Suprachoroidal CLS-TA Improves Visual Acuity and Macular Edema in Noninfectious Uveitis: Results of the Phase 3 PEACHTREE Study

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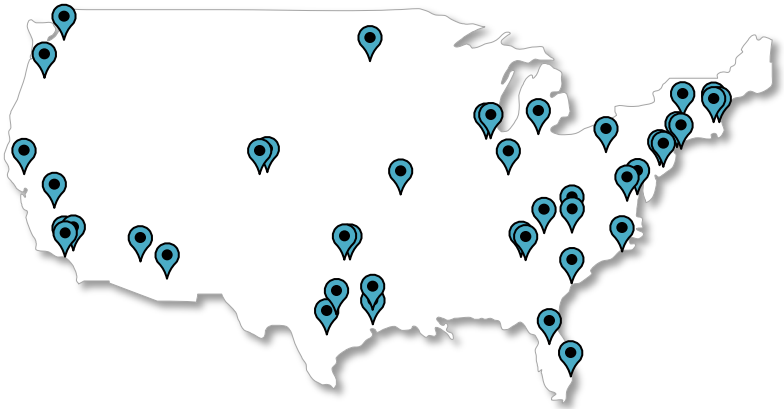
Thank You to the PEACHTREE Investigators!

USA

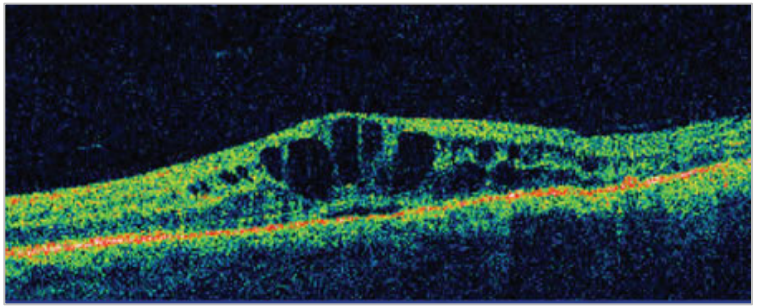


India

Israel

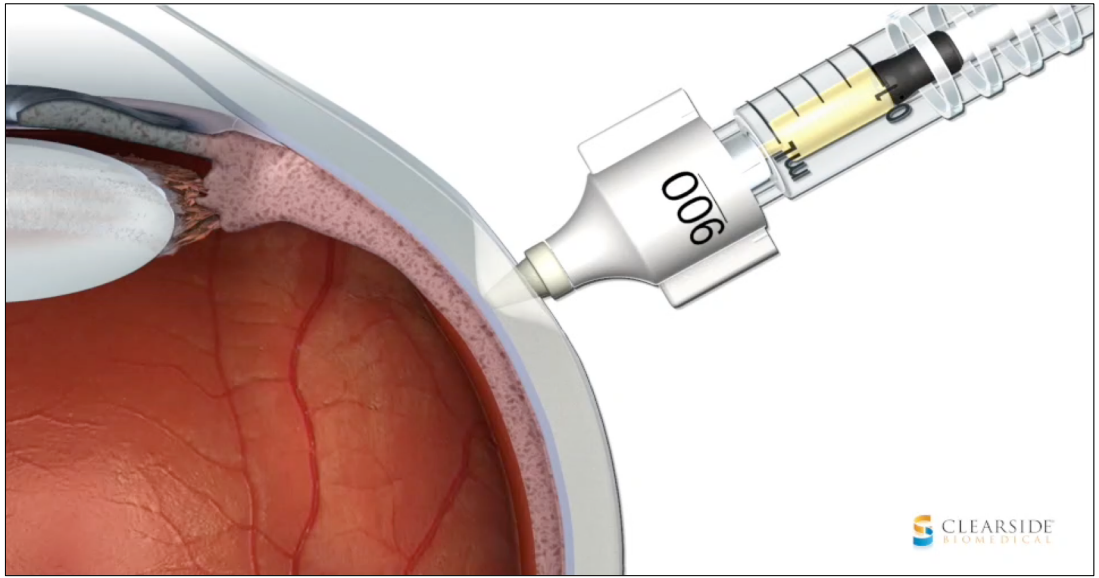
Macular Edema Due to Noninfectious Uveitis

- Macular edema (ME) is the leading cause of vision impairment and vision loss in uveitis[1]
- Commonly observed across anatomic subtypes of uveitis
  - 34-66% of intermediate, posterior, panuveitis
  - 11% of anterior uveitis
- Macular edema may persist despite adequate control of inflammation



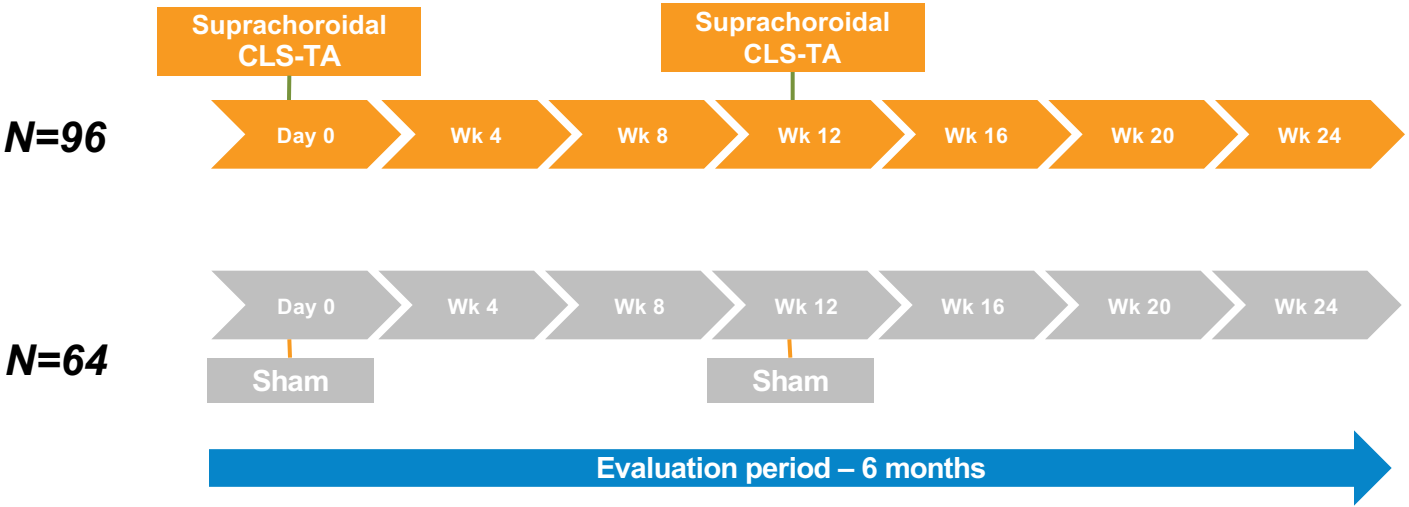
1. Dick AD, *Br J Ophthalmol*. 1994;78:1-2;
2. Lardenoye CWTA et al, *Ophthalmology*. 2006;113:1446-1449;
3. Tomkins-Netzer et al, *Ophthalmology*. 2015;122:2351-2359.

Suprachoroidal Injection for Posterior Segment Disease



- **Favorable drug concentrations:** Retina, RPE, choroid >> Anterior segment
- Potential for uveitic macular edema with fewer side effects

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



Both Arms: Rescue therapy at any time according to pre-specified criteria

- **Primary endpoint:** Proportion of subjects gaining ≥15 ETDRS letters in BCVA at week 24
- 3:2 randomization of suprachoroidal CLS-TA vs. sham procedure

Key Inclusion and Exclusion Criteria

Inclusion

- Macular edema with central subfield thickness ≥300 microns
- Noninfectious uveitis of any associated diagnosis/etiology
- Any anatomic location: anterior, intermediate, posterior and panuveitis
- Disease activity: Active or controlled inflammation
- Visual acuity: 20/800 to 20/40 (≥5 to ≤70 ETDRS letters)

Exclusion

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

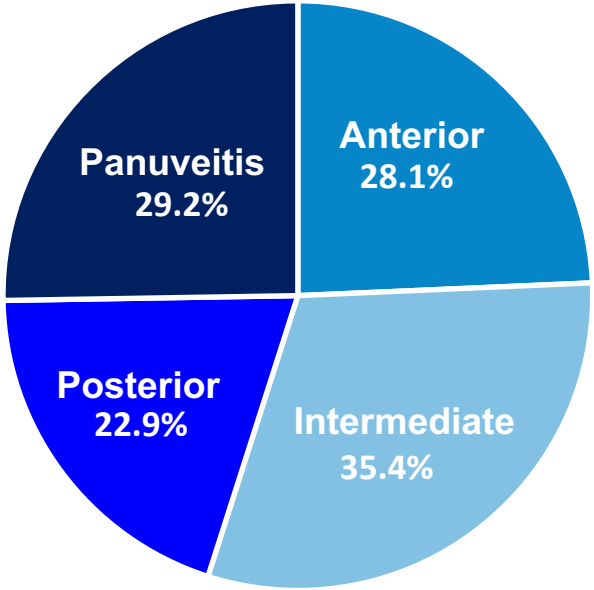
Baseline Subjects Characteristics - Similar Between Treatment Groups

Characteristics	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 (14.2)	50.0 (15.1)	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)

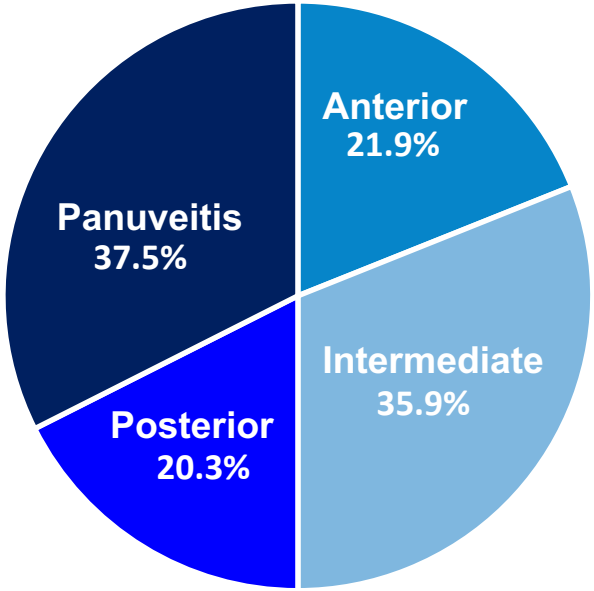
CST: central subfield thickness; ETDRS: Early Treatment Diabetic Retinopathy Study

All Anatomic Subtypes Enrolled

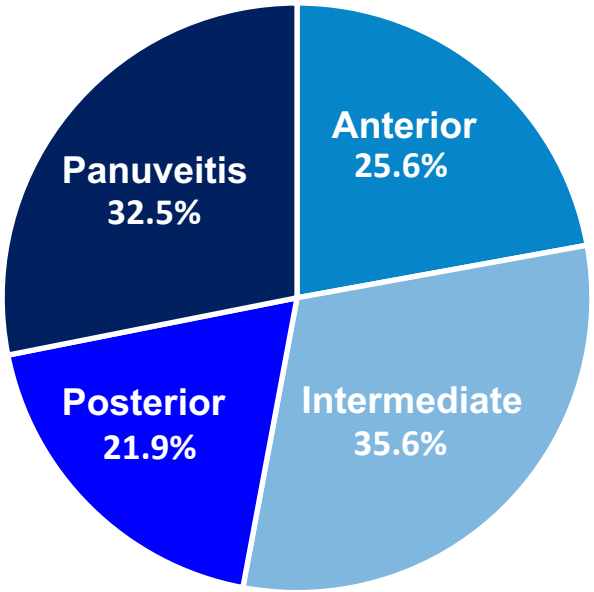
CLS-TA (N=96)



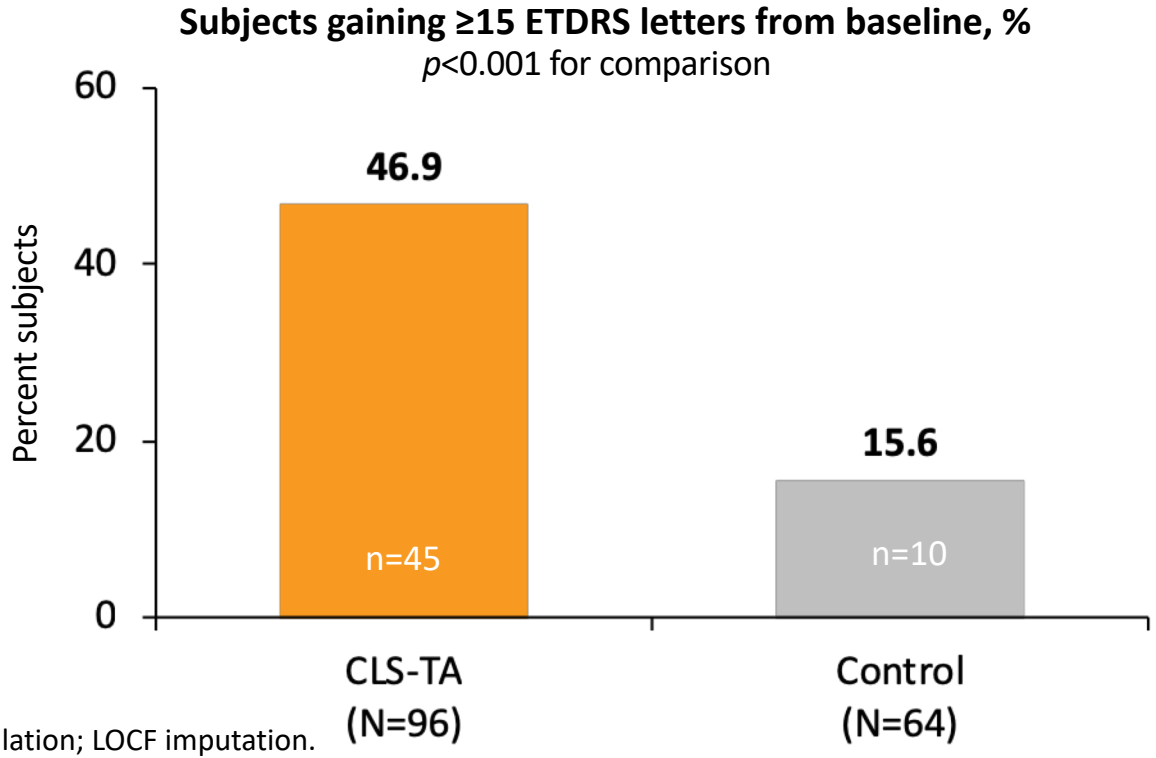
Control (N=64)



Overall (N=160)



PEACHTREE Met Its Primary Efficacy Endpoint

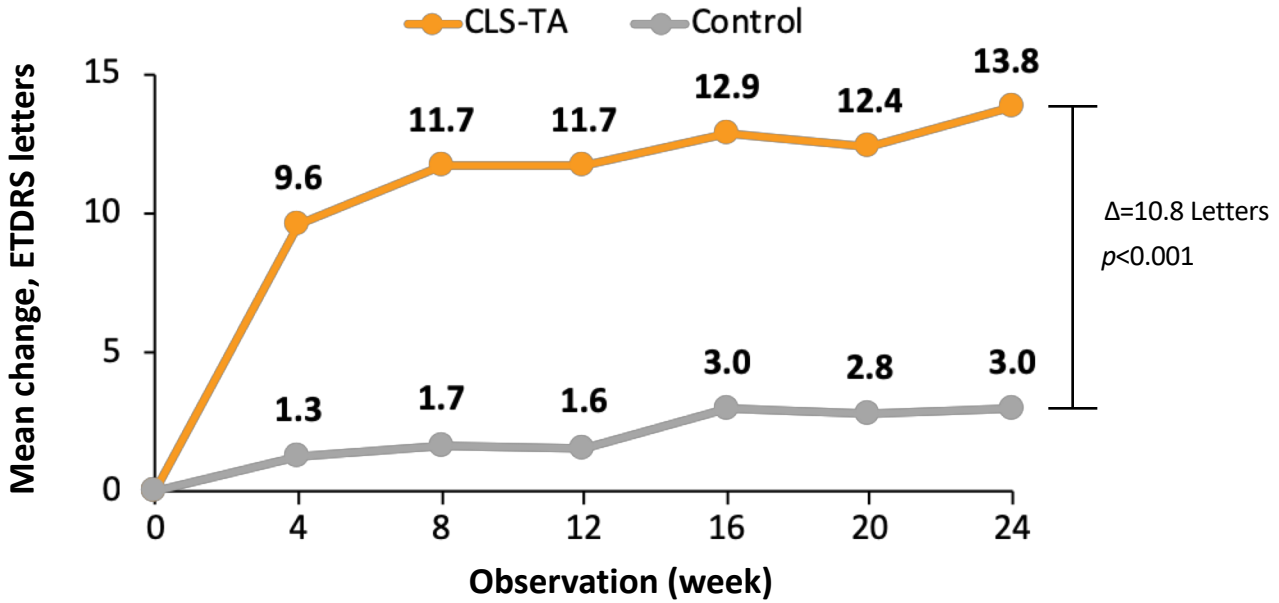


Intention-to-treat population; LOCF imputation.

The *p*-value is based on a CMH 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

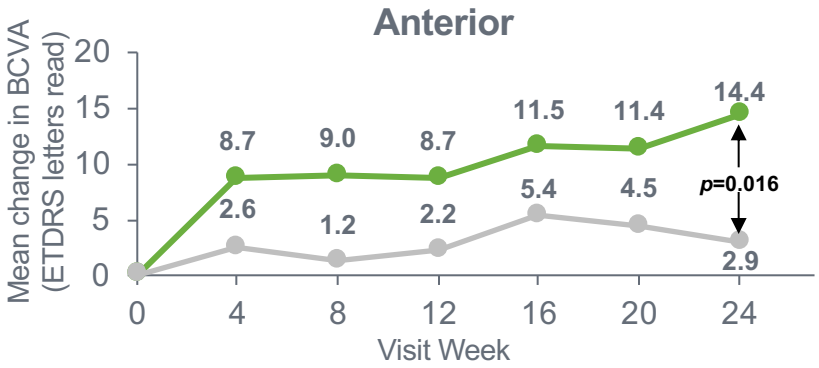


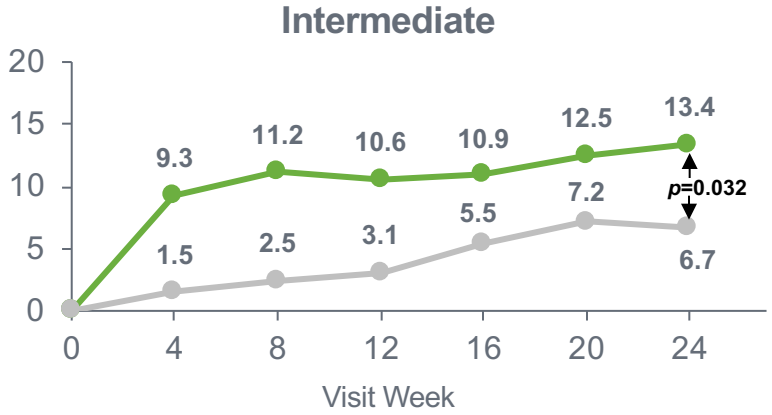
Intention-to-treat population; LOCF imputation.

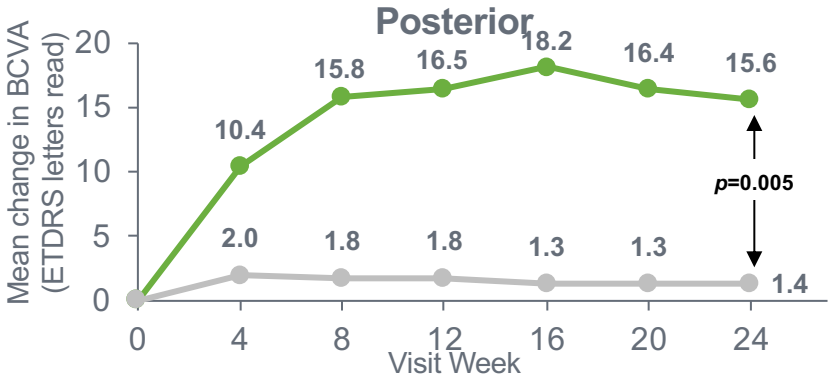
t-test. Differences between the CLS-TA and control arms were significant at each visit.

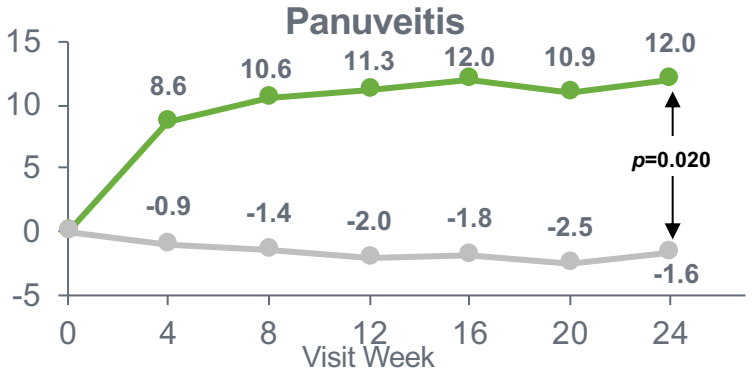
BCVA, best corrected visual acuity.

BCVA Mean Change from Baseline by Anatomic Location



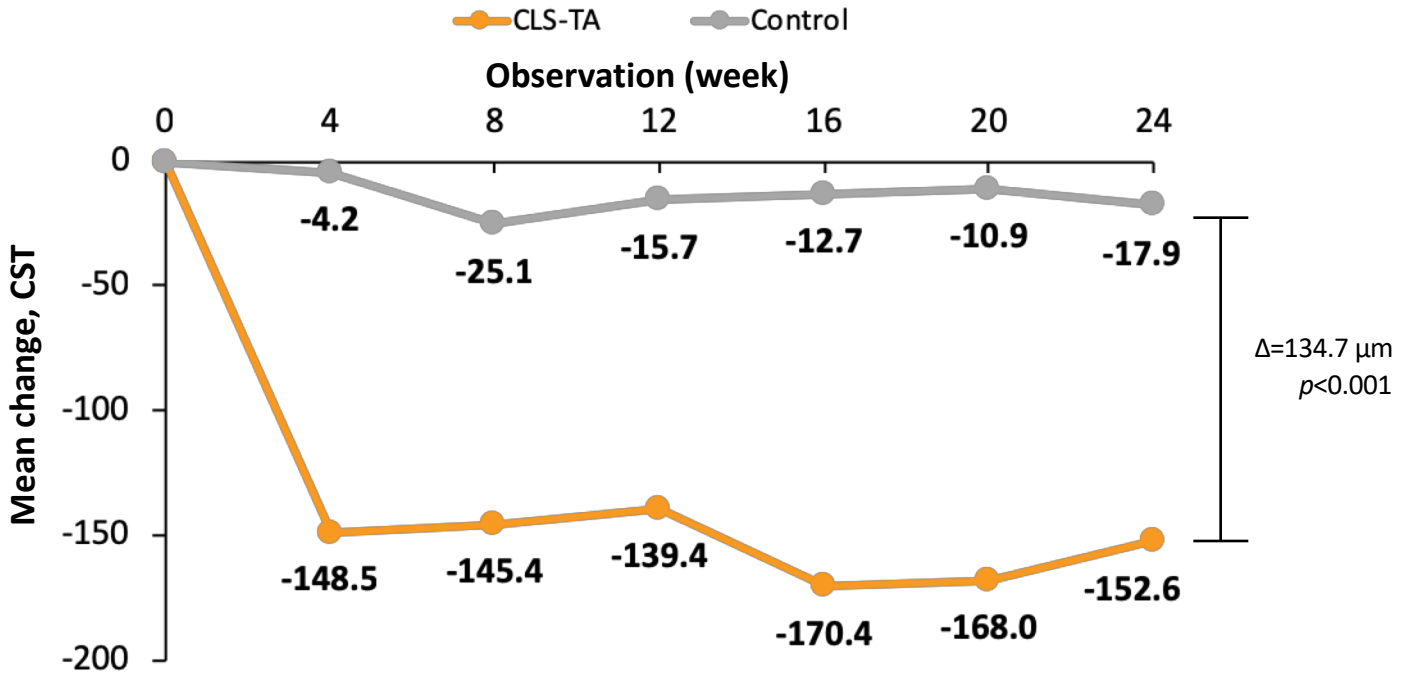






Mean Change in Central Subfield Thickness

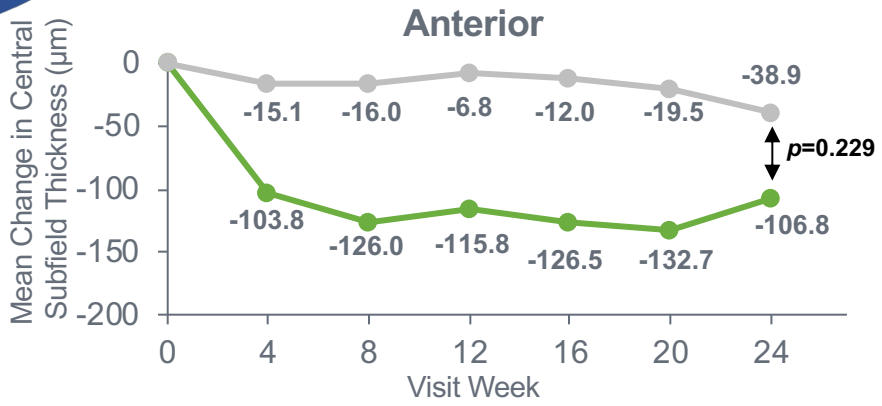
Improvement From as Early as Week 4 through Week 24 in CLS-TA Arm

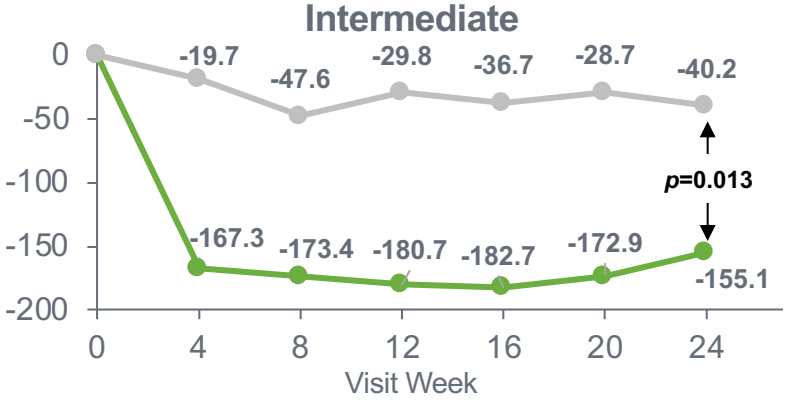


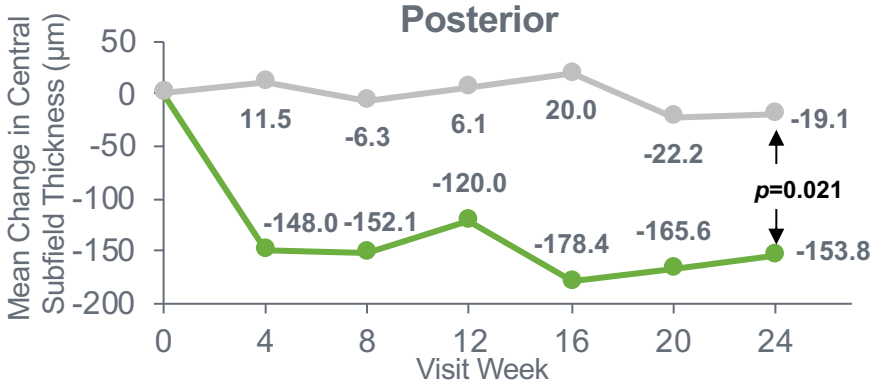
Intention-to-treat population; LOCF imputation.

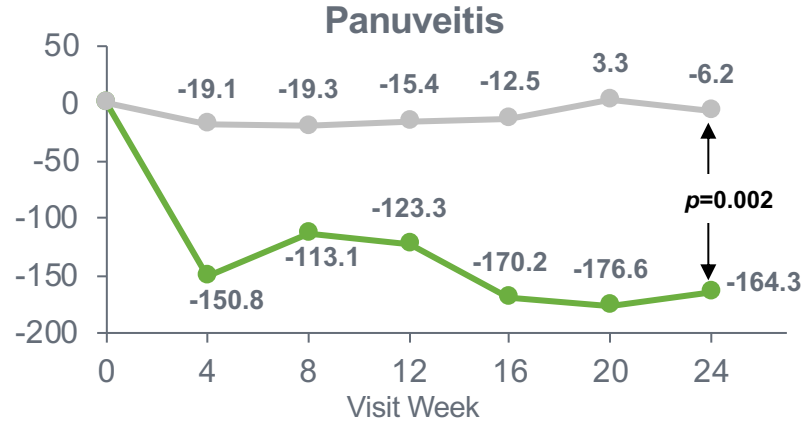
CST, central subfield retinal thickness.

Mean Change from Baseline in CST by Anatomic Location

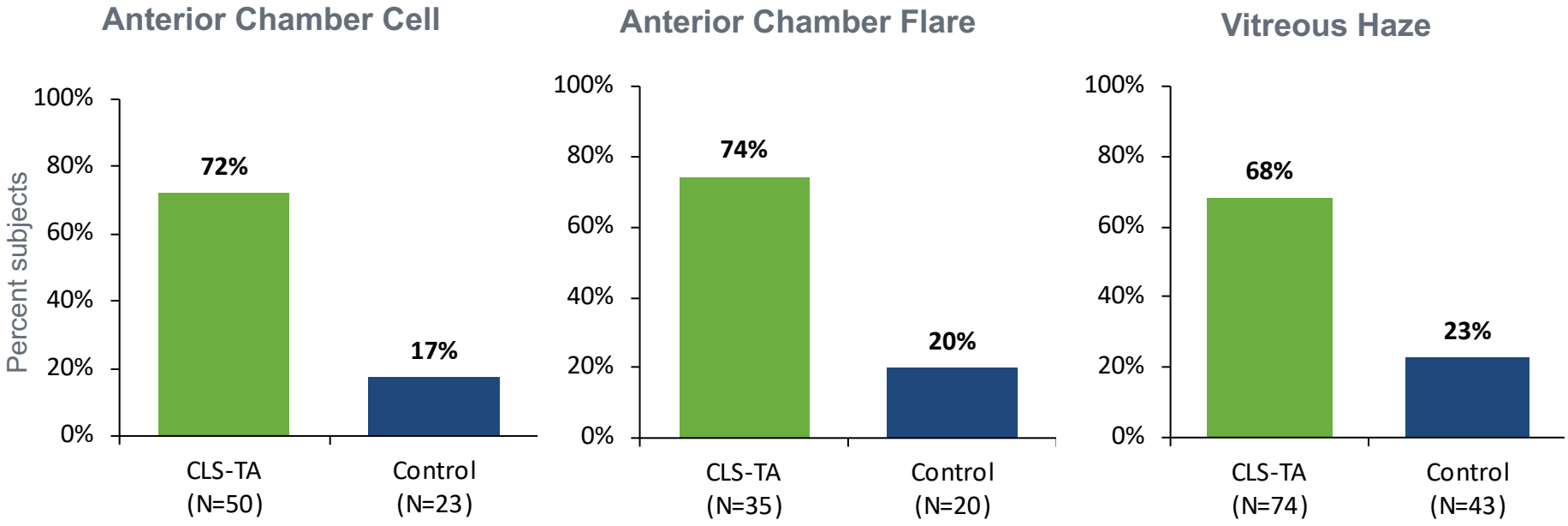






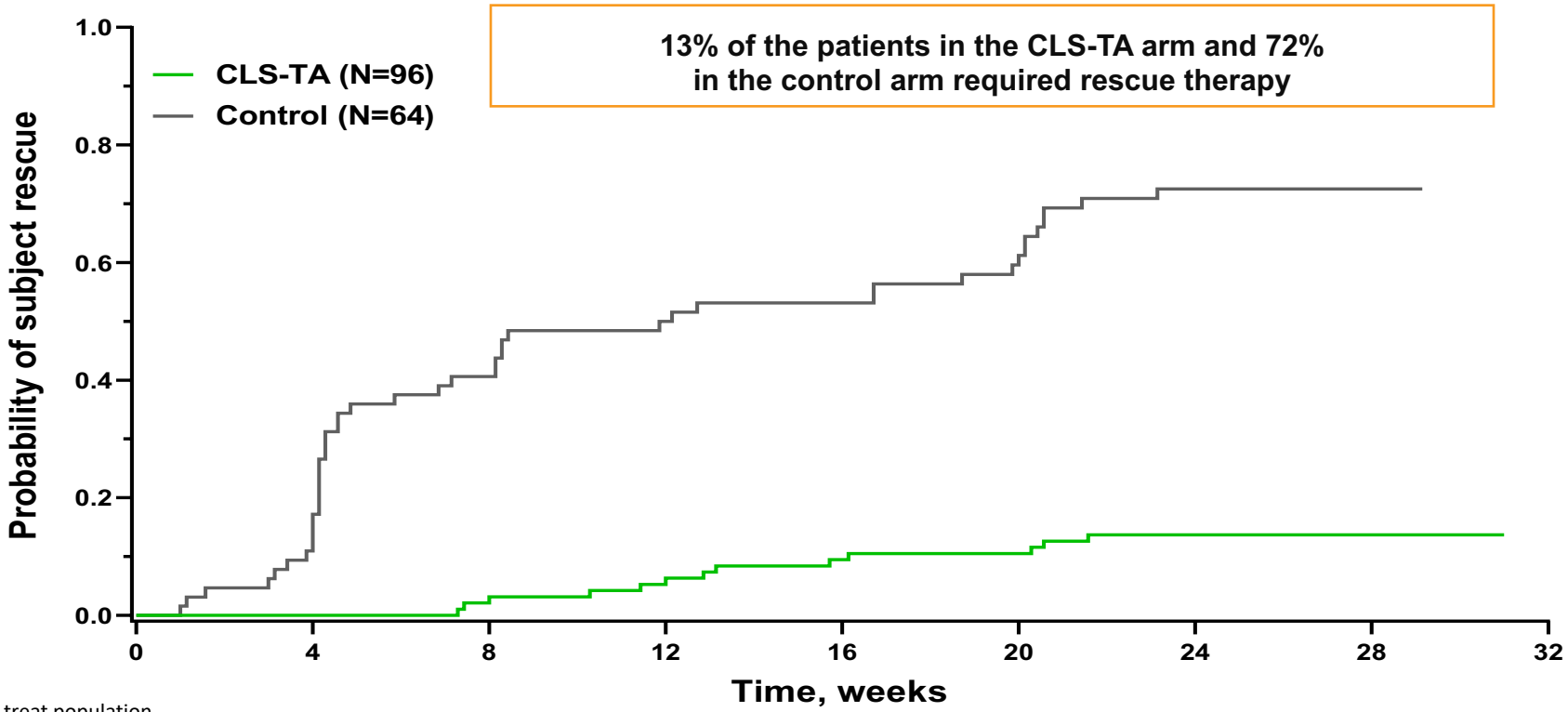


Anterior Chamber and Vitreous Inflammation: % Subjects with Resolution, Week 24



P<0.001 for all comparisons (AC Cell, AC Flare, Vitreous Haze)

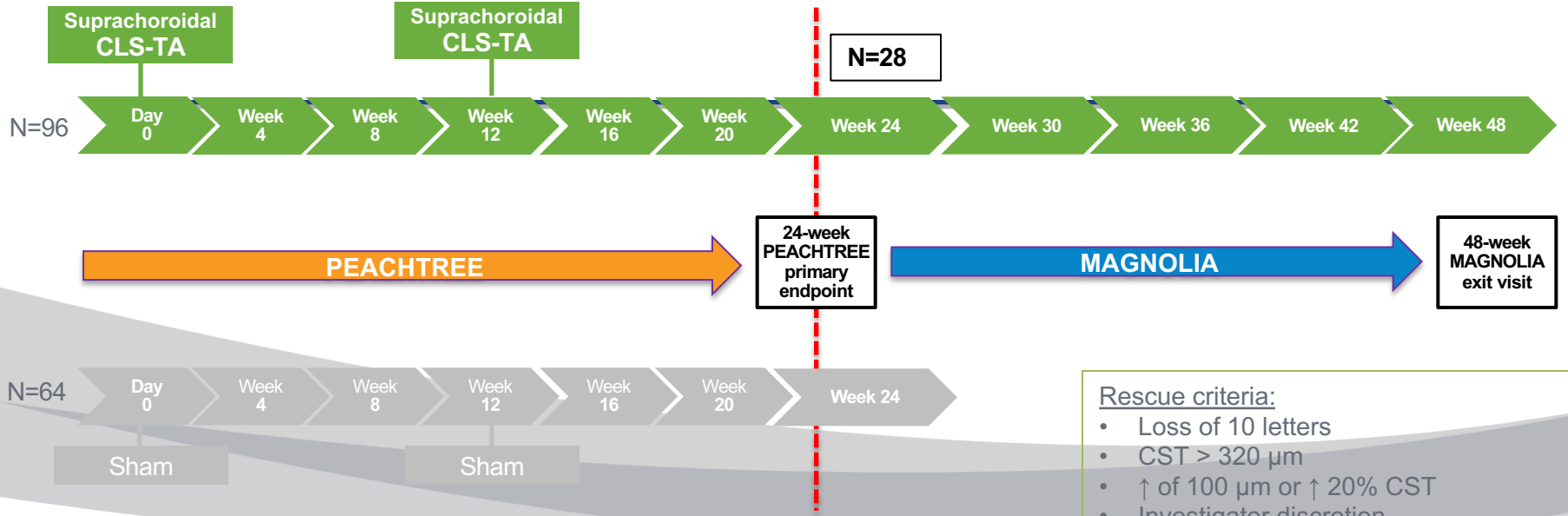
Kaplan-Meier Analysis: Time to Rescue



Intention-to-treat population

MAGNOLIA: Prospective, Non-interventional, Masked, Observational 24-week Extension Trial

- To be eligible for MAGNOLIA, subjects must have completed PEACHTREE and **NOT** have received rescue medication
- Primary Endpoint: Time to rescue therapy relative to Day 0 of PEACHTREE

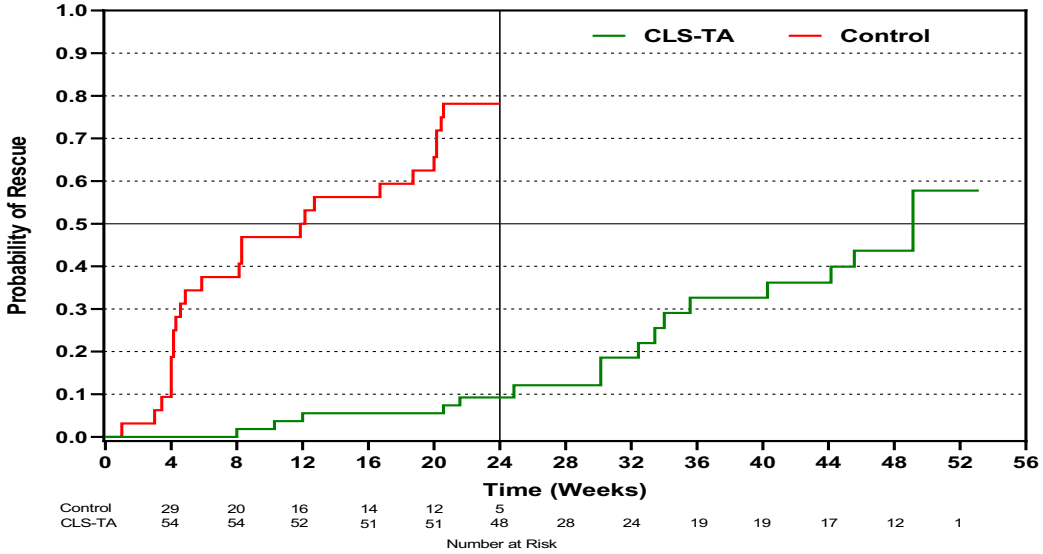


Rescue criteria:

- Loss of 10 letters
- CST > 320 µm
- ↑ of 100 µm or ↑ 20% CST
- Investigator discretion

Kaplan-Meier: Time to First Rescue – Primary Endpoint

PEACHTREE | MAGNOLIA



- 50% of CLS-TA subjects did not receive any additional medication through Week 48
- 9 months from last CLS-TA dose

Safety

Serious AEs

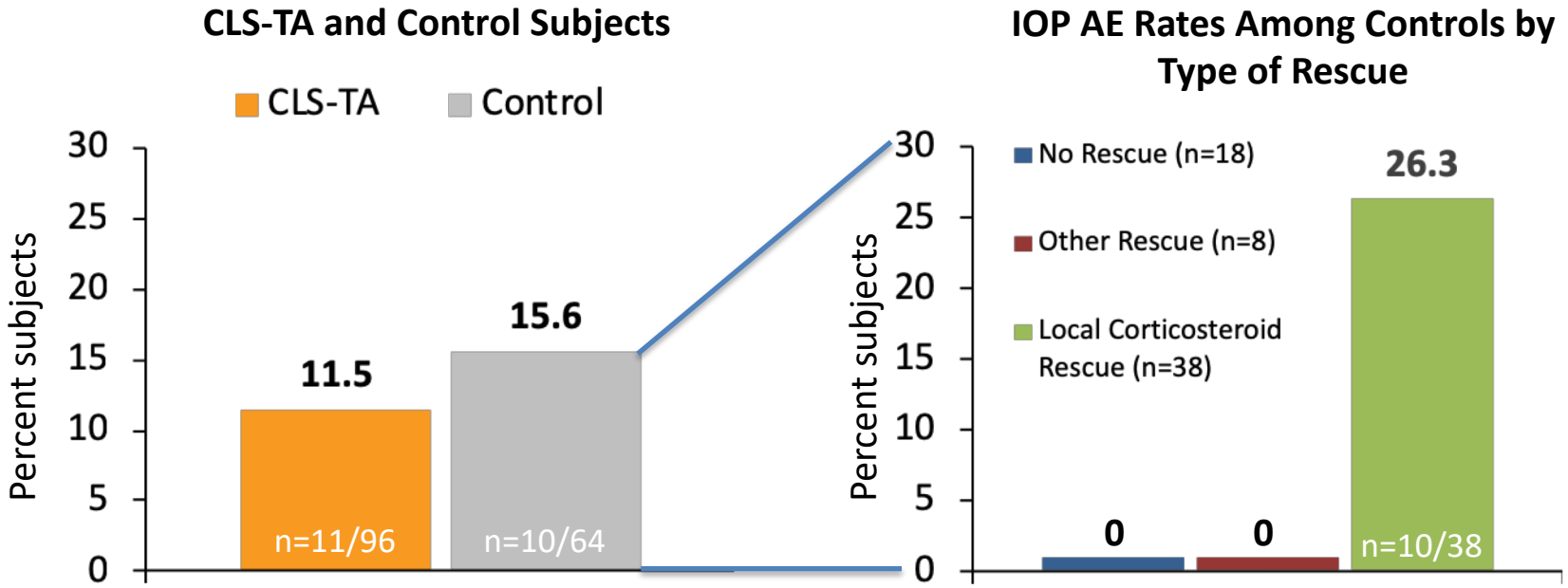
- No deaths
- Three SAEs in CLS-TA arm: none considered treatment-related
  - Two non-ocular (sialoadenitis, lumbar vertebral fracture)
  - One ocular (retinal detachment approximately 8 weeks after injection)

Ocular AEs, 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)

Ocular AEs

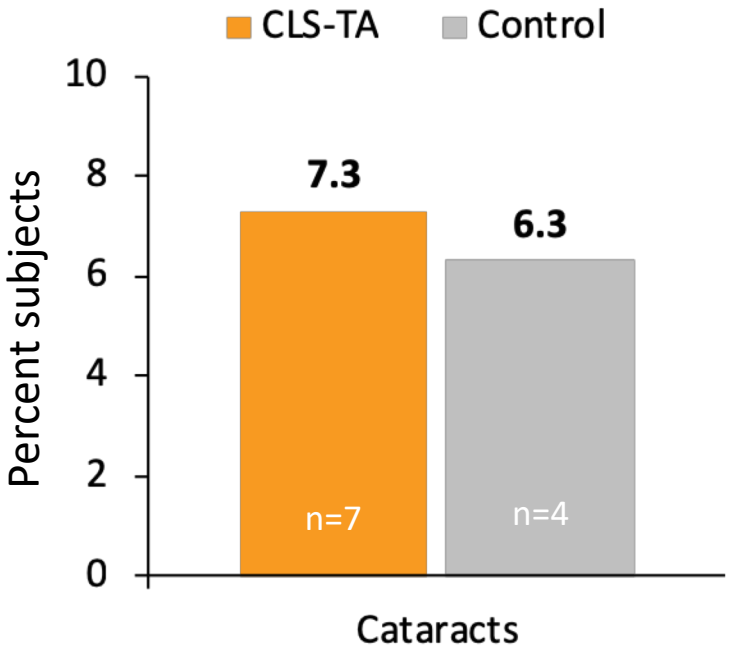
- AEs occurring in >5% subjects in the CLS-TA arm included: elevated IOP, eye pain, cataract

Elevated IOP Adverse Events



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

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) cataract subcapsular, and (c) cataract nuclear.

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 uveitis at all anatomical locations
- Anterior segment and vitreous inflammation resolved in the majority of CLS-TA patients

Safety

- Low rates of elevated IOP and cataract
- No SAEs attributed to CLS-TA

THANK YOU