THE UNIVERSITY OF CHICAGO
MEDICINE & BIOLOGICAL SCIENCES

# Suprachoroidally Injected CLS-TA Results in Rapid and Sustained Resolution of Macular Edema in a Majority of Patients

## *Results of DOGWOOD, PEACHTREE, and AZALEA Studies*


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# Disclosures

- Consultant or Speaker's Bureau
  - Clearside Biomedical, EyePoint Pharmaceuticals, Allergan, Alimera Sciences, Alcon, OD-OS, Novartis, Spark, and Regeneron

# 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 a sensible choice 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 1996
2. Lardenoye 2006
3. Durrani 2004

# Mechanisms for Local Corticosteroid Administration

## Challenges exist with all current methods to locally administer steroids

- Incomplete delivery
- Inconsistent delivery
  - Uncertain concentration of TA suspensions in syringe when preparing drug
  - Amount of drug diffusing to retina and choroid is uncertain
- Side effect profile: IOP elevation and cataract formation
  - 35–39% develop a moderate IOP elevation with TA[1]
  - 1–5% develop a significant IOP elevation requiring IOP lowering surgery[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 efficacy is found with as little as 1/10$^{th}$ of intravitreal steroid dose

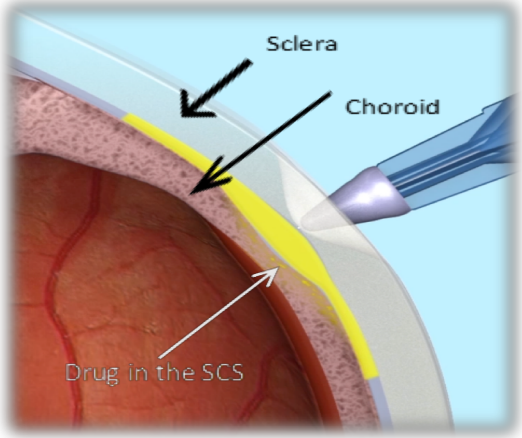


1. Razeghineja MR *et al.* Steroid-induced iatrogenic glaucoma. *Ophthalmic Res.* 2012;47(2):66-80.
2. Becker B. Intraocular pressure response to topical corticosteroids. *Invest Ophthalmol.* 1965;4:198-205.

# 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 1000 µm in length
- Proposed benefits of suprachoroidal corticosteroid
  - Efficacy advantages due to high bioavailability
  - Longer duration of effect
  - Fewer side effects as TA substantially spares anterior structures




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

# Suprachoroidal Corticosteroid Noninfectious Uveitis Trials

- **DOGWOOD- Phase 2 Trial**
  - 8 weeks / 22 Patients
- **PEACHTREE- Phase 3**
  - 24 weeks / 160 Patients
- **AZALEA- Phase 3 Trial**
  - 24 weeks / 38 Patients
- A single SC injection of CLS-TA was given at baseline in each study. No additional medication was administered through week 12.
- In *PEACHTREE* and *AZALEA* that ran 24 weeks, a second protocol mandated SC injection of CLS-TA was given at week 12. No additional medication was administered from week 12 through week 24.

# DOGWOOD, PEACHTREE, and AZALEA Studies

- Reduction in retinal thickness in patients with ME secondary to uveitis was evaluated following suprachoroidal injection of 4 mg of CLS-TA
  - For this post-hoc analysis, resolution was defined as a retinal thickness <300 microns by SD-OCT
- Patients were evaluated for the presence of intraretinal and subretinal fluid every 4 weeks through week 24

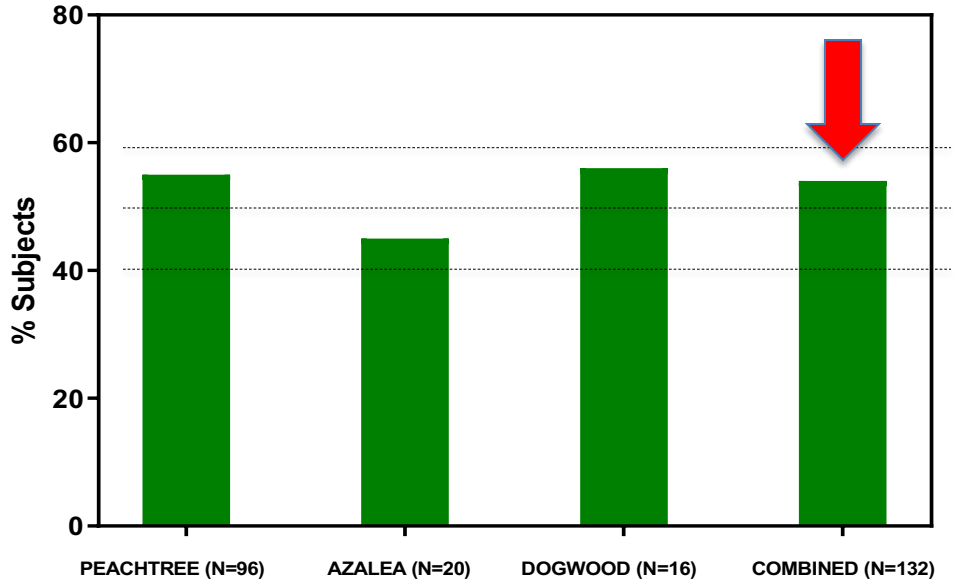
# Demographics

| Baseline | DOGWOOD N = 16 | PEACHTREE N = 160 | AZALEA N = 20 |
|---|---|---|---|
| **Age in years Mean (SD)** | 51.8 (20.2) | 50.2 (14.5) | 56.3 (14.5) |
| **Females** | 50% | 55% | 60% |
| **Duration of uveitis in months Mean (SD)** | 69 (81) | 37 (51) | 32 (35) |
| **CST in µm Mean (SD)** | 537 (128.8) | 499 (156) | 399 (64.9) |
| **ETDRS letters read Mean (SD)** | 60.5 (13.4) | 54.2 (13.5) | 65.7 (21.7) |

# Resolution in a Majority of Patients is Observed Rapidly

Percentage of patients with resolution of macular edema at **week 4**

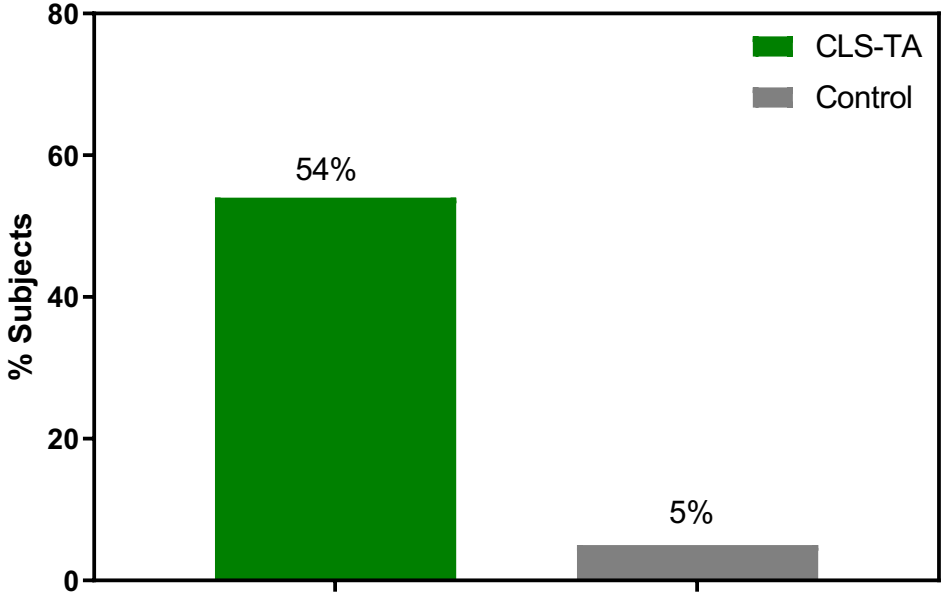
(*individual* study data and *combined* data)




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

# Reduction in Retinal Thickness to <300 µm at Week 4

Percentage of patients with resolution of macular edema at **week 4**



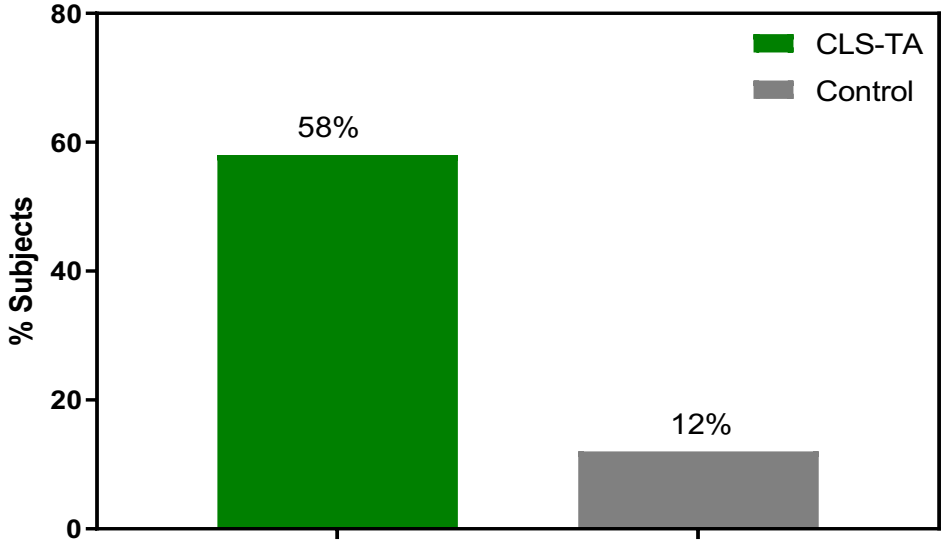

The effect of suprachoroidal CLS-TA on CST appears to be rapid.



CST: central subfield retinal thickness

# Reduction in Retinal Thickness to <300 µm at Week 8

Percentage of patients with resolution of macular edema at **week 8**




The effect of suprachoroidal CLS-TA on CST appears to be sustained through week 8 with no additional CLS-TA administered.



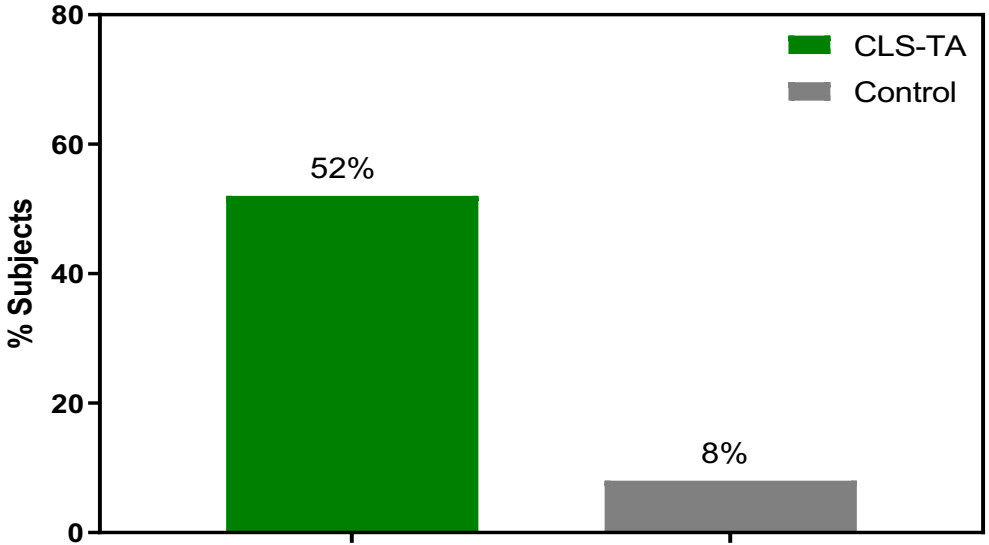
CST: central subfield retinal thickness

# PEACHTREE and AZALEA Trials were 24 Weeks Long

- 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

# Reduction in Retinal Thickness to <300 µm at Week 12

Percentage of patients with resolution of macular edema at **week 12**



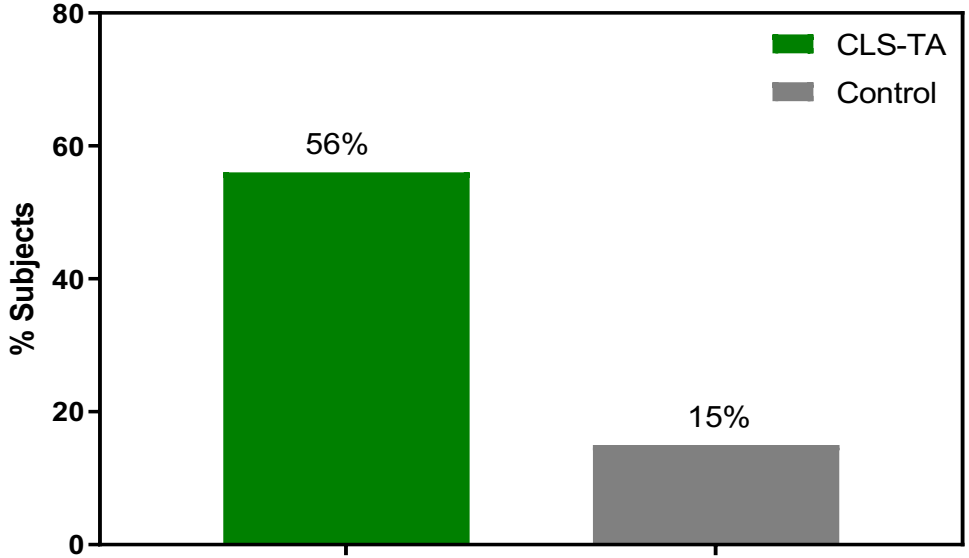

The effect of suprachoroidal CLS-TA on CST appears to be sustained through week 12 with no additional CLS-TA administered.



CST: central subfield retinal thickness

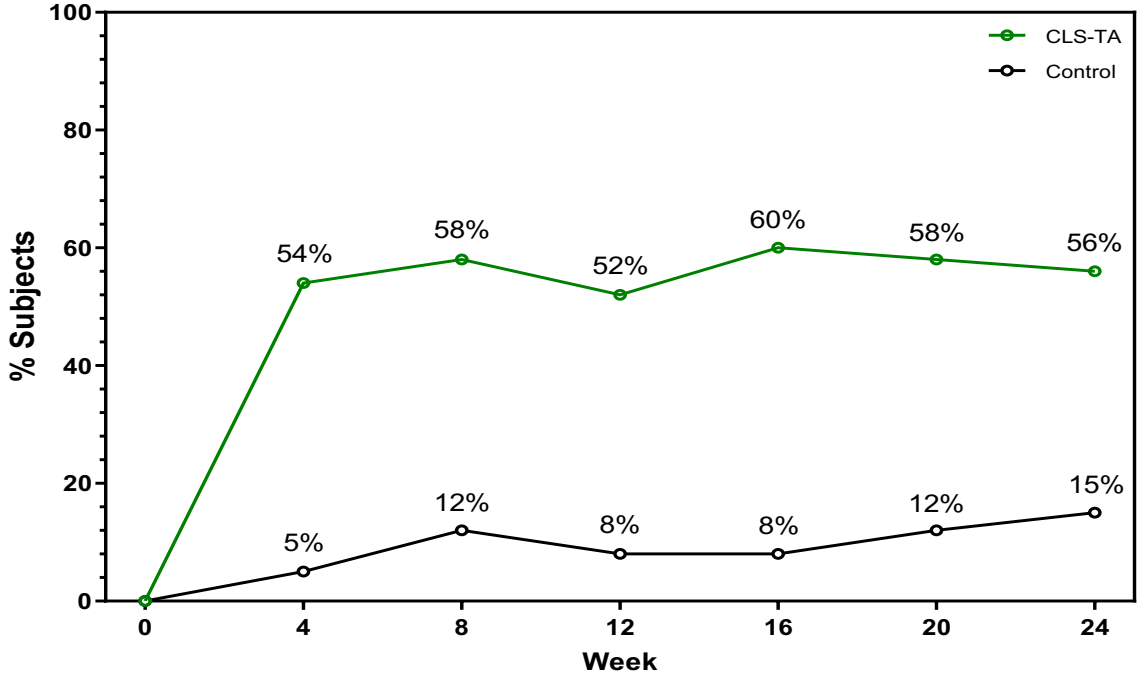
# Reduction in Retinal Thickness to <300 µm at Week 24

Percentage of patients with resolution of macular edema at **week 24**



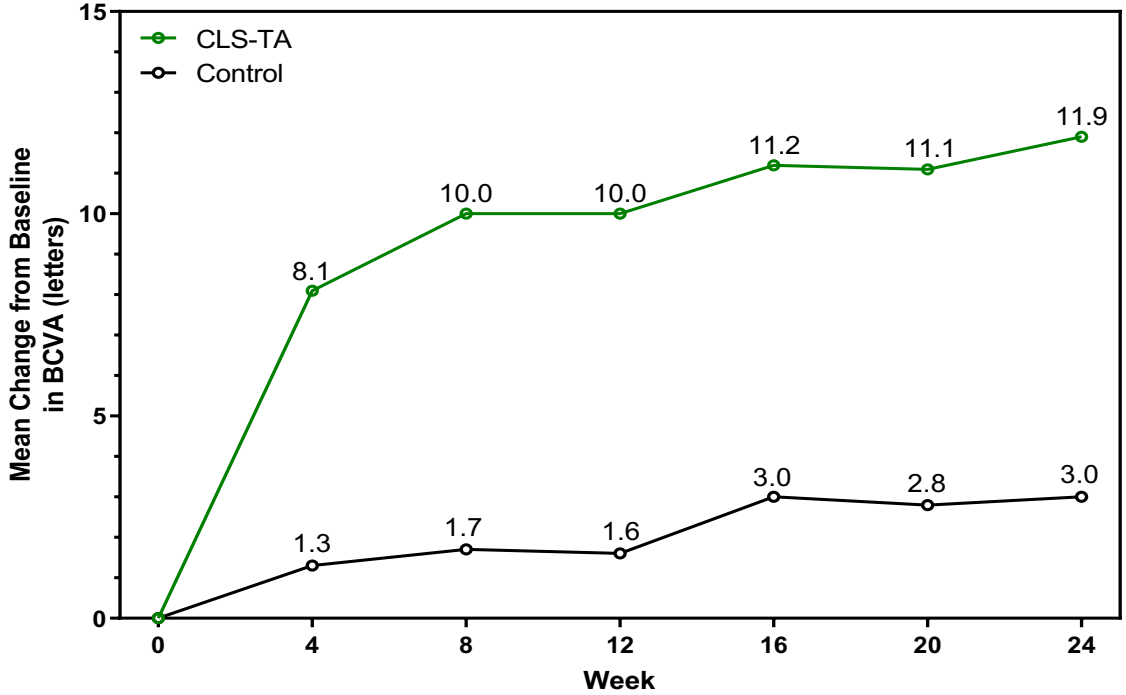

The effect of suprachoroidal CLS-TA on CST appears to be sustained between weeks 12 and 24 with no additional CLS-TA administered.

# Time Course of ME change 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.

# Time Course of ETDRS Letter change through Week 24




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

# 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

# THANK YOU