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Suprachoroidal Administration of Triamcinolone Acetonide (CLS-TA) for the Treatment of Macular Edema in Noninfectious Uveitis: Pooled Results of Three Clinical Trials

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Disclosures

Consultant:

- Abbvie
- Clearside
- EyeGate
- EyePoint
- Eyevensys
- Gilead
- Santen

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- Abbvie
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Purpose

To conduct a post-hoc evaluation of resolution of macular edema following suprachoroidally injected CLS-TA across 3 prospective, multicenter, clinical trials in patients with noninfectious uveitis

- Macular edema is the most common cause of vision impairment in patients with uveitis[1]
- Corticosteroids are commonly used to treat this condition as inflammatory cytokines result in a dysfunctional blood-retinal barrier that results in accumulation of fluid[2]
- The cumulative effect of chronic uveitis and the recurrence or persistence of macular edema can result in permanent tissue damage and irreversible vision loss[3]

1. Rothova et al. Causes and frequency of blindness in patients with intraocular inflammatory disease. Br J of Ophthalmology 1996; 80:332-336.
2. Lardenoye et al. Impact of Macular Edema on Visual Acuity in Uveitis. Ophthalmology 2006; 113:1446-1449.
3. Durrani et al. Degree, duration, and causes of visual loss in uveitis. Br J of Ophthalmology 2004; 88:1159-1162.

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Mechanisms for Local Corticosteroid Administration

Challenges exist with current methods to locally administer steroids

- Incomplete and/or inconsistent delivery
- Side effect profile: IOP elevation and cataract formation
  - 39-50% develop secondary ocular hypertension and elevated IOP ranges between 20-65% with IVT TA[1]
  - 22% require IOP lowering medications and 12% require IOP-lowering surgery with Periocular TA[2]
  - 20% require IOP-lowering medications and 6% require IOP-lowering surgery with IVT TA[2]
  - 24% require IOP-lowering medications and 15% required IOP-lowering surgery with IVT Dexamethasone Implant[2]

Suprachoroidal administration is a novel treatment approach for the eye

- In preclinical animal models, drug administered suprachoroidally had high posterior tissue bioavailability
  - Drug distributes preferentially to the choroid and retina
  - Drug level in the anterior segment is minimal
  - Comparable resolution of inflammation observed with as little as 1/10th of intravitreal steroid dose

1. Razeghineja *et al.* Steroid-induced iatrogenic glaucoma. *Ophthalmic Res*. 2012;47(2):66-80.
2. Thorne *et al*. Periocular TA vs. Intravitreal TA vs. Dexamethasone Implant for the treatment of Uveitic Macular Edema: The POINT Trial. Opthalmology. 2018:1-13

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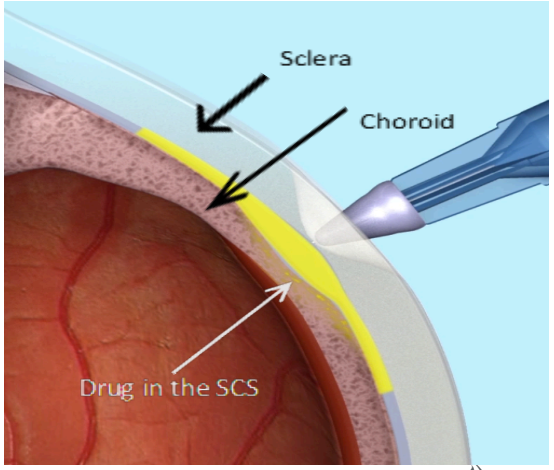
Suprachoroidal Administration for Treatment of Noninfectious Uveitis

Suprachoroidal injection could become a useful approach for the treatment of ocular conditions affecting the posterior segment of the eye

- Novel technique developed for suprachoroidal injection utilizing a proprietary microinjector syringe device
  - 30g needle approximately 900 or 1100 µm in length

- Proposed benefits of suprachoroidal corticosteroid
  - Efficacy advantages due to high bioavailability
  - Maintains durability of effect
  - Fewer side effects as TA substantially spares anterior structures



In three distinct trials using suprachoroidal CLS-TA to treat ME secondary to noninfectious uveitis, consistent efficacy was observed with a reasonable safety profile

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Suprachoroidal Corticosteroid Noninfectious Uveitis Trials

- **DOGWOOD - Randomized Phase 2 Trial**
  - 8 weeks / 22 subjects
    - CLS-TA 4.0 mg N = 17; CLS-TA 0.8 mg N = 5

- **PEACHTREE - Randomized Phase 3 Trial**
  - 24 weeks / 160 subjects
    - CLS-TA 4.0 mg N = 96; Sham N = 64

- **AZALEA - Open-Label Phase 3 Trial**
  - 24 weeks / 38 subjects received CLS-TA 4.0 mg

- A single SC injection of CLS-TA was given at baseline in each study.

- In *PEACHTREE* and *AZALEA* that ran 24 weeks; the protocols mandated a second SC injection of CLS-TA at week 12. No additional medication was administered from week 12 through week 24.

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DOGWOOD, PEACHTREE, And AZALEA Studies

- Reduction in retinal thickness in subjects with ME secondary to noninfectious uveitis was evaluated following suprachoroidal injection of 4 mg of CLS-TA
  - For this post-hoc analysis, macular edema resolution was defined as a retinal thickness <300 microns by SD-OCT

- Subjects were evaluated for the presence of intraretinal and subretinal fluid every 4 weeks through week 24

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Demographics – ME Resolution Analysis

Baseline	DOGWOOD CLS-TA 4.0 mg N = 16	AZALEA CLS-TA 4.0 mg N = 20	PEACHTREE CLS-TA 4.0 mg N = 96	PEACHTREE Sham Control N = 64
Age in years Mean (SD)	51.8 (20.2)	56.3 (14.5)	50.4 (14.2)	50 (15.1)
Females	50%	60%	56%	53%
Duration of uveitis in months Mean (SD)	69 (81)	32 (35)	44 (59)	27 (34)
CST in µm Mean (SD)	537 (128.8)	399 (64.9)	480.9 (153.2)	525.4 (158.1)
ETDRS letters read Mean (SD)	60.5 (13.4)	65.7 (21.7)	54.7 (13.9)	53.5 (12.9)

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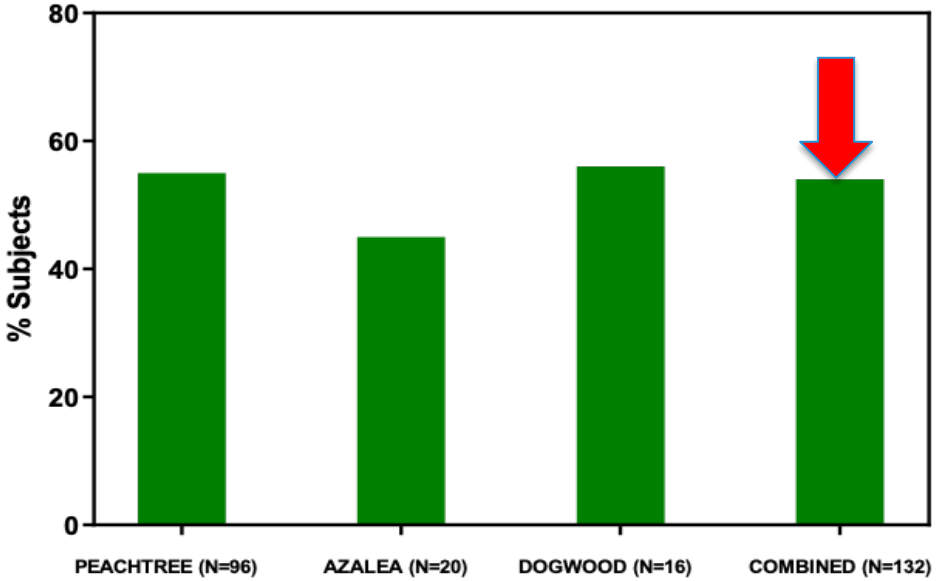
Resolution in a Majority of Patients is Observed Rapidly

Percentage of patients with resolution of macular edema at **Week 4**
(individual study data and *combined* data)



Data are consistent across the three studies, showing that approximately 50% of patients are below 300 microns in retinal thickness at 4 weeks.

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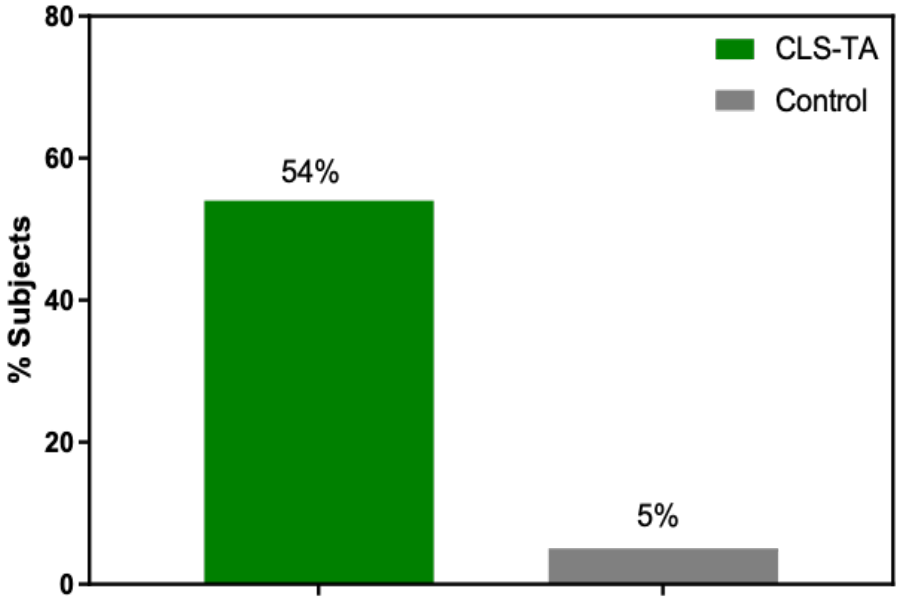
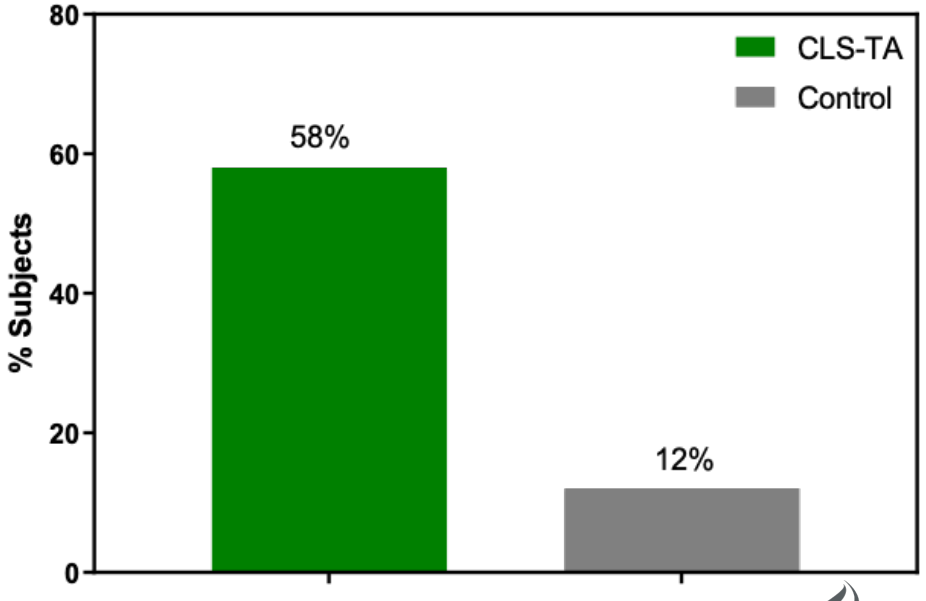
Reduction in Retinal Thickness to < 300 µm at Week 4 and Week 8

Percentage of patients with resolution of macular edema
Week 4



Percentage of patients with resolution of macular edema
Week 8



The effect of suprachoroidal CLS-TA on CST appears to be rapid.

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PEACHTREE and AZALEA were 24-Week Trials

- A protocol mandated second injection of CLS-TA was administered at week 12 only in PEACHTREE and AZALEA
  - Injection was administered despite over 50% of the patients in these trials showing resolution of ME and having improved vision at this time point

- After the 2nd CLS-TA injection at week 12, no additional CLS-TA was administered to these patients through week 24

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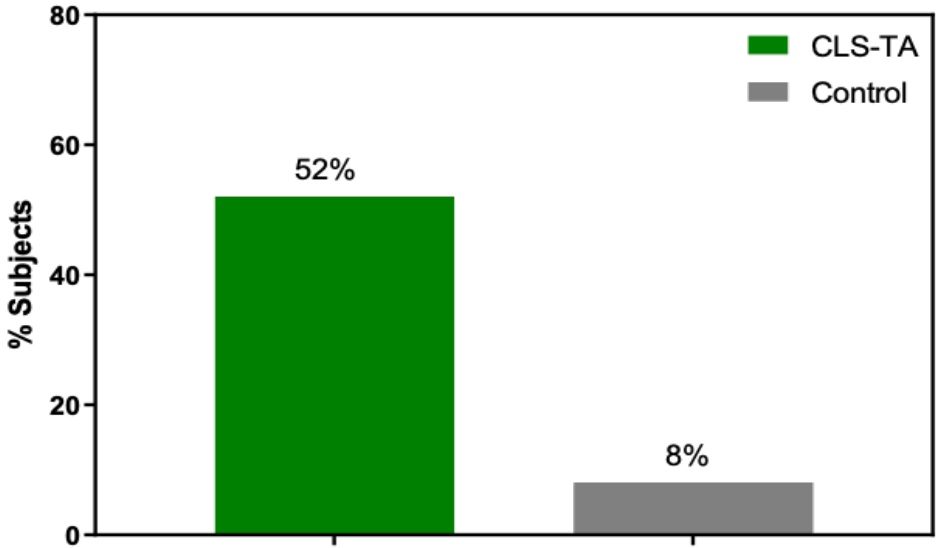
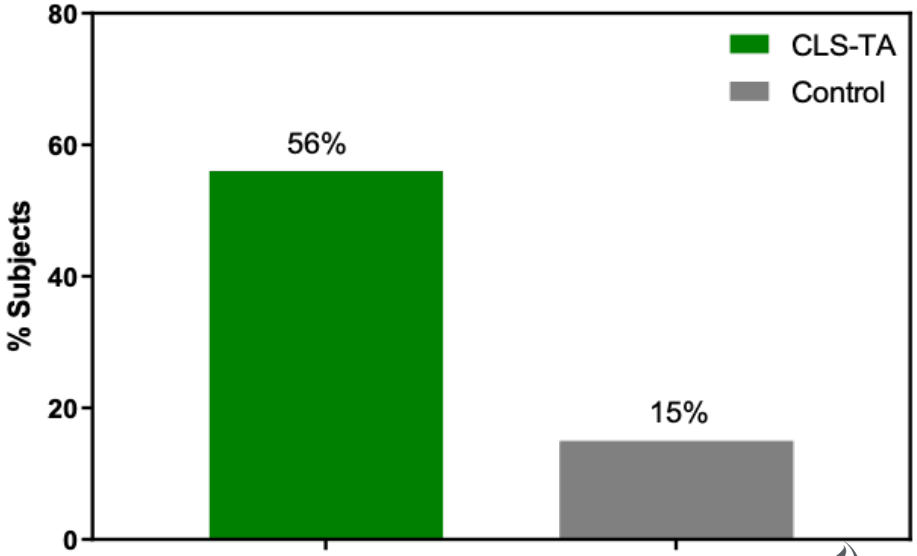
Reduction in Retinal Thickness to < 300 µm at Week 12 and Week 24

Percentage of patients with resolution of macular edema
Week 12



Percentage of patients with resolution of macular edema
Week 24



The effect of suprachoroidal CLS-TA on CST appears to be sustained through week 12 with no additional CLS-TA administered.

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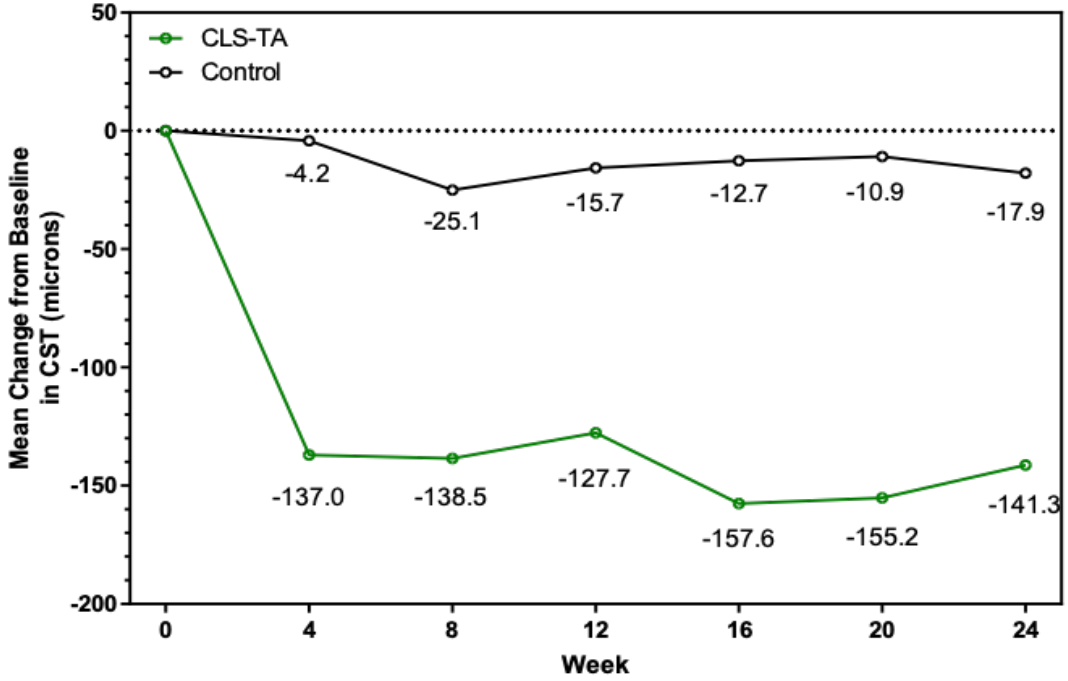
Mean Change in CST through Week 24



The rapid reduction in retinal thickness in a majority of patients, first observed at week 4, is sustained at each observation through 24 weeks.

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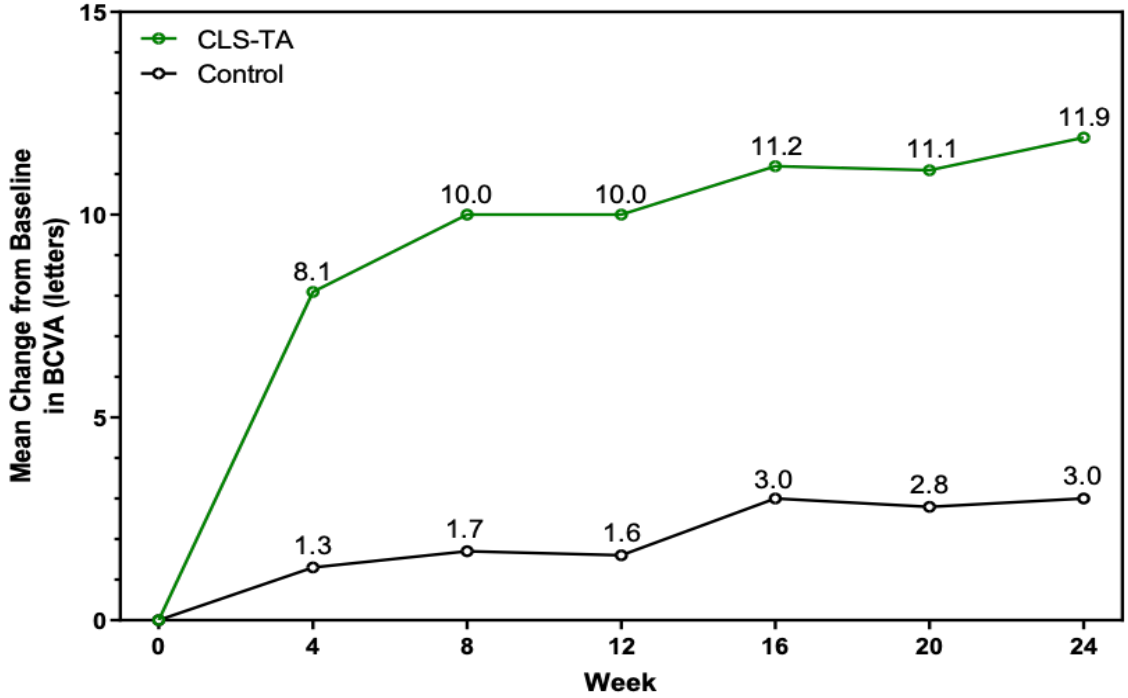
Mean Change in ETDRS BCVA Letters through Week 24



Similar to the reductions in retinal thickness, improvements in BCVA are rapid and sustained through week 24.

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PEACHTREE: Summary of Adverse Reactions

n (%)	CLS-TA 4.0 mg N=96	Control N=64
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
Cataract**	7 (7.3)	4 (6.3)

*Based on elevated intraocular pressure adverse reactions
**Includes adverse event reports of cataract, cataract cortical, and cataract subcapsular; no subject required cataract surgery due to AE
***IOP lowering medications administered for 30 days or more
Safety population; includes subjects in the control group who received rescue medication

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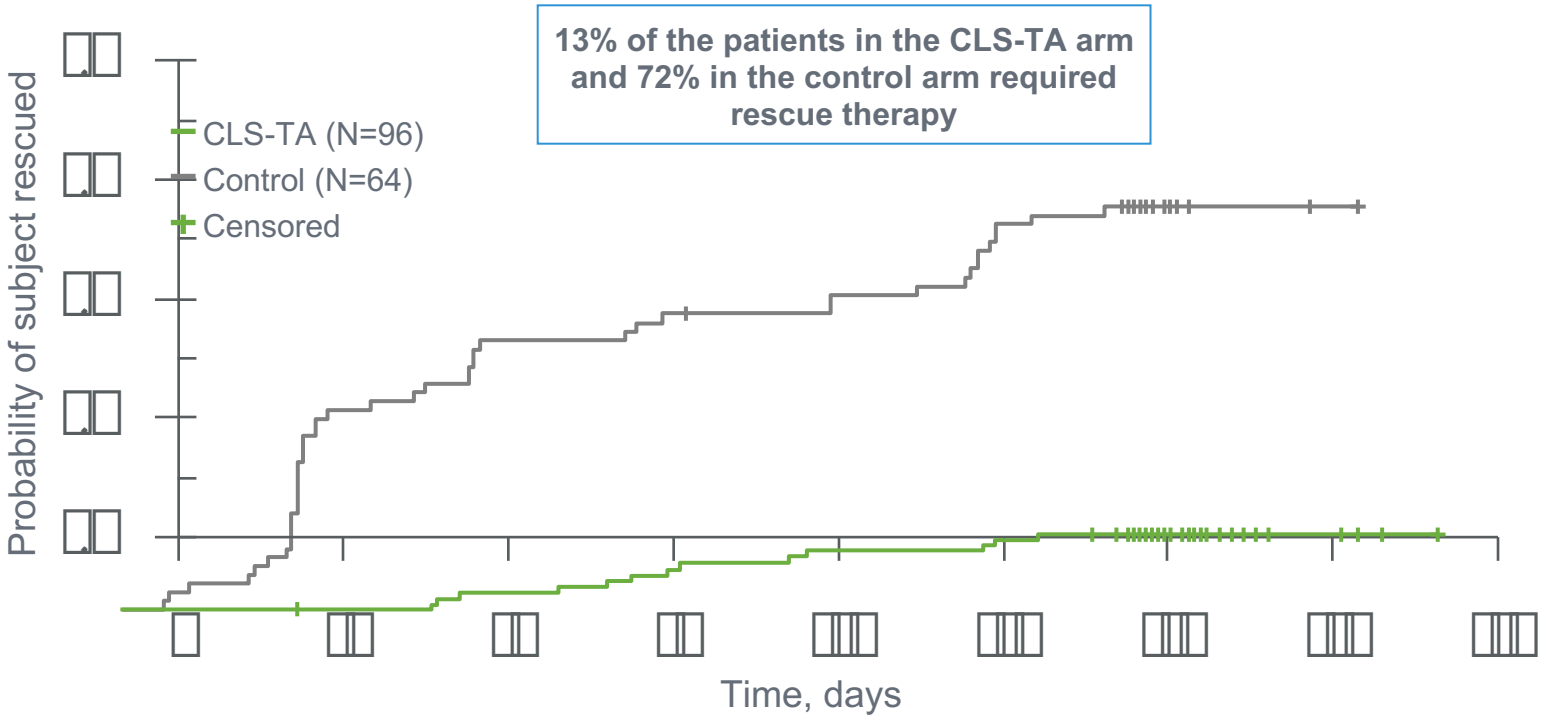
PEACHTREE: Kaplan Meier Time to Rescue



Intention-to-treat population

SC CLS-TA in Uveitis Macular Edema Analysis of 3 Clinical Trials: Summary

> 50% patients	• Resolution of ME at Week 4
> 50% patients	• Sustained effect at Week 12
> 50% patients	• No ME at Week 24 (12 weeks after 2nd injection*)
> 10 ETDRS letters gain	• At 24 weeks

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Key Findings

- Use of CLS-TA to treat macular edema secondary to noninfectious uveitis results in a rapid (by week 4) reduction in retinal thickness
  - Resolution observed in over 50% of subjects following a single suprachoroidal injection

- Rapid resolution is sustained in a majority of patients through week 12 with no additional CLS-TA (or other treatment) administered
- A protocol mandated second injection of CLS-TA was administered at week 12 in two of the studies, PEACHTREE and AZALEA
  - Evaluation of the data show that over 50% of the patients in each of these trials showed resolution of ME and improved vision at this time point prior to the second injection
  - Data observed through Week 24 reveal a majority of patients continued to show macular edema resolution and did not require additional treatment

- Vision improvements are consistent with ME reduction results- approximately 10 ETDRS letters gained from baseline observed at week 24

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Thank You PEACHTREE Investigators!

USA

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Israel

Thank You

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