Anatomical Subtype Stratification for Evaluating the Safety and Efficacy of CLS-TA in Noninfectious Uveitis-Related Macular Edema: Insights from a Post-hoc Analysis of PEACHTREE

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SONOMA EYE

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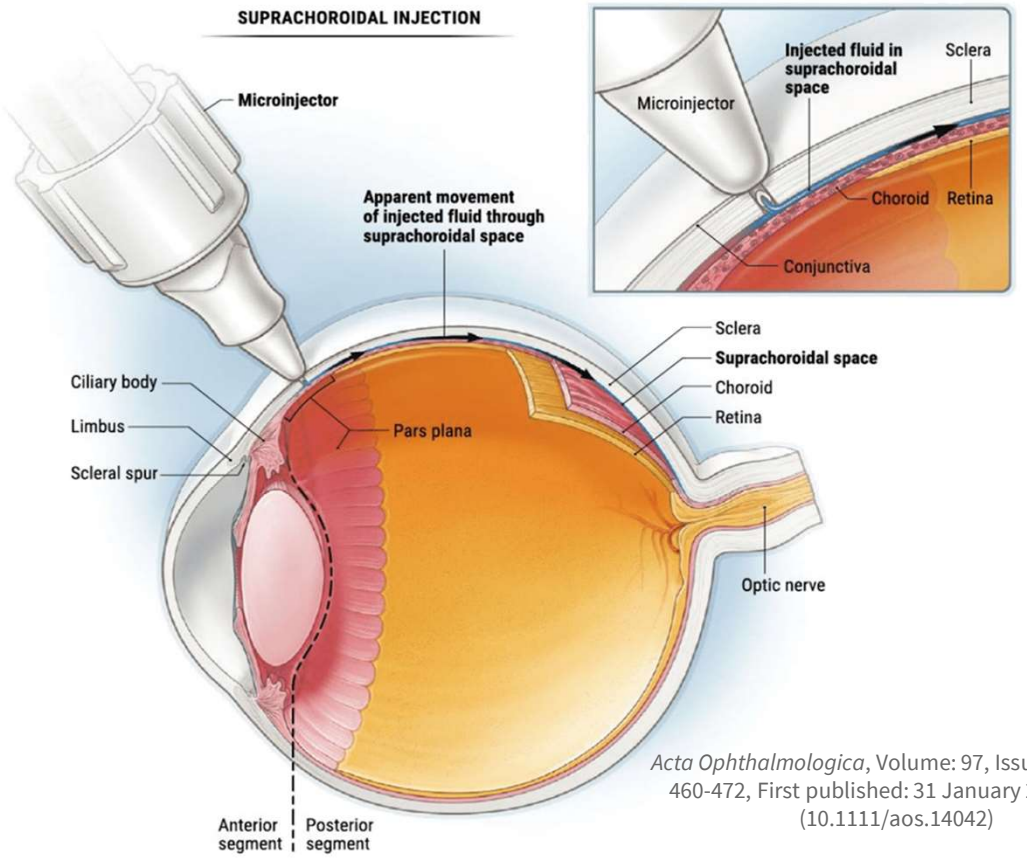
Financial Disclosures

I have the following financial interests or relationships to disclose:

- Clearside Biomedical: Grant Support

Suprachoroidal Triamcinolone Acetonide Injectable Suspension (SCS-TA; XIPERE®)

- 1st FDA-approved therapy for the treatment of macular edema associated with uveitis[1] (October 2021)
- Proprietary steroid formulation delivered via unique modality to the suprachoroidal space using the SCS Microinjector®[1]
- Suprachoroidal microinjection selectively delivers drug to the posterior segment while sparing the anterior chamber[2]



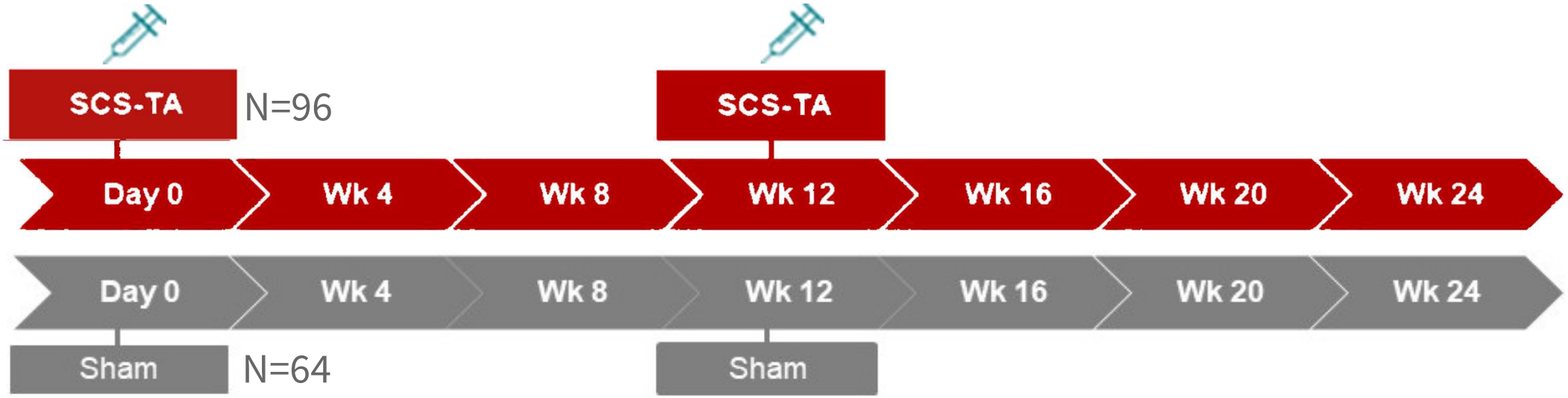
Acta Ophthalmologica, Volume: 97, Issue: 5, Pages: 460-472, First published: 31 January 2019, DOI: (10.1111/aos.14042)

1. XIPERE® (triamcinolone acetonide injectable suspension), for suprachoroidal use [package insert]. Bridgewater, NJ: Bausch & Lomb Americas Inc.; 2022. 2. Muya L, Kansara V, Cavet ME, Ciulla T. *J Ocul Pharm Ther.* 2022; 38(6):459-467

FDA, United States Food and Drug Administration; SCS, suprachoroidal space.

Suprachoroidal Triamcinolone Acetonide Injectable Suspension (SCS-TA; XIPERE®)

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



- Patients randomized 3:2 to SCS-TA injection vs Sham injection
- SCS-TA injections administered at Day 0 and 12 weeks

SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension; Wk, week.

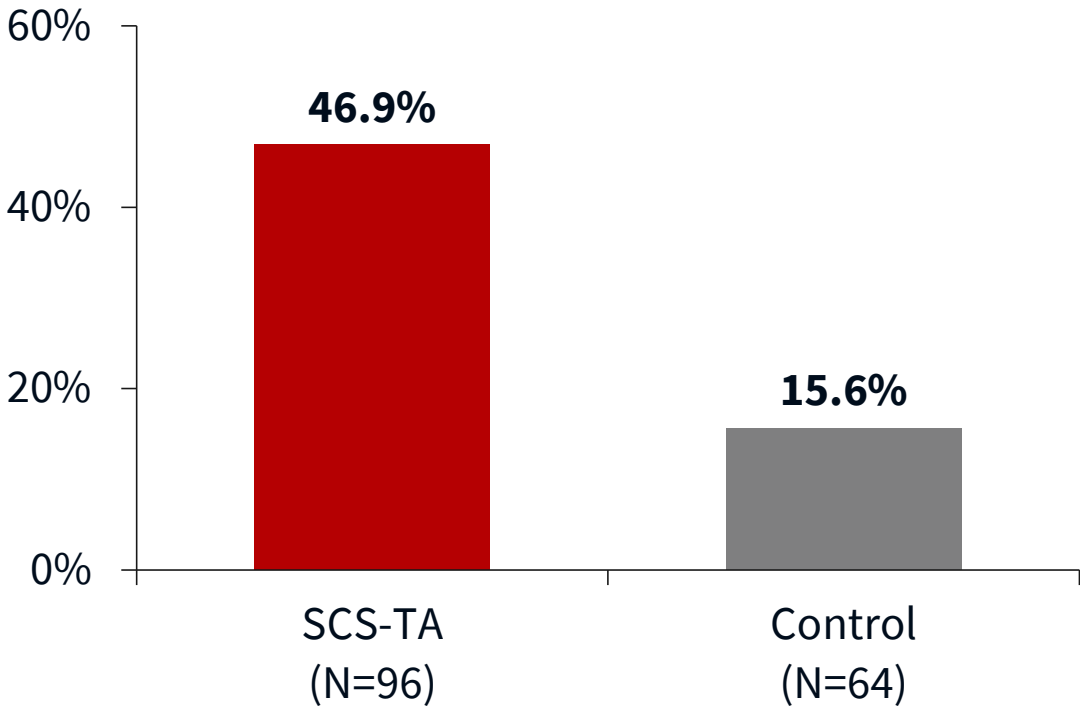
PEACHTREE: Efficacy and Safety Established

- Demonstrated the efficacy and safety of SCS-TA in NIU with macular edema across pooled anatomic subtypes
- <u>Efficacy</u>

  Primary endpoint achieved with 47% of SCS-TA treated patients gaining ≥15 ETDRS letters
- <u>Safety</u>

  Low rates of IOP elevation and cataract
  No SAEs reported

Primary Endpoint: % of patients gaining ≥15 BCVA letters from baseline at Week 24



BCVA, best corrected visual acuity; ETDRS; Early Treatment Diabetic Retinopathy Study; IOP, intraocular pressure; NIU, noninfectious uveitis; SAE, serious adverse event; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension.

Yeh S, Khurana RN, Shah M, et al. *Ophthalmology*. 2020;127(7):948-955.

Post-hoc Analysis: Evaluating Outcomes of PEACHTREE by Discrete Anatomic Subtype

Objective: To assess the response of suprachoroidal triamcinolone acetonide injectable suspension (SCS-TA) for treatment of uveitic macular edema (UME) by various subtypes

Methods: Post hoc analysis of Phase 3 PEACHTREE trial was performed evaluating SCS-TA (injected at baseline and 12 weeks) for treatment of UME

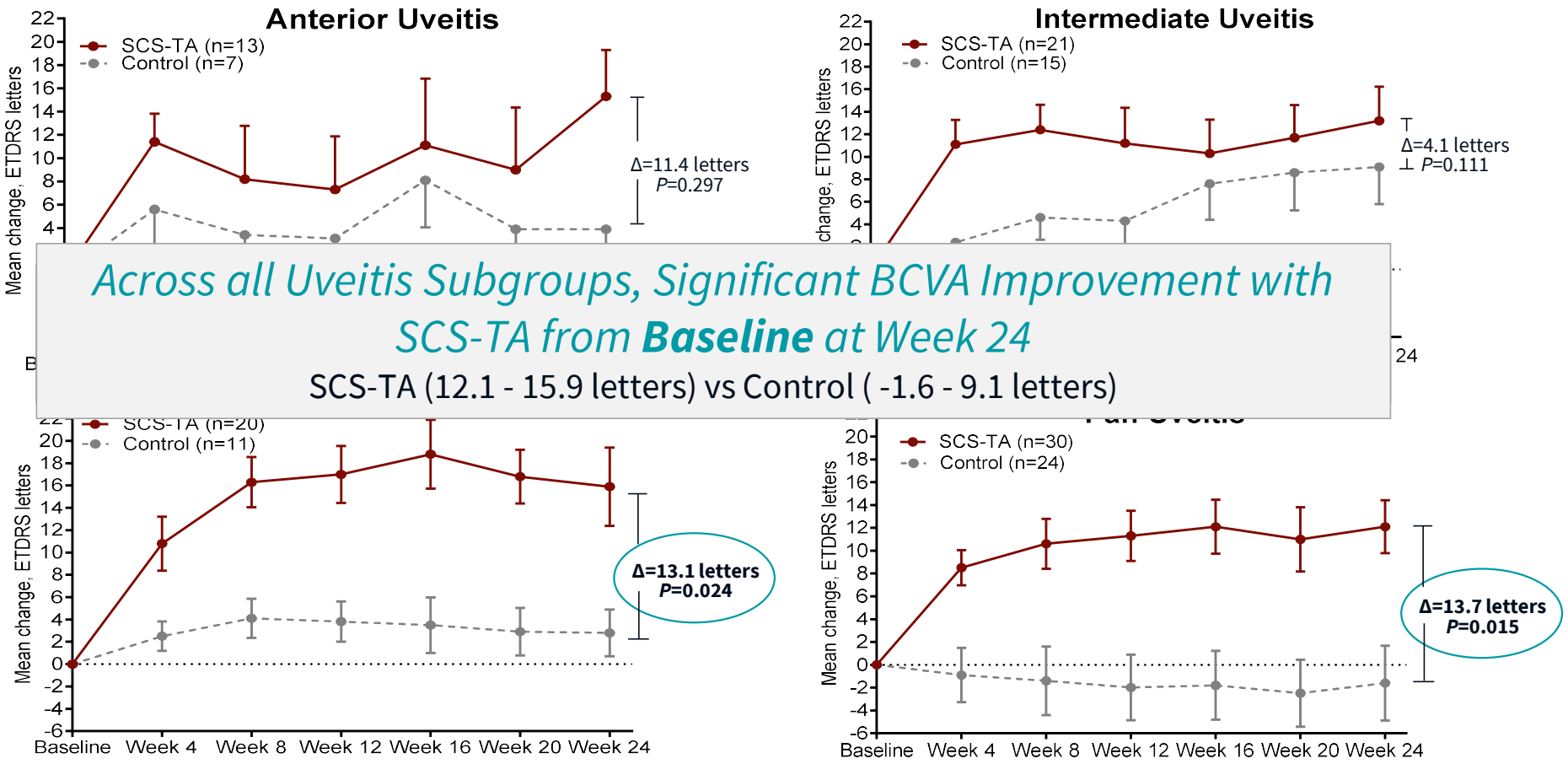
Trial participants were categorized by

A. Discrete anatomic location of uveitis
B. Subgroup with chronic uveitis (persistent uveitis with relapse in <3 months after treatment)

Outcomes reviewed: mean change in BCVA, CST, IOP, and incidence of adverse events

BCVA, best corrected visual acuity; CST, central subfield thickness; IOP, intraocular pressure; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension; UME, uveitic macular edema.

Mean Change in Best Corrected Visual Acuity by Anatomic Subtype



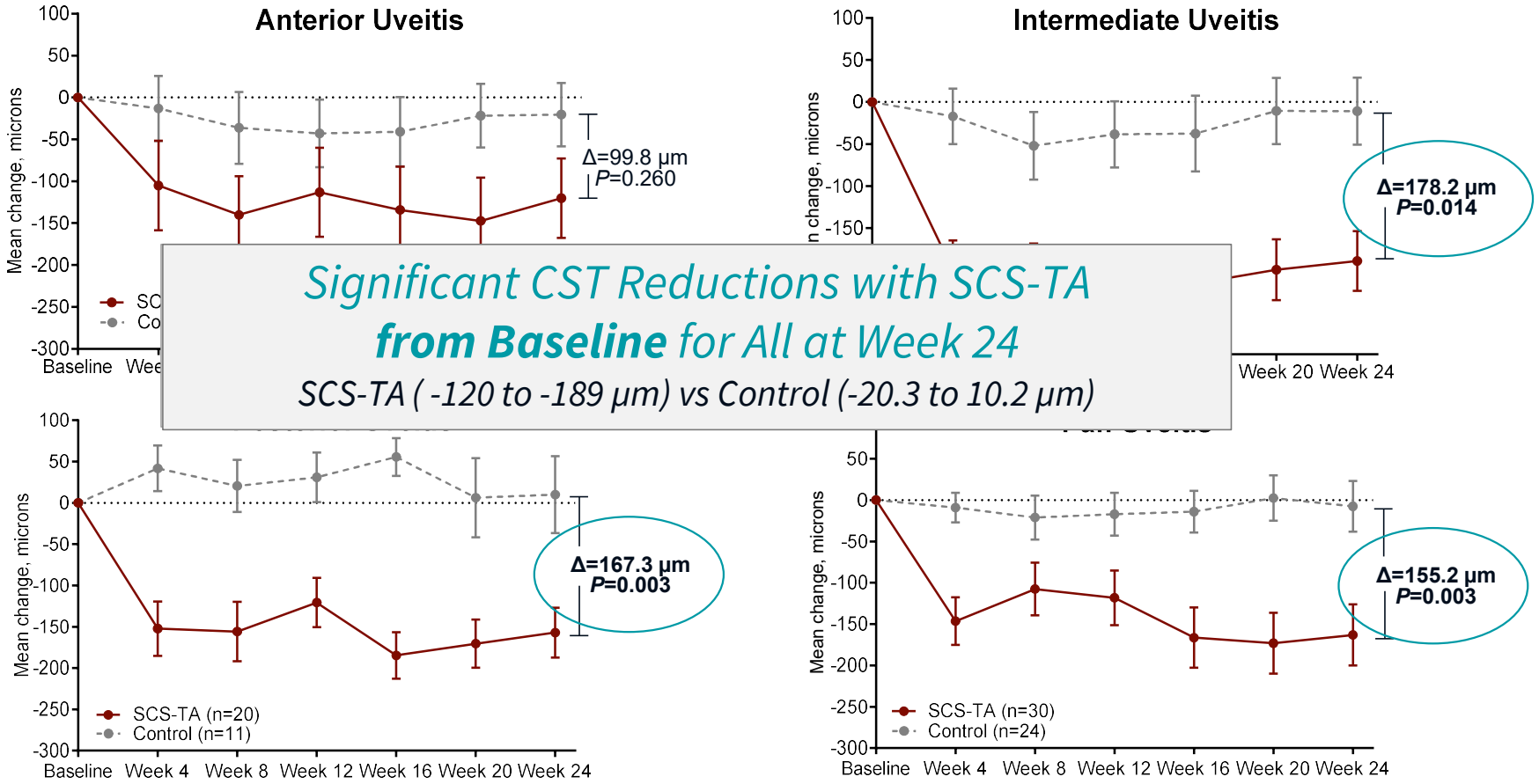
*Across all Uveitis Subgroups, Significant BCVA Improvement with SCS-TA from **Baseline** at Week 24*

SCS-TA (12.1 - 15.9 letters) vs Control (-1.6 - 9.1 letters)

All improvements from baseline with SCS-TA were significant except for anterior uveitis, Weeks 8-20; *P*≤0.002 for SCS-TA vs baseline at Week 24

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension; UME, uveitic macular edema.

Mean Change in Central Subfield Thickness by Anatomic Subtype

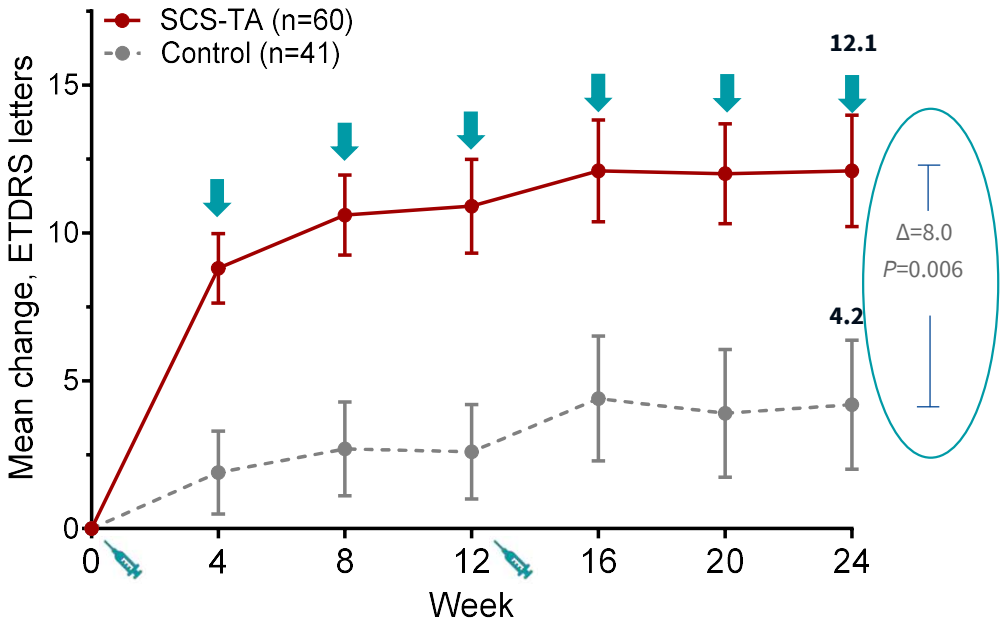


All improvements from baseline with SCS-TA were significant except for anterior uveitis, Weeks 4 and 16; $P \leq 0.028$ for SCS-TA vs baseline at Week 24

CST, central subfield thickness; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension.

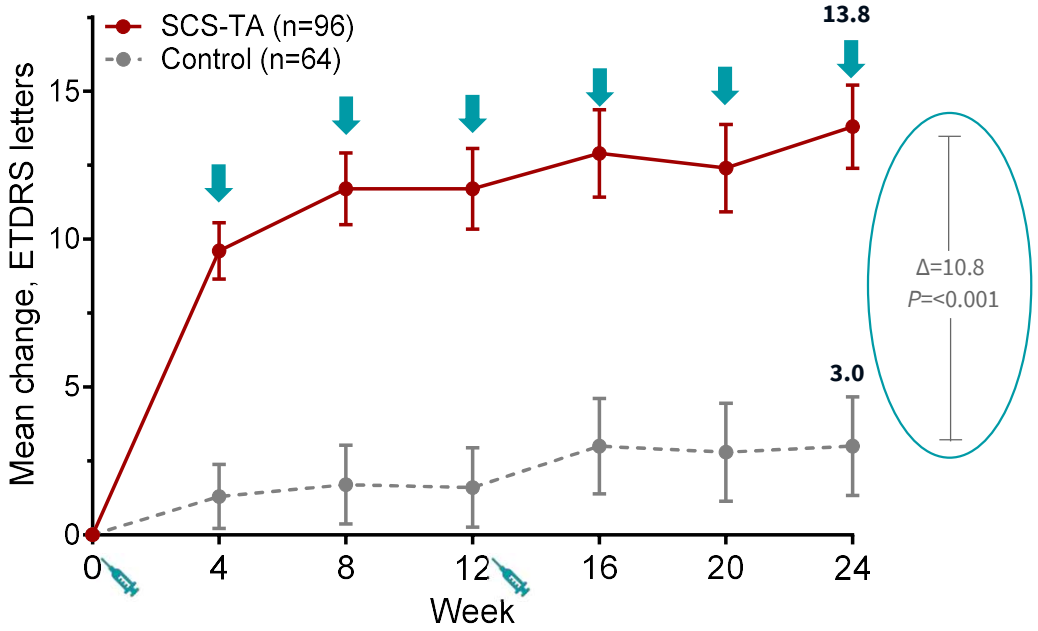
Significant Improvements in Visual Acuity with SCS-TA in Patients with Chronic Uveitis

Chronic Uveitis Patients



P<0.001 vs baseline and *P*≤0.006 vs control at all time points
Mean BCVA at baseline: 54.0 in the SCS-TA group and 50.2 in the control group

All Uveitis Patients



P<0.001 vs baseline and P<0.001 vs control at all time points
Mean BCVA at baseline: 54.7 in the SCS-TA group and 53.5 in the control group

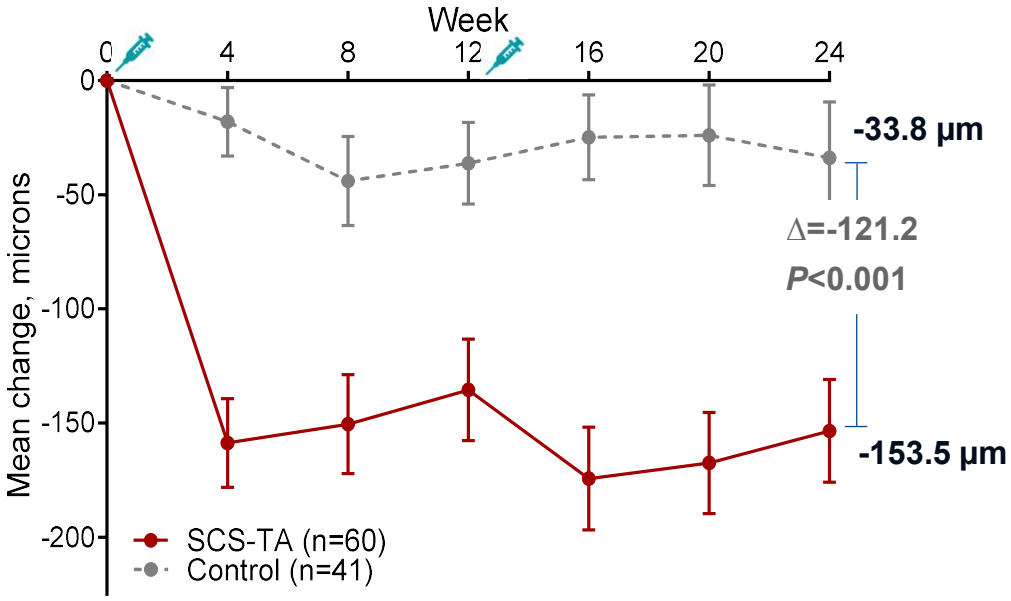
Data = mean (SEM); Intent-to-Treat Population, LOCF imputation
P-value vs baseline based on a t-test
P-value vs control based on an ANOVA with fixed effects for treatment group and pooled country

Yeh S, Khurana RN, Shah M, et al. *Ophthalmology.* 2020;127(7):948-955.

BCVA, best corrected visual acuity; ETDRS; Early Treatment Diabetic Retinopathy Study; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension.

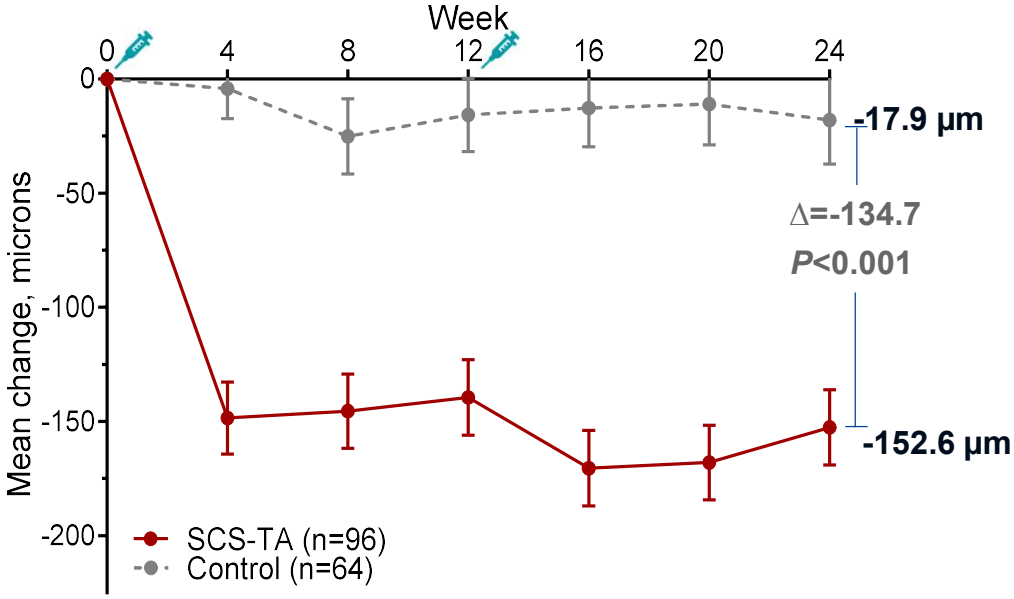
Significant Improvements in CST with SCS-TA in Patients with Chronic Uveitis

Chronic Uveitis Patients



P<0.001 vs baseline and *P*≤0.002 vs control at all time points
Mean CST at baseline: 492.7 in the SCS-TA group and 531.0 in the control group

All Uveitis Patients



P<0.001 vs baseline and *P*<0.001 vs control at all time points
Mean CST at baseline: 480.9 in the SCS-TA group and 525.4 in the control group

Data = mean (SEM); Intent-to-Treat Population, LOCF imputation
P-value vs baseline based on a t-test
P-value vs control based on an ANOVA with fixed effects for treatment group and pooled country

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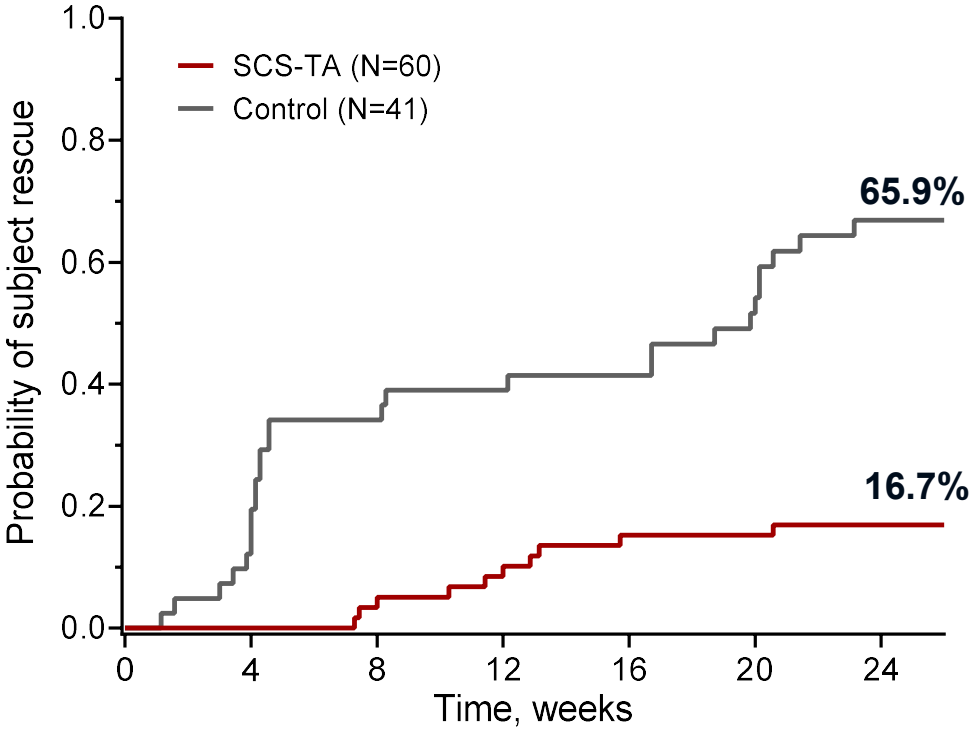
CST, central subfield thickness; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension.

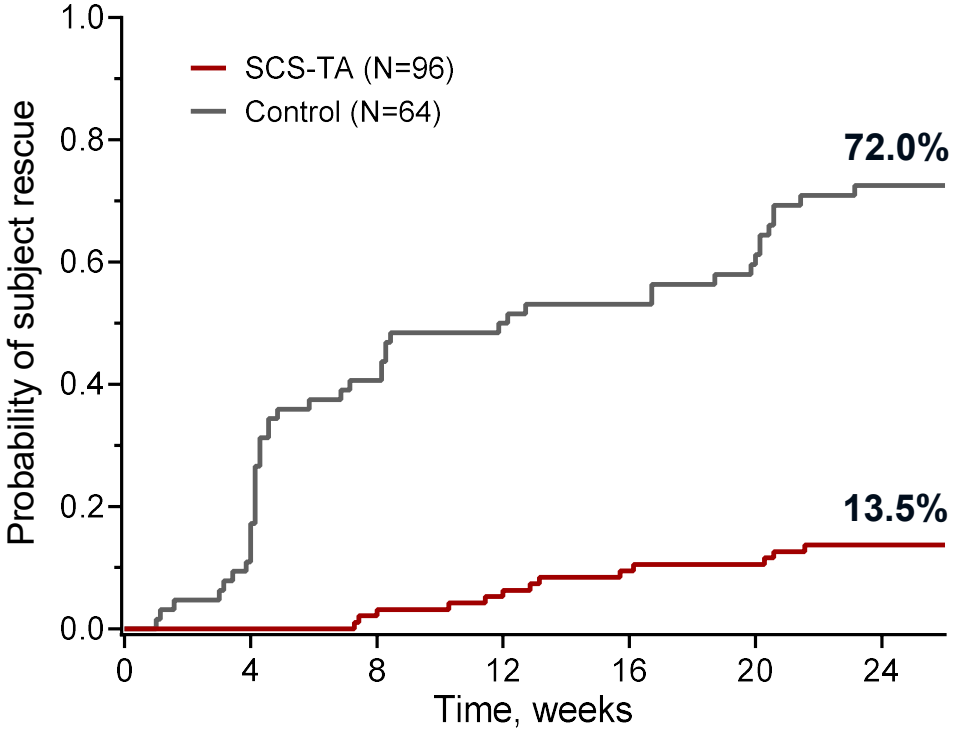
Time to Rescue in SCS-TA and Control Patients with Chronic Uveitis

Time to Rescue in Patients Treated with SCS-TA and Control

Chronic Uveitis Patients



All Uveitis Patients



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SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension.

SCS-TA was Well Tolerated Across Anatomic Subtypes

Ocular Adverse Reactions Across Anatomic Subtypes

Adverse Reaction	Anterior Uveitis		Intermediate Uveitis		Posterior Uveitis		Pan Uveitis	
	SCS-TA N=13 n (%)	Control N=7 n (%)	SCS-TA N=21 n (%)	Control N=15 n (%)	SCS-TA N=20 n (%)	Control N=11 n (%)	SCS-TA N=30 n (%)	Control N=24 n (%)
Cataract[a]	0	0	4 (19.0)	1 (6.7)	2 (10.0)	1 (9.1)	1 (3.3)	2 (8.3)
Cystoid macular edema	0	2 (28.6)	0	4 (26.7)	0	2 (18.2)	0	1 (4.2)
Eye pain: acute[b]	0	0	0	0	0	0	3 (11.1)	0
Eye pain: non-acute[c]	0	0	4 (19.0)	0	1 (5.0)	0	6 (22.2)	0
Elevated IOP:[d] acute	1 (7.7)	0	0	0	1 (5.0)	0	3 (11.1)	0
Elevated IOP: non-acute	1 (7.7)	1 (14.3)	3 (14.3)	1 (6.7)	3 (15.0)	2 (18.2)	4 (14.8)	2 (8.7)
Uveitis	0	1 (14.3)	1 (4.8)	3 (20.0)	1 (5.0)	1 (9.1)	0	1 (4.2)
Vitreous detachment	1 (7.7)	0	1 (4.8)	0	2 (10.0)	0	1 (3.3)	0

At Week 24, IOP mean change from baseline was (0.5 to 3.1 mmHg) in SCS-TA-groups vs (-1.2 to 1.7 mmHg) in control groups

[a] Cataract includes the preferred terms cataract, cataract subcapsular, cataract nuclear, and cataract cortical.
[b] Defined as occurring on the day of the injection procedure and resolving the same day.
[c] Defined as not occurring on the day of the injection procedure or occurring on the day of the injection procedure and not resolving the same day.
[d] "Elevated IOP" includes the preferred terms Intraocular pressure increased, and ocular hypertension.

IOP, intraocular pressure; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension.

SCS-TA was Well Tolerated Among Patients with Chronic Uveitis

Ocular Adverse Reactions Comparison

Adverse Reaction	Chronic Uveitis		All Uveitis Patients	
	SCS-TA N=60 n (%)	Control N=41 n (%)	SCS-TA N=96 n (%)	Control N=64 n (%)
Cataract[a]	6 (10.0)	0	7 (7.3)	4 (6.3)
Cystoid macular edema	0	6 (14.6)	0	11 (17.2)
Eye pain: acute[b]	3 (5.0)	0	3 (3.1)	0
Eye pain: non-acute[c]	6 (10.0)	0	11 (11.5)	0
Elevated IOP:[d] acute	3 (5.0)	0	6 (6.3)	0
Elevated IOP: non-acute	10 (16.7)	3 (7.3)	13 (13.5)	9 (14.1)
Uveitis	2 (3.3)	2 (4.9)	2 (2.1)	7 (10.9)
Vitreous detachment	1 (1.7)	0	5 (5.3)	1 (1.6)

- **Cataract (24 weeks)**
- Incidence similar between Chronic Uveitis group and All Uveitis group
  - Approximately 6-7 %
- **Non-acute IOP elevation (24 weeks)**
  - Similar rates of elevation among groups
  - **Mean** Δ IOP from baseline was 1.7 mmHg for Chronic Uveitis and All Uveitis group
- Overall, **no meaningful differences** in adverse effects between the two groups

[a] Cataract includes the preferred terms cataract, cataract cortical and cataract subcapsular.
[b] Defined as occurring on the day of the injection procedure and resolving the same day.
[c] Defined as not occurring on the day of the injection procedure or occurring on the day of the injection procedure and not resolving the same day.
[d] "Elevated IOP" includes the preferred terms Intraocular pressure increased and ocular hypertension.

Conclusion

- **Across discrete anatomic NIU subtypes,** SCS-TA treated patients showed
  - Significant BCVA gains from **baseline** at Week 24 ($P \leq 0.002$)
  - Significant CST improvements from **baseline** at Week 24 ($P \leq 0.028$)
- **Comparing (SCS-TA vs control),** treatment arm subjects showed
  - Higher gains in BCVA with SCS-TA in posterior- and pan-uveitis at week 24, and achieved statistical significance
  - Similarly, CST reductions were greater vs control for most discrete anatomic subtypes of uveitis
- **In patients with chronic uveitis**
  - SCS-TA significantly improved BCVA and decreased CST ($P \leq 0.006$)
  - Time-course for rescue was similar to total uveitis cohort

BCVA, best corrected visual acuity; CST, central subfield thickness; NIU, noninfectious uveitis; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension.

Conclusion

In Summary, SCS-TA resulted in BCVA and CST improvements, was well tolerated, and had comparable safety findings irrespective of anatomic subtypes in NIU

THANK YOU

BCVA, best corrected visual acuity; CST, central subfield thickness; NIU, noninfectious uveitis; SCS-TA, suprachoroidal triamcinolone acetonide injectable suspension.

Full Publication Describing Results from the PEACHTREE Trial by Anatomic Location of Inflammation is Available

OCULAR IMMUNOLOGY AND INFLAMMATION
https://doi.org/10.1080/09273948.2023.2262015

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ORIGINAL ARTICLE

OPEN ACCESS

Safety and Efficacy of CLS-TA by Anatomic Location of Inflammation: Results from the Phase 3 PEACHTREE Clinical Trial

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ABSTRACT

Purpose: To explore the efficacy of CLS-TA, a proprietary suprachoroidal injectable suspension of triamcinolone acetonide, in noninfectious uveitis (NIU) with macular edema (ME), categorized by anatomic subtype.
Methods: Patients diagnosed with ME associated with NIU of any etiology and anatomic subtype were eligible for the phase 3 PEACHTREE trial of CLS-TA. Post-hoc analyses were performed, stratified by discrete anatomic subtype of uveitis (anterior, intermediate, posterior, and panuveitis.)
Results: Across all anatomic subtypes at 24 weeks, patients receiving CLS-TA at baseline and week 12 demonstrated mean increases in BCVA ranging from +12.1 to +15.9 letters, mean central subfield thickness (CST) improvement ranging from −120.1 µm to −189.0 µm, and IOP changes ranging from +0.5 to +2.1 mmHg. Overall, reports of adverse events were similar among subtypes.
Conclusions: Irrespective of the uveitic anatomic subtype among patients treated for ME associated with NIU, a clinical benefit in participants treated with CLS-TA was demonstrated, with a comparable safety profile.

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KEYWORDS
Non-Infectious Uveitis; uveitic Macular Edema; suprachoroidal injection; triamcinolone Acetonide

Uveitis is a heterogeneous collection of inflammatory ocular conditions and a leading cause of vision loss globally. Non-infectious uveitis (NIU) accounts for up to 90% of cases, affecting approximately 350,000 patients in the United States.[1] NIU can be divided into subtypes based on the anatomic location of inflammation; anterior uveitis affects the iris and ciliary body; intermediate uveitis affects the vitreous and pars plana region; posterior uveitis affects the retina and the choroid; and panuveitis can affect all parts of the uvea. Periocular and intravitreal corticosteroids are often utilized in the treatment of uveitis but can be associated with the development of cataract and intraocular pressure (IOP) elevations.

Macular edema (ME) affects approximately one-third of uveitic patients and is the leading cause of uveitis vision loss, for which there has historically been no specifically approved treatment.[2] However, in October 2021, XIPERE® (CLS-TA triamcinolone acetonide injectable suspension) for suprachoroidal (SC) use was approved by the United States Food and Drug Administration (FDA), becoming the first such treatment specifically approved for ME associated with uveitis. The approval was based on the successful phase 3 PEACHTREE trial results (ClinicalTrials.gov Identifier NCT02595398) using suprachoroidal CLS-TA to treat ME associated with NIU.[3] PEACHTREE was a 6-month, randomized, multicenter, double-masked, sham-controlled study in patients with ME associated with anterior-, intermediate-, posterior-, or pan-uveitis.

In PEACHTREE, patients were treated at baseline and week 12, and there was a clinically meaningful gain of 15 letters or more from baseline in Early Treatment of Diabetic Retinopathy Study (ETDRS) best corrected visual acuity (BCVA) for 47% of patients treated with CLS-TA, along with a clinically meaningful 153 µm reduction of central subfield thickness (CST) at 24 weeks among all patients in the Active arm.[3] Suprachoroidal injection of CLS-TA is thought to result in more targeted delivery of drug to the affected chorioretinal tissues while relatively sparing the anterior segment, resulting in lower risk of corticosteroid associated adverse events (AEs), such as cataract formation and IOP elevations.[4,5] In PEACHTREE, elevated IOP occurred in 11.5% and 15.6% of the CLS-TA and control groups, respectively, while cataract adverse event rates were comparable (7.3% and 6.3%, respectively).[3]

In addition, PEACHTREE demonstrated clinically and statistically significant resolution of anterior and posterior segment inflammation in approximately 70% of patients.[3] However, while PEACHTREE enrolled patients with ME associated with various anatomic subtypes (anterior, intermediate, posterior, or panuveitis), there has been limited information on outcomes stratified by these anatomic locations. The POINT study, a comparative study evaluating three arms of corticosteroid treatments for uveitic ME, analyzed OCT reduction in CST and visual acuity gains; however, these endpoints

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Prior Presentations: This data has been presented at: AAO 2022, October 032022, Chicago, IL.
This article has been corrected with minor changes. These changes do not impact the academic content of the article.

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