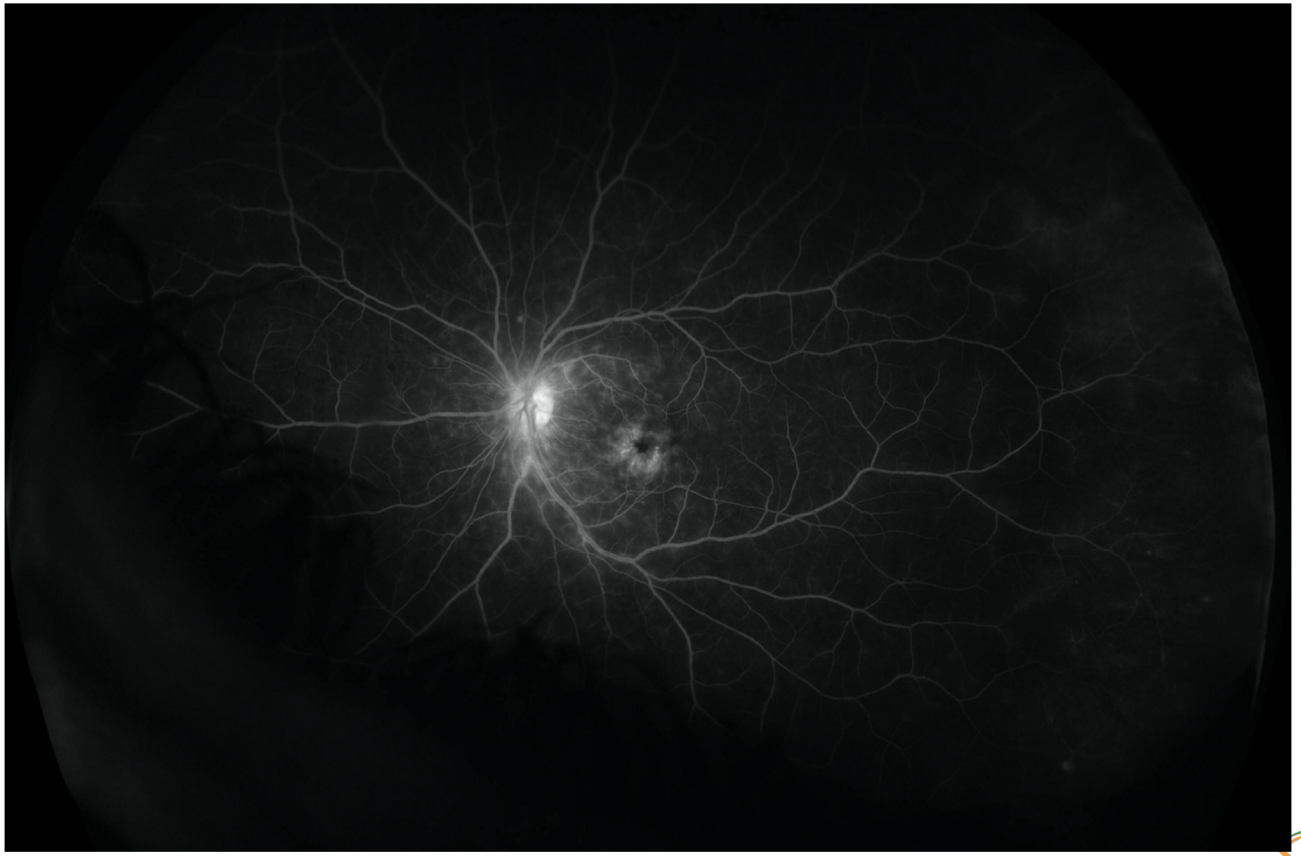
Baseline IOP: 9 OD, 14 OS

Anterior Segment: 2+ anterior chamber cells, 2+ flare, posterior synechiae from 4-10, Few brown granulomatous KPs inferior OS

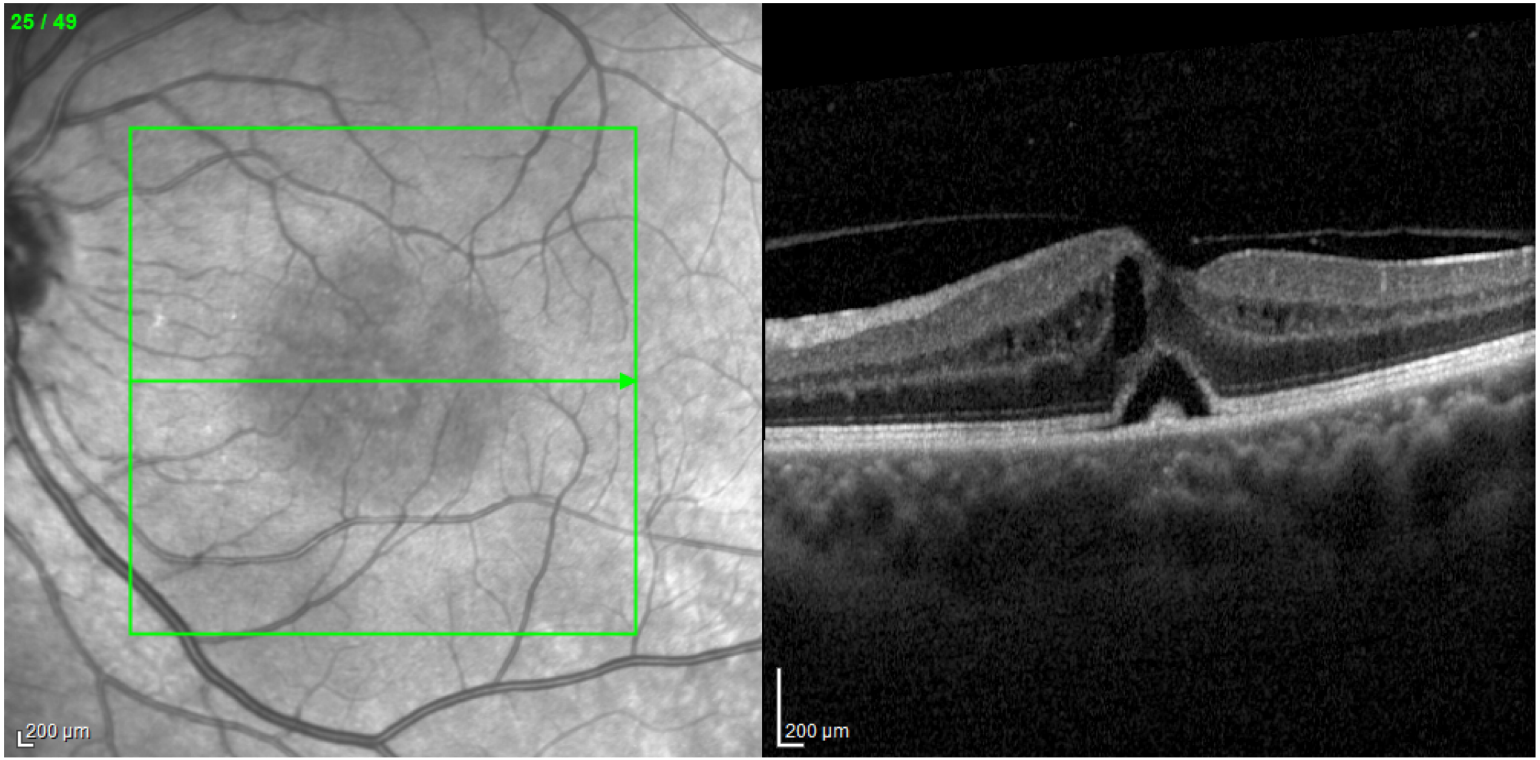
Posterior Segment: 1+ vitreous cells, 1+ vitreous haze, Few inferior snowballs, No chorioretinal lesions OS

"Cataract" includes (a) cataract, (b) cataract subcapsular, and (c) cataract nuclear.

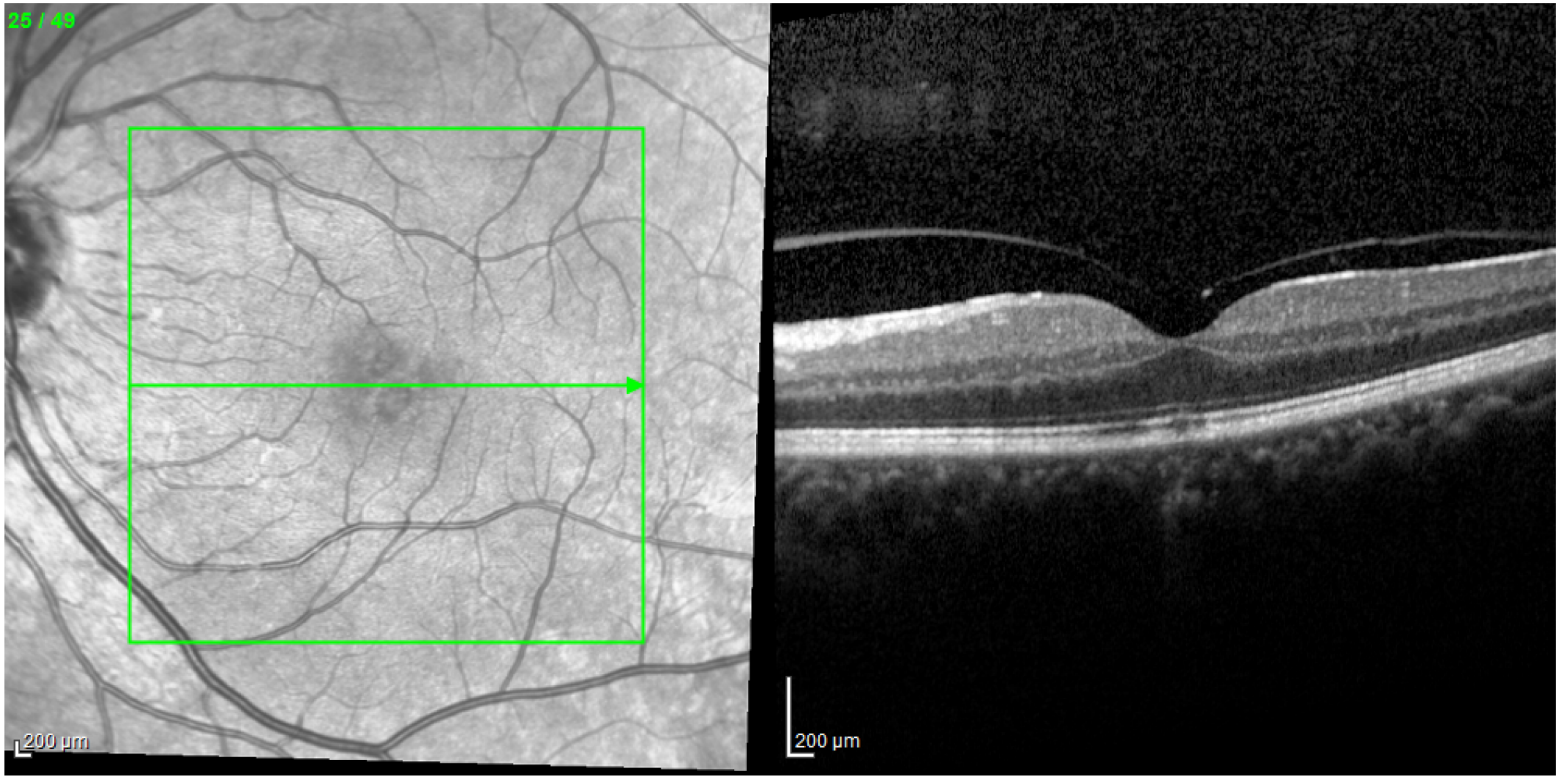
Baseline: 20/40 OS, CST 466, IOP 14



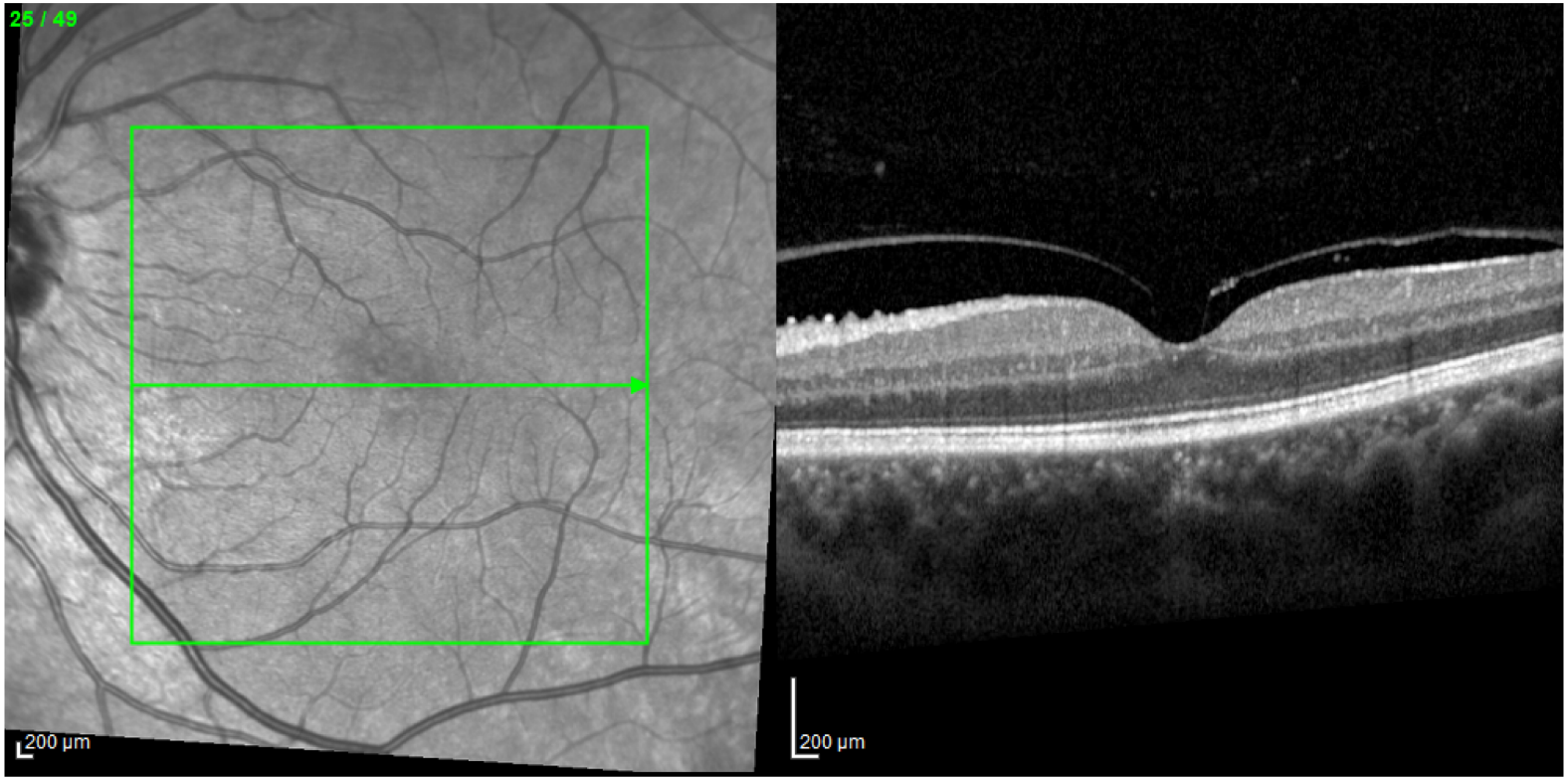
Baseline: 20/40 OS, CST 466, IOP 14



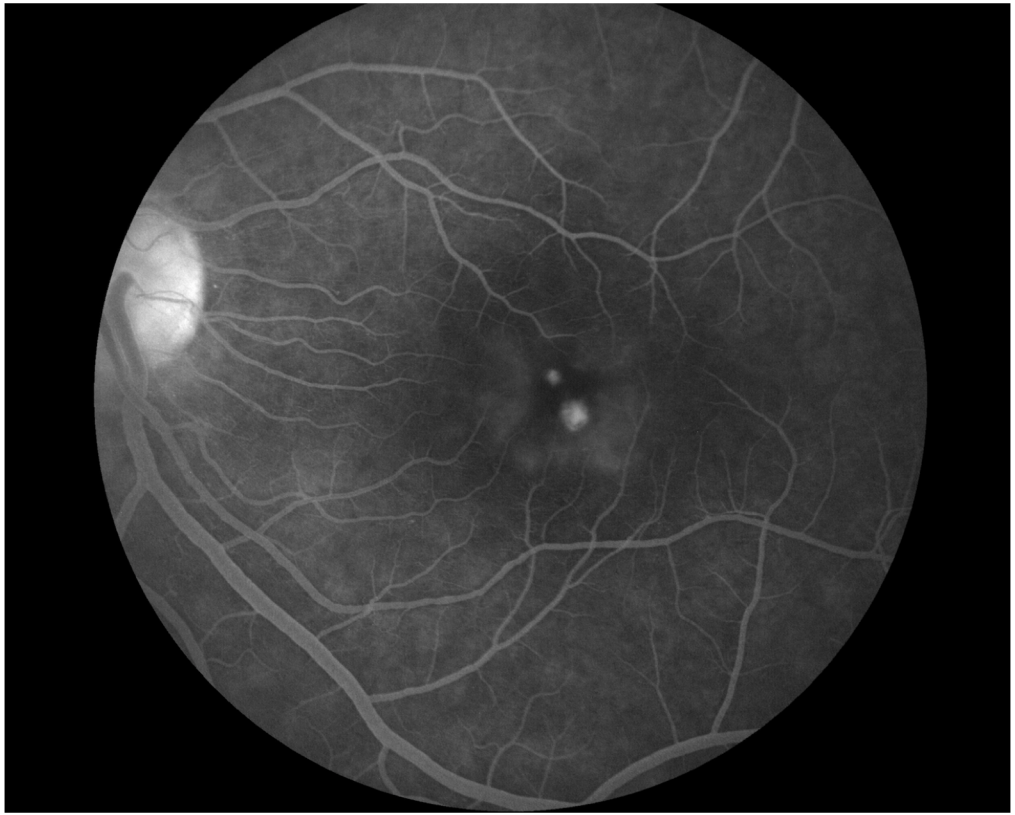
3 months: 20/12.5 OS, CST 315, IOP 10



6 months: 20/12.5 OS, CST 303, IOP 12



6 months: 20/12.5 OS, CST 303, IOP 12



PEACHTREE: Take Home Points

Efficacy

- PEACTHREE Primary endpoint was met, with ~47% of patients gaining ≥15 ETDRS letters.
- Suprachoroidally injected CLS-TA significantly improved vision and macular edema.
- Visual acuity and macular edema improved irrespective of the anatomic location of uveitis.
- The majority of CLS-TA patients with active inflammation at baseline had resolution of anterior chamber cells, anterior chamber flare and vitreous haze.

Safety

Low rates of elevated IOP and cataract

Thank You

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