

Efficacy and Safety of Suprachoroidal CLS-TA for Macular Edema Secondary to Noninfectious Uveitis

Phase 3 Randomized Trial

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Purpose: Injection of pharmacotherapy into the suprachoroidal space, between the sclera and choroid, is an alternative delivery technique developed with the rationale of providing higher drug concentrations to posterior ocular structures compared with other intraocular and periocular injection procedures. This study was conducted to evaluate the safety and efficacy of suprachoroidally injected triamcinolone acetonide formulation (CLS-TA), a suspension of triamcinolone acetonide, in improving vision among patients with noninfectious uveitis complicated by macular edema (ME).

Design: Phase 3 masked, randomized trial.

Participants: One hundred sixty patients with ME secondary to noninfectious uveitis. Patients were required to have a best-corrected visual acuity (BCVA) of 5 or more Early Treatment Diabetic Retinopathy Study (ETDRS) letters (Snellen equivalent, 20/800) and 70 or fewer ETDRS letters read (Snellen equivalent, 20/40) in the study eye.

Methods: Patients were randomized 3:2 to suprachoroidally injected CLS-TA or sham treatment, with administrations at day 0 and week 12.

Main Outcome Measures: The primary end point was improvement from baseline of 15 or more ETDRS letters in BCVA at week 24. The secondary end point was reduction from baseline in central subfield thickness (CST) at week 24.

Results: In the CLS-TA arm, 47% of patients gained 15 or more ETDRS letters in BCVA versus 16% in the control arm ($P < 0.001$), meeting the primary end point. Mean reductions in CST from baseline were 153 μm versus 18 μm ($P < 0.001$). No serious adverse events (AEs) related to treatment were reported. Corticosteroid-associated AEs of elevated intraocular pressure occurred in 11.5% and 15.6% of the CLS-TA and control groups, respectively. Cataract AE rates were comparable (7.3% and 6.3%, respectively).

Conclusions: Patients in the CLS-TA study arm experienced clinically significant improvement in vision relative to the sham procedure, demonstrating the efficacy of suprachoroidal injection of CLS-TA for the treatment of ME in a vision-threatening disorder. *Ophthalmology* 2020;127:948-955 © 2020 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



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Suprachoroidal administration, an alternative technique for delivering ocular therapies, may facilitate more targeted delivery of therapeutic agents to chorioretinal structures than intravitreal injection¹ (Fig S1, available at www.aaojournal.org). Targeted delivery was demonstrated in preclinical ocular distribution studies in which suprachoroidal injection of an investigational triamcinolone acetonide formulation (CLS-TA) yielded high levels of the corticosteroid in the retina, retinal pigmented epithelium, and choroid detectable for more

than 3 months (Edelhauser HF, et al. Suprachoroidal microinjection delivers triamcinolone acetonide to therapeutically-relevant posterior ocular structures and limits exposure in the anterior segment. Poster presented at: Association for Research in Vision and Ophthalmology Annual Meeting; Seattle, WA, May 1st–5th, 2016).² Suprachoroidal injection also may limit corticosteroid exposure to the anterior chamber, iris–ciliary body, and lens, offering the potential to decrease adverse events (AEs) such as cataracts, intraocular pressure (IOP) elevation, and

exacerbation of glaucoma that commonly arise from intra-vitreous and periocular corticosteroids (Edelhauser HF, et al. Suprachoroidal microinjection delivers triamcinolone acetonide to therapeutically-relevant posterior ocular structures and limits exposure in the anterior segment. Poster presented at: Association for Research in Vision and Ophthalmology Annual Meeting; Seattle, WA, May 1st–5th, 2016).²

We report the first phase III study assessing a suprachoroidally administered therapy. Specifically, suprachoroidally administered CLS-TA was assessed in a randomized, controlled, double-masked, phase III study (PEACHTREE) to evaluate its ability to improve vision in patients with macular edema (ME) associated with noninfectious uveitis (NIU). Uveitis, a heterogeneous group of diseases characterized by intraocular inflammation, accounts for 10% to 15% of cases of blindness in the developed world,^{3,4} nearly one third of which are the result of uveitis-associated ME.⁵ Intravitreal corticosteroids are commonly used and effective treatments for reducing uveitic ME and inflammation, but they are associated with elevations in IOP ranging in incidence from 20% to 60%,^{6–11} exacerbation of glaucoma, and cataract development or progression^{8,12} resulting from corticosteroid exposure to the anterior segment and the lens.^{13,14} These observations highlight the unmet need for a targeted drug delivery approach for treating vision loss resulting from uveitis.

Methods

Study Design

This trial was conducted in the United States, India, and Israel from November 2015 through January 2018. The study population included 160 patients enrolled at 53 sites. Only 1 eye could serve as the study eye, even if both eyes were eligible. Patient eligibility was established during screening (day –14 to –1). Eligible patients returned to the clinic for the baseline visit (day 0), when they were assigned randomly in a 3:2 ratio to the treatment or control group. Patients received a single unilateral suprachoroidal injection of CLS-TA, 4 mg (0.1 ml of 40 mg/ml), or a unilateral sham procedure (control) at day 0 and at week 12. The control group underwent a sham procedure to maintain masking; the procedure mimicked the suprachoroidal injection, but no drug or vehicle was administered. To maintain masking and to minimize bias, investigators who administered study medications were distinct from masked investigators who assessed patients. Patients attended 8 clinic visits over 27 weeks (Fig S2, available at www.aaojournal.org). Ocular assessments were conducted as follows: screening and exit were performed on both eyes, IOP was collected for both eyes, and all other ocular assessments were performed on the study eye only. Follow-up visits were conducted every 4 weeks up to 24 weeks, when a final evaluation was conducted.

The trial protocol was approved by an independent ethics committee or institutional review board at each study site (full list of study sites appear in the [Supplementary Appendix](#), available at www.aaojournal.org), and the trial was performed in compliance with the provisions of the Declaration of Helsinki, International Conference on Harmonization Good Clinical Practice guidelines, and

applicable local regulations. Patients provided written informed consent before the study commenced. PEACHTREE was registered prospectively at ClinicalTrials.gov (identifier, NCT02595398).

Patients

Patients 18 years of age or older were eligible if they had a diagnosis of NIU of any cause and had ME secondary to uveitis, defined as having intraretinal or subretinal fluid along with a retinal thickness of 300 μ m or more in the central subfield as measured by spectral-domain OCT. Patients were required to have a best-corrected visual acuity (BCVA) of 5 or more Early Treatment Diabetic Retinopathy Study (ETDRS) letters (Snellen equivalent, 20/800) and 70 or fewer letters read (Snellen equivalent, 20/40) in the study eye. Patients were excluded if they had any active ocular disease or infection in the study eye except uveitis, IOP of more than 22 mmHg, or uncontrolled glaucoma. In patients with IOP of 22 mmHg or less, the use of up to 2 IOP-lowering medications was allowed. Additionally, the trial did not limit inclusion by anatomic subtype but included all eligible patients with either anterior uveitis, intermediate uveitis, posterior uveitis, or panuveitis (Table S1, available at www.aaojournal.org). Patients were allowed to take systemic corticosteroids at doses of 20 mg/day or less for oral prednisone (or equivalent for other corticosteroids), stable (≥ 2 weeks) doses of systemic immunomodulatory therapies, or both.

Efficacy Assessments

The 24-week, prespecified, primary end point was the proportion of patients with change from baseline of 15 or more ETDRS letters in BCVA (≥ 3 lines of vision). The secondary end point was mean change from baseline in central subfield thickness (CST) measured by spectral-domain OCT at 24 weeks. Additional end points included mean change in BCVA in ETDRS letters by visit, mean change in CST by visit, and changes in signs of inflammation as evaluated by the Standardization of Uveitis Nomenclature scales¹⁵ for anterior chamber cells, anterior chamber flare, and vitreous haze.

Safety

The safety population included all randomized patients. Safety end points included (1) frequency of treatment-related AEs and serious AEs, grouped by organ system, relatedness to study medication determined by the study investigator, and severity; (2) percentage of patients whose IOP increases were more than 10 mmHg from their baseline measurement; (3) percentage of patients whose IOP increased to more than 30 mmHg; and (4) percentage of patients who were introduced to 1 or more IOP-lowering medications. The IOP evaluations pertaining to corticosteroid were at any follow-up visit except for evaluations after injection on treatment days. Intraocular pressure assessment is described in the [Appendix](#) (available at www.aaojournal.org).

Rescue Therapy

Beginning at week 4 (visit 3), rescue therapy could be introduced if certain criteria were met in the study eye or if the patient was not improving (Table S2, available at www.aaojournal.org). Any additional therapy administered was per the study investigator's discretion.

Table 1. Baseline Characteristics and Demographics

Characteristic	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)	50.4 (14.2)	50.0 (15.1)	50.2 (14.5)
Race, n (%)			
American Indian/Alaska Native	0	0	0
Asian	44 (45.8)	28 (43.8)	72 (45.0)
Black/African American	11 (11.5)	11 (17.2)	22 (13.8)
Native Hawaiian/other Pacific Islander	0	0	0
White	40 (41.7)	25 (39.1)	65 (40.6)
Other	1 (1.0)	0	1 (0.6)
BCVA, study eye (ETDRS letters read)			
Mean (SD)	54.7 (13.9)	53.5 (12.9)	54.2 (13.5)
Median (range)	57.0 (9, 89)	54.0 (12, 79)	56.0 (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)
Uveitis anatomic location, n (%) [*]			
Anterior	27 (28.1)	14 (21.9)	41 (25.6)
Intermediate	34 (35.4)	23 (35.9)	57 (35.6)
Posterior	22 (22.9)	13 (20.3)	35 (21.9)
Panuveitis	28 (29.2)	24 (37.5)	52 (32.5)
Time Since Uveitis Diagnosis (Weeks)			
n	96	64	160
Mean (STD)	177.4 (235.91)	107.1 (134.70)	149.3 (204.04)
Median	66.0	60.5	65.5
Min, Max	0, 1262	0, 648	0, 1262
Lens Status, n (%) [*]			
Phakic	47 (49.0%)	42 (65.6%)	89 (55.6%)

BCVA, best corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study.

^{*}Percentages based on number of patients in respective groups.

Statistical Analysis

The intent-to-treat (ITT) population was used for all efficacy analyses and consisted of all randomized patients. Randomized assignment of patients to treatment arms was performed by interactive response technology. This study had more than 90% power to detect a difference between treatments. A Cochran-Mantel-Haenszel test was used to test differences in the proportion of patients in the 2 groups who showed 15 or more letters of improvement in BCVA at the week 24 visit after adjusting for country effects. The last observation carried forward method was used to impute data for all data points after rescue medication had been administered or to impute missing data in the ITT efficacy analyses.

Results

Patients

A total of 160 patients were randomized. The ITT population for efficacy analyses consisted of 96 and 64 patients in the CLS-TA and control groups, respectively. Overall, 97% (155/160) completed the study, including 95.8% (92/96) in the CLS-TA group and 98.4% (63/64) in the control group (Fig S3, available at www.aaojournal.org). Discontinuations in the CLS-TA arm (n = 4) were the result of patient withdrawal of consent (n = 2), patient noncompliance (n = 1), and loss to follow-up (n = 1). One

patient in the control arm withdrew consent. Demographics and baseline features were balanced across groups, with slightly more women than men (Table 1, Table S3 available at www.aaojournal.org). Mean age in both arms was approximately 50 years. Mean BCVA in the study eye was 55 and 54 ETDRS letters (approximate Snellen equivalent, 20/80) read in the CLS-TA and control arms, respectively. Overall, the distribution of anatomic subtypes of uveitis was as follows: anterior (26%), intermediate (36%), posterior (22%), and panuveitis (32%). The distribution was comparable between the 2 arms. The mean time since uveitis diagnosis was 177.4 weeks in the CLS-TA arm versus 107.1 weeks in the control arm. The CLS-TA and control arms included 47 and 42 phakic patients, respectively.

Efficacy

Primary end point analysis showed the percentage of patients with BCVA gain from baseline of 15 or more ETDRS letters was 46.9% (45/96) in the CLS-TA group compared with 15.6% (10/64; $P < 0.001$) in the control group at week 24 (Fig 1A). Improvements from baseline were observed early in follow-up; at week 4, a mean change of 9.6 ETDRS letters was observed compared with 1.3 ETDRS letters for the control arm. This improvement was maintained through week 24, with 13.8 and 3.0 ETDRS letters gained for the CLS-TA and control groups, respectively ($P < 0.001$; Fig 1B). At week 8, 49% of CLS-TA patients had attained vision of 70 ETDRS letters or better (approximate Snellen equivalent, 20/40) versus 15% of control

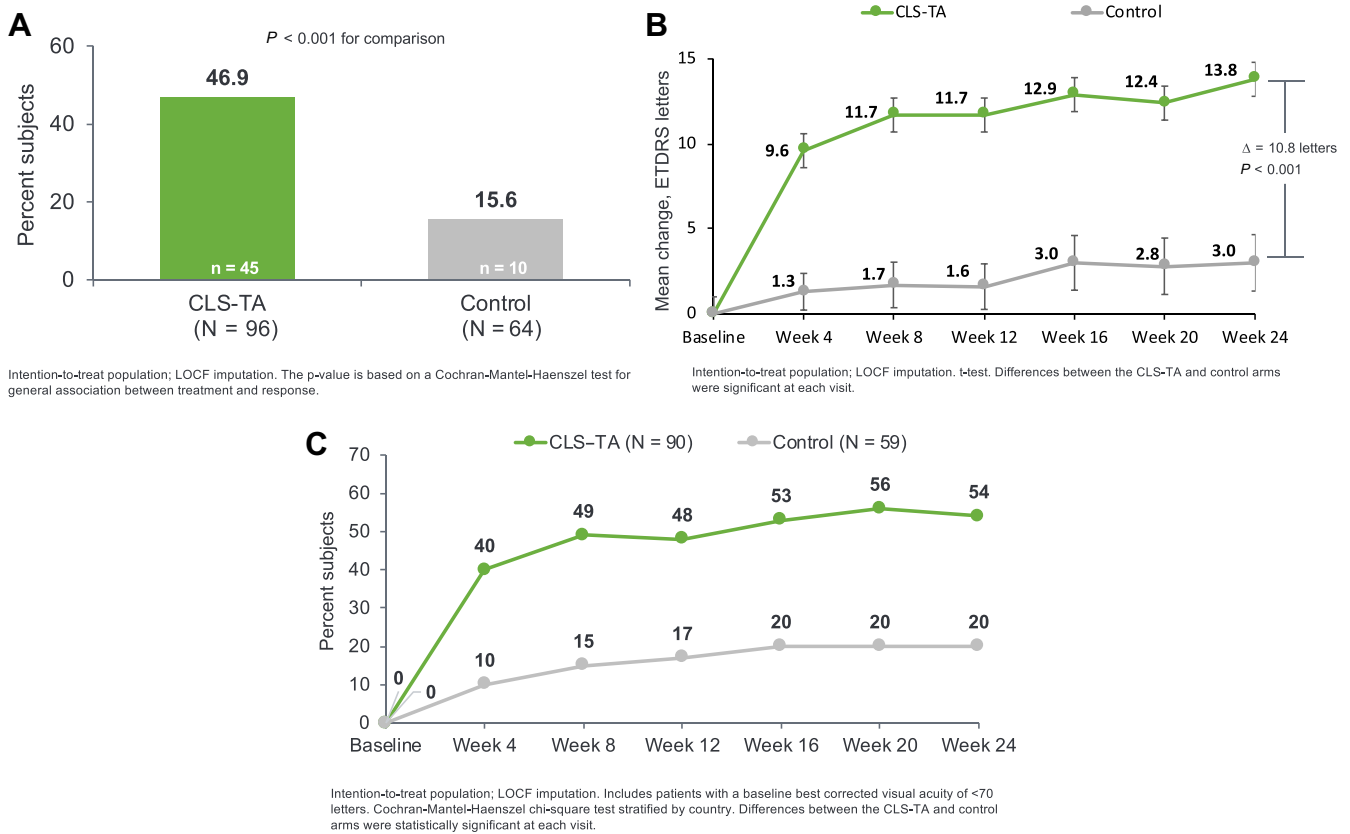


Figure 1. A, Bar graph showing percent of patients gaining 15 or more Early Treatment Diabetic Retinopathy Study (ETDRS) letters from baseline at week 24. B, Graph showing mean $\pm$ standard error of the mean change from baseline in best-corrected visual acuity in ETDRS letters read at each visit. C, Graph showing percent of patients reading 70 or more ETDRS letters (approximately 20/40 or better) at each visit. CLS-TA = triamcinolone acetonide formulation; LOCF = last observation carried forward.

patients ($P < 0.001$; Fig 1C). This difference between arms was maintained through week 24 and was statistically significant at all time points. Proportions of patients in CLS-TA versus control groups achieving other specified thresholds of BCVA improvement at week 24 were as follows: 5 or more letters, 76% versus 39%, respectively; 10 or more letters, 60% versus 30%, respectively; and 15 or more letters, 47% versus 16%, respectively.

At baseline, the CLS-TA and control groups showed similar degrees of ME, at 481 μm and 525 μm , respectively ($P > 0.05$; Table 1). Central subfield thickness was reduced from baseline in CLS-TA patients by 153 μm compared with a reduction of 18 μm in the control group at week 24, a difference of 135 μm ($P < 0.001$; Fig 2A). A more than 100- μm difference in CST reductions between study arms was observed starting at week 4

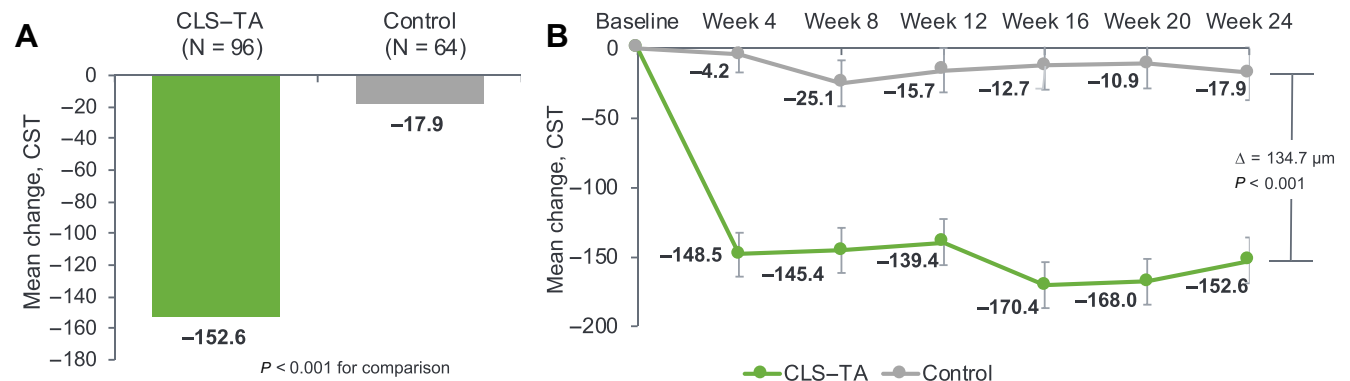


Figure 2. Graphs showing mean $\pm$ standard error of the mean change from baseline in central subfield thickness (CST; in micrometers) at (A) week 24 and at (B) each visit. CLS-TA = triamcinolone acetonide formulation; LOCF = last observation carried forward.

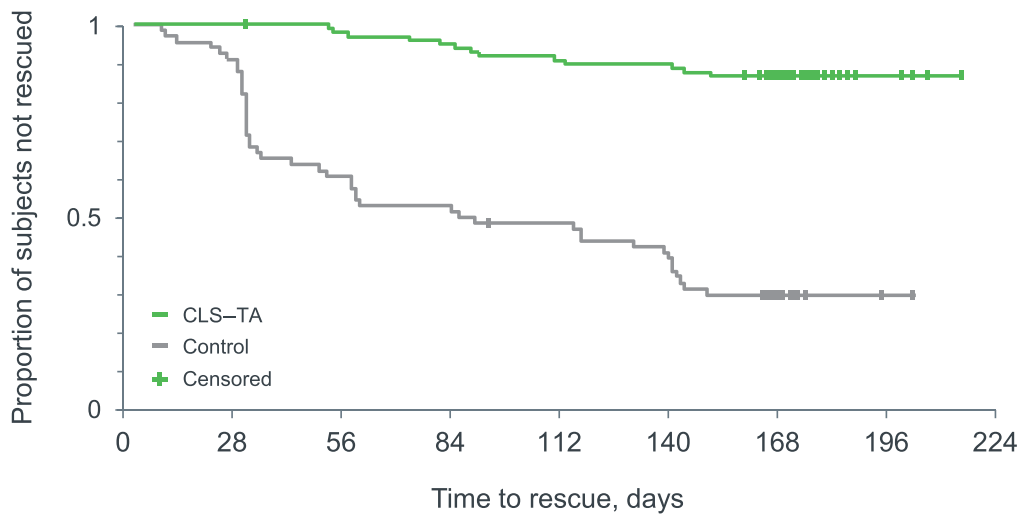


Figure 3. Kaplan-Meier graph showing time to rescue in the triamcinolone acetonide suspension (CLS-TA) and in sham control arms.

($-148\ \mu\text{m}$ vs. $-4\ \mu\text{m}$) and continued through week 24 (Fig 2B). The percentage of patients with ME resolution (CST $<300\ \mu\text{m}$) was 53% at week 4 in the CLS-TA group and 2% in the control group (Fig S4, available at www.aaojournal.org). This difference in ME resolution between the CLS-TA and control arms was maintained through week 24. A higher proportion of patients experienced a clinically meaningful 20% or more reduction in CST¹⁶ in the CLS-TA arm at each visit (Fig S5, available at www.aaojournal.org).

At least two thirds of the patients with active inflammation at baseline in the CLS-TA arm experienced resolution of inflammation (Standardization of Uveitis Nomenclature scores of 0 for

anterior chamber cell, anterior chamber flare, and vitreous haze) at week 24. The percentages of patients requiring rescue therapy were 13.5% (13/96) in the CLS-TA arm and 72% (46/64) in the control arm over 24 weeks (Fig 3). Among rescued patients, median time to first rescue was 89 days in the CLS-TA arm versus 36 days in the control arm ($P < 0.001$).

A post hoc analysis was performed to compare efficacy results from the unrescued CLS-TA patients with the rescued control patients (observed data from the ITT population, without data imputation from the time point of rescue). As noted previously, predefined criteria were established for the administration of rescue therapy, and the type of rescue therapy was administered at the

Table 2. Ocular Adverse Events

Study Eye, n (%)	CLS-TA 4.0 mg N=96 n (%)	Control N=64 n (%)
Total number of ocular adverse events	122	54
Number of patients with ≥ 1 ocular AE	49 (51.0)	37 (57.8)
Treatment-related ocular AEs	29 (30.2)	8 (12.5)
Serious ocular AEs	1 (1.0)	0
Treatment-related serious AEs	0	0
TEAEs leading to study drug discontinuation	5 (5.2)	5 (7.8)
Number of patients with ≥ 1 eye disorder	41 (42.7)	34 (53.1)
Adverse events in $\geq 5\%$ of patients in either treatment group		
Cataract*	7 (7.3)	4 (6.3)
Cystoid macular edema	0	11 (17.2)
Eye pain: time of procedure	12 (12.5)	3 (4.7)
Eye pain: any time post procedure	6 (6.3)	0
Elevated IOP†: time of procedure	8 (8.3)	0
Elevated IOP†: pertaining to corticosteroid‡	11 (11.5)	10 (15.6) [§]
Uveitis	2 (2.1)	7 (10.9)
Vitreous detachment	5 (5.2)	1 (1.6)

AE, adverse event; IOP, intraocular pressure; TEAE, treatment-emergent adverse event.

A TEAE was any AE temporally associated with the use of the study drug, whether or not considered causally related to the study drug, that occurred after the subject received the first dose of study drug.

*Cataract includes the preferred terms (a) cataract, (b) cataract subscapular, and (c) cataract nuclear.

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

‡Includes all events of elevated IOP that did not occur on the day of the procedure.

§All IOP adverse events in the control group occurred after rescue with local corticosteroid administration.

investigators' discretion; intravitreal or periocular corticosteroids were prescribed in 37 of 46 (80.4%) rescued control patients. The estimate of the between-treatment difference, 95% confidence interval (CI), and *P* value was based on an analysis of covariance model with fixed effects for treatment group. In 83 of 96 (86.4%) unrescued CLS-TA patients, mean baseline BCVA was 55.6 letters, and in 46 of 64 (71.9%) rescued control patients, mean baseline BCVA was 53.8 letters (95% CI for difference, -2.9 to $+7.0$ letters; *P* = 0.414). At week 24, 79 of 92 (85.9%) unrescued CLS-TA patients who completed the study showed a mean improvement of 15.7 letters, compared with a 10.9-letter improvement in 46 of 63 (73.0%) rescued control patients who completed the study (95% CI for difference, -0.5 to $+9.6$ letters; *P* = 0.080). Analysis of CST showed a similar trend. In 83 of 96 (86.4%) unrescued CLS-TA patients, mean baseline CST was 480.6 μ m, and in 46 of 64 (71.9%) rescued control patients, mean baseline CST was 519.7 μ m (95% CI for difference, -95.1 to $+20.8$ μ m; *P* = 0.207). At week 24, 77 of 90 (85.6%) unrescued CLS-TA patients who completed the study with gradable images showed a 174.0- μ m improvement, compared with the 148.5- μ m improvement in 44 of 61 (72.1%) rescued control patients who completed the study with gradable images (95% CI for difference, -88.2 to -2.0 μ m; *P* = 0.040).

Safety

The percentage of patients with 1 or more ocular AEs was 51% in the CLS-TA arm and 58% in the control arm (Table 2 and S4, available at www.aaojournal.org). The incidence of AEs considered by the investigator to be treatment related was 29 (30.2%) in the CLS-TA arm and 8 (12.5%) in the control arm. The 3 most frequent ocular AEs were cystoid ME (0% vs. 17.2% of patients in CLS-TA and control arms, respectively), eye pain at time of procedure (12.5% vs. 4.7%, respectively), and elevated IOP associated with corticosteroid (11.5% vs. 15.6%, respectively). All patients who experienced AEs of elevated IOP in the control arm had undergone rescue therapy with local corticosteroids, with elevated IOP AEs in 10 of the 37 control arm patients (27.0%) who were administered intravitreal or periocular corticosteroid injection as additional therapy. Cataract incidence was comparable between the CLS-TA and control groups: 7.3% and 6.3%, respectively.

Three serious AEs occurred, all of which were identified in the CLS-TA arm: sialadenitis, posttraumatic lumbar compression fracture, and a retinal detachment. The retinal detachment occurred approximately 8 weeks after the suprachoroidal injection procedure and was in a different quadrant than the procedure. It was assessed by the study investigator as possibly related to underlying disease state. None of the serious AEs were deemed treatment related by the study investigator or led to study discontinuation.

Discussion

PEACHTREE was the first phase III trial to evaluate suprachoroidal injection of a therapeutic agent for the treatment of an ocular disease. In preclinical studies, suprachoroidally administered CLS-TA rapidly achieved high levels in the choroid and retina, detectable for more than 3 months (Edelhauser HF, et al. Suprachoroidal microinjection delivers triamcinolone acetonide to therapeutically relevant posterior ocular structures and limits exposure in the anterior segment. Poster presented at: Association for Research in Vision and Ophthalmology Annual Meeting; Seattle, WA, May 1–5, 2016),² which

could explain, in part, the functional and anatomic improvements observed in NIU patients with ME in this clinical trial setting. PEACTHREE also was the first phase III pivotal uveitis trial to study changes in visual acuity as a primary end point and showed that suprachoroidally injected CLS-TA significantly improved vision in patients with ME secondary to uveitis, with visual acuity gains of 3 lines or more (≥ 15 ETDRS letters) in nearly half of patients receiving treatment. This clinically meaningful improvement represents a doubling of the visual angle (i.e., patients were able to read ETDRS letters half the size after study therapy compared with study entry). Moreover, patients receiving suprachoroidal CLS-TA derived a mean visual acuity benefit of approximately 14 letters versus the 3 letters gained in the control arm at 24 weeks. A difference of 2 lines of improved vision was observed between groups starting at week 4, the first evaluation time point. By week 8, the next evaluation time point, the proportion of patients with 20/40 or better visual acuity (i.e., legal driving vision in most states of the United States) approached 50% after suprachoroidal CLS-TA administration. Improvement in vision was accompanied by significant reduction of ME and normalization of retinal architecture, with resolution of ME in more than 50% of patients treated with CLS-TA. Improvement in functional and anatomic end points occurred regardless of the primary anatomic site of inflammation, including anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis.

Although suprachoroidal administration of CLS-TA was not compared with other treatments in PEACHTREE, the data suggest that suprachoroidal CLS-TA may provide a valuable addition to the therapeutic armamentarium. Although cross-trial comparisons have limitations, a retrospective cohort analysis of more than 1000 patients with uveitic ME who were treated with systemic immunosuppressive therapy demonstrated that approximately one half of patients gained 10 letters or more in vision at 6 months.¹⁷ In PEACHTREE, approximately one half of patients treated with CLS-TA gained 15 letters or more at 6 months. For additional context, the recent Periocular and Intravitreal Corticosteroids for Uveitic Macular Edema Trial (ClinicalTrials.gov identifier, NCT02374060), a National Institutes of Health-funded prospective clinical trial, compared 3 commonly administered local corticosteroids for uveitic ME. The 6-month results showed that intravitreal triamcinolone acetonide and intravitreal dexamethasone outperformed periocular corticosteroid treatment, both achieving approximately 9 letters of improvement compared with approximately 4 letters gained in the periocular arm.¹⁸ In PEACHTREE, the mean gain in visual acuity was approximately 14 letters at 6 months.

With respect to safety, reported rates of IOP elevation with the use of local triamcinolone acetonide in the eye range from 20% to 60%,¹⁹ compared with the 11.5% rate observed in PEACHTREE for 2 CLS-TA injections during the 24-week trial. In the Periocular and Intravitreal Corticosteroids for Uveitic Macular Edema Trial, approximately 24% to 33% of patients in each arm required IOP-lowering medication. Although cross-trial comparisons have limitations, 7.3% of patients in the treatment arm of

PEACHTREE required medication to lower IOP. These data suggest an IOP-sparing benefit, arguably because of the unique compartmentalization and ocular distribution inherent to the suprachoroidal administration of CLS-TA. Preclinical studies investigating suprachoroidal administration support this assertion, demonstrating low corticosteroid exposure within the anterior chamber and trabecular meshwork (Edelhauser HF, et al. Suprachoroidal microinjection delivers triamcinolone acetonide to therapeutically relevant posterior ocular structures and limits exposure in the anterior segment. Poster presented at: Association for Research in Vision and Ophthalmology Annual Meeting; Seattle, WA, May 1–5, 2016).² This benefit is supported further by the control arm of PEACHTREE, which showed that 27.0% of patients receiving intravitreal or periocular corticosteroid injection rescue demonstrated IOP AEs.

Limitations of this trial include a lack of comparison with other local corticosteroid therapies and only 6 months of efficacy and safety follow-up. Nonetheless, the PEACHTREE study showed robust outcomes that were observed as early as week 4 and were sustained through week 24, with longer-term outcomes to be assessed in the MAGNOLIA follow-up study ([ClinicalTrials.gov](https://clinicaltrials.gov) identifier, NCT02952001).

In summary, the results of PEACHTREE support the clinical use of suprachoroidally injected CLS-TA as a new treatment option for patients with ME associated with NIU, demonstrating clinically meaningful improvements in vision for nearly half of the patients treated. As the first phase III trial to evaluate suprachoroidal injection for the treatment of an ocular disease, PEACHTREE also paves the way for research on suprachoroidal administration to deliver other therapeutics in a targeted approach to choroidal and retinal tissues. Suprachoroidal administration could enhance delivery of therapies for a variety of ophthalmic conditions in which a precise anatomic drug application may yield safety, efficacy, and durability benefits over current therapies (Edelhauser HF, et al. Suprachoroidal microinjection delivers triamcinolone acetonide to therapeutically relevant posterior ocular structures and limits exposure in the anterior segment. Poster presented at: Association for Research in Vision and Ophthalmology Annual Meeting; Seattle, WA, May 1–5, 2016).¹ In the future, suprachoroidal administration may even be assessed for some gene therapies, because preclinical work supports the potential for minimally invasive targeted ocular gene therapy, without the risks of vitrectomy surgery and subretinal administration (Taraborelli D, et al. A one-week study to evaluate safety, tolerability, and retinal cell transfection of non-viral DNA nanoparticles administered by suprachoroidal injection. Poster presented at: Association for Research in Vision and Ophthalmology Annual Meeting; Honolulu, HI, April 29–May 3, 2018).²⁰

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*A complete listing of the members of the PEACHTREE Study Group is available in the [Appendix](#) (available at www.aaojournal.org)

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HUMAN SUBJECTS: Human subjects were included in this study. The human ethics committees/IRB at each site approved the study (see [supplementary appendix](#) [available at www.aaojournal.org] for full list of sites and investigators). All research adhered to the tenets of the Declaration of Helsinki. All participants provided informed consent.

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Abbreviations and Acronyms:

AE = adverse event; **AMD** = age-related macular degeneration; **BCVA** = best-corrected visual acuity; **CST** = central subfield thickness; **ETDRS** = Early Treatment Diabetic Retinopathy Study; **IOP** = intraocular pressure; **ITT** = intent-to-treat; **ME** = macular edema; **NIU** = noninfectious uveitis; **POINT** = PeriOcular and INTravitreal Corticosteroids for Uveitic Macular Edema Trial.

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