Ophthalmol Ther (2023) 12:577–591
https://doi.org/10.1007/s40123-022-00603-x

BRIEF REPORT

Triamcinolone Acetonide Suprachoroidal Injectable Suspension for Uveitic Macular Edema: Integrated Analysis of Two Phase 3 Studies

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Received: September 21, 2022 / Accepted: October 18, 2022 / Published online: November 18, 2022

ABSTRACT

Introduction: Macular edema, a common complication of uveitis, may result in vision loss. The aim of this analysis was to report integrated phase 3 trial data for triamcinolone acetonide injectable suspension for suprachoroidal use (SCS-TA) in the treatment of macular edema secondary to noninfectious uveitis using strict inclusion criteria.

Methods: This analysis included patients with central subfield thickness (CST) ≥ 300 μm and best-corrected visual acuity (BCVA) of ≥ 5 and ≤ 70 Early Treatment Diabetic Retinopathy Study (ETDRS) letters at both screening and baseline who received ≥ 1 study treatment in either PEACHTREE (randomized, double-masked SCS-TA or sham control) or AZALEA (open-label SCS-TA). Patients received SCS-TA 4.0 mg (0.1 ml of 40 mg/ml) or control at baseline and week 12.

Results: In the SCS-TA group (n = 95), 47.4% of patients gained ≥ 15 ETDRS letters from baseline to week 24 versus 16.7% of patients in the control group (n = 60; $P < 0.001$). Mean change in BCVA in the SCS-TA group was 9.6 letters at week 4 and 13.9 letters at week 24. CST also improved rapidly in the SCS-TA group (mean change: − 158.4 μm at week 4), with sustained reduction throughout the study (mean change: − 163.9 μm at week 24 versus − 19.3 μm in the control group; $P < 0.001$). No treatment-related serious adverse events (AEs) were reported. Incidence of AEs pertaining to elevated intraocular pressure was 12.6% and 15.0% in the SCS-TA and control groups, respectively; incidence of cataract formation/worsening AEs was 7.4% and 6.7%, respectively.

Conclusion: In this integrated analysis utilizing strict inclusion criteria, SCS-TA was found effective in the treatment of patients with macular edema associated with noninfectious uveitis and was generally well tolerated.

Trial registration: ClinicalTrials.gov identifier: NCT02595398, NCT03097315.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40123-022-00603-x.

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Keywords: Central subfield thickness; Macular edema; Suprachoroidal; Triamcinolone acetonide; Uveitis

Key Summary Points

Why carry out this study?

Administration of ocular therapies via the suprachoroidal space selectively targets drug delivery to chorioretinal structures.

Triamcinolone acetonide injectable suspension for suprachoroidal use (SCS-TA) has demonstrated efficacy in phase 3 trials in patients with macular edema associated with noninfectious uveitis.

What did the study ask?

What was the safety and efficacy of SCS-TA on integrated analysis of clinical trial data from two pivotal studies that employed strict inclusion criteria for macular edema and visual acuity impairment in patients with uveitis?

What was learned from the study?

In addition to confirming the improvement in best-corrected visual acuity and reducing retinal thickness in the central subfield, SCS-TA led to the resolution of anterior chamber and vitreous inflammation in the majority of patients.

SCS-TA provides clinicians with an effective treatment option for macular edema associated with uveitis, with a route of administration that targets posterior segment ocular tissues.

The incidence of elevations in intraocular pressure was low.

INTRODUCTION

Uveitis refers to a group of heterogeneous intraocular conditions characterized by inflammation of the uveal tissues that may also affect adjacent structures (e.g., vitreous, retina) [1, 2]. Macular edema (ME), a common complication of uveitis, is the primary cause of vision loss in patients with uveitis [3, 4]. Uveitis has detrimental effects on health-related quality of life, particularly among patients with reduced visual acuity [5, 6] who may experience difficulties with activities such as reading and driving, leading to potential loss of independence. The presence of ME secondary to noninfectious uveitis (NIU) is associated with increased vision loss and healthcare utilization and costs compared with NIU alone [7].

Corticosteroids, including periocular or intravitreal injections and intravitreal implants, are the mainstay of treatment for ME associated with NIU [8, 9]. Although corticosteroids have robust anti-inflammatory and immunosuppressive properties, their long-term ocular use is limited by numerous adverse events (AEs) including elevated intraocular pressure (IOP) and the development or progression of cataracts [8, 9].

Administration of ocular therapies via the suprachoroidal space (SCS) provides drug delivery that is targeted to chorioretinal structures [10–12]. Triamcinolone acetonide injectable suspension for suprachoroidal use (SCS-TA; XIPERE), administered as a suprachoroidal injection via the SCS Microinjector (Clearside Biomedical, Alpharetta, GA), provides a minimally invasive, alternative, office-based therapeutic approach for the treatment of ME associated with NIU (Supplementary Fig. 1) [13, 14]. In preclinical pharmacokinetic studies, TA concentrations were high in the choroid and retina following suprachoroidal injections of TA suspensions, including SCS-TA, with limited anterior segment exposure; TA was detectable in chorioretinal tissues for up to 3 months [15–17]. SCS-TA has been evaluated in phase 2 and phase 3 clinical trials [18–20] and is approved by the US Food and Drug Administration for the treatment of ME associated with uveitis [21].

Here we report results from an integrated analysis of the efficacy and safety of SCS-TA for the treatment of ME in patients with NIU across two phase 3 clinical trials (PEACHTREE and AZALEA), including integrated outcomes for other clinical signs of ocular inflammation. Stringent inclusion criteria were used in this integrated analysis; specifically, only data from patients with confirmed ME and visual acuity impairment at both screening and baseline visits were included from PEACHTREE, as opposed to those meeting such criteria solely at screening in prior analyses. To augment the study population, data from patients that met these same criteria from AZALEA were also included.

METHODS

Study Design and Patients

This is an integrated analysis of data from two phase 3 clinical trials that evaluated the efficacy and/or safety of SCS-TA. Details of study methodology have been reported previously [19, 20]. Each study protocol was approved by an institutional review board or independent ethics committee at each study site. Studies were conducted in accordance with the Good Clinical Practice guideline of the International Conference on Harmonisation and the ethics principles of the Declaration of Helsinki, and all patients provided written informed consent before study procedures were initiated.

PEACHTREE was a phase 3, randomized, masked, sham-controlled trial; all patients were required to have ME secondary to NIU (central subfield thickness [CST] $\geq$ 300 μm) and best-corrected visual acuity (BCVA) $\geq$ 5 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (Snellen equivalent, 20/800) and $\leq$ 70 letters (Snellen equivalent, 20/40) in the study eye at screening. AZALEA was a phase 3, single-arm, open-label safety study that enrolled patients with NIU (active or inactive), with or without ME, and an ETDRS BCVA score of $\geq$ 5 letters in the study eye. In both studies, ocular health was otherwise stable, with no other active ocular disease and no IOP > 22 mmHg or uncontrolled glaucoma. Concomitant medications could include $\leq$ 2 IOP-lowering medications, systemic corticosteroids at doses equivalent to oral prednisone $\leq$ 20 mg/day and/or systemic immunomodulatory therapies (at stable doses for $\geq$ 2 weeks) provided there was no expectation of a dosage increase during the study.

The population for this integrated efficacy and safety analysis included patients from PEACHTREE and AZALEA with baseline CST $\geq$ 300 μm and baseline BCVA of $\geq$ 5 and $\leq$ 70 ETDRS letters who met these inclusion criteria at both the screening and baseline visits and received $\geq$ 1 study treatment (active or sham).

Treatment and Assessments

In both studies, patients received a single injection in the designated study eye on day 0 and week 12. In PEACHTREE, patients were randomized in a 3:2 ratio to receive active treatment (suprachoroidal injection of SCS-TA 4.0 mg [0.1 ml of 40 mg/ml]) or a sham procedure (that mimicked the suprachoroidal injection but used a needle-less hub on the microinjector with no drug or vehicle administered). In AZALEA, all patients received open-label suprachoroidal injection of SCS-TA 4.0 mg (0.1 ml of 40 mg/ml). In both studies, assessments were conducted every 4 weeks through week 24.

The studies included similar assessments of efficacy and safety; however, efficacy endpoints were designated as primary in PEACHTREE and safety endpoints were designated as primary in AZALEA. Key efficacy endpoints were the proportion of patients with an increase from baseline BCVA of $\geq$ 15 ETDRS letters ($\geq$ 3 lines of vision) at week 24 and mean change from baseline CST (measured by spectral domain optical coherence tomography [SD-OCT]) at week 24. Additional efficacy endpoints included changes in other indicators of uveitic inflammation using the Standardization of Uveitis Nomenclature working group criteria for anterior chamber (AC) cells (assessed by slit-lamp biomicroscopy and rated using a standardized grading scale [2] ranging from 0 to 4+), AC flare

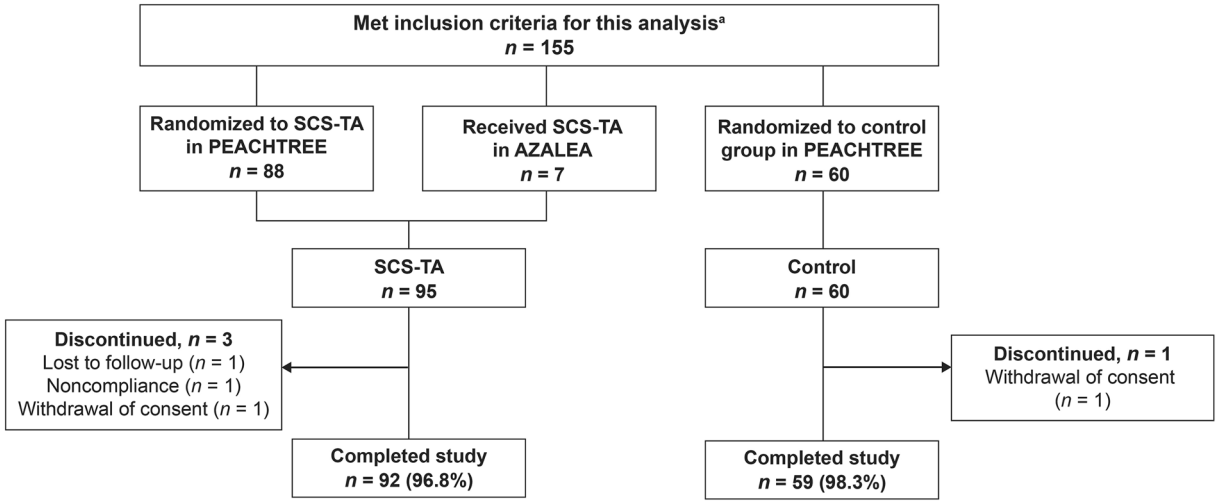

Fig. 1 Patient disposition. [a]Baseline CST ≥ 300 µm and baseline BCVA of ≥ 5 and ≤ 70 ETDRS letters. *BCVA* best-corrected visual acuity, *CST* central subfield thickness, *ETDRS* Early Treatment Diabetic Retinopathy Study, *SCS-TA* triamcinolone acetonide injectable suspension for suprachoroidal use

(assessed by slit-lamp biomicroscopy and rated using a standardized grading scale [2] ranging from 0 to 4+) and vitreous haze (assessed via indirect ophthalmoscopy and rated using a standardized photographic scale [22, 23] ranging from 0 to 4). Safety endpoints included the incidence of AEs and serious AEs and changes in IOP. In both studies, rescue therapy was permitted beginning at week 4 following protocol-defined criteria; selection of rescue treatment was made at the discretion of the investigator.

Statistical Analysis

Change in BCVA (ETDRS letters) and change in CST from baseline through week 24 were compared for SCS-TA versus control at each assessment time point using an analysis of variance model with treatment and pooled country (USA + Israel, India) as fixed effects. Cochran-Mantel-Haenszel chi-square tests, with stratification by pooled country, were used to evaluate differences between the SCS-TA group versus the control group in the proportion of patients who met specified outcome criteria. Missing data (including post-rescue time points) were imputed using the method of last observation carried forward. The type I error rate (alpha) was set at 0.05, without adjustment for multiple comparisons.

RESULTS

Patients

The integrated analysis population included 95 patients who received SCS-TA ($n = 88$ of 96 from PEACHTREE, $n = 7$ of 38 from AZALEA) and 60 patients (of 64) who received the sham control procedure in PEACHTREE (Fig. 1). Overall, the analysis population included 54.8% males; mean age was 50.5 (range, 18–92) years. Demographic and baseline clinical characteristics were similar between the SCS-TA and control groups (Table 1), except for time since diagnosis of uveitis, which was longer, on average, in the SCS-TA group (40.2 months versus 26.1 months).

Visual Acuity Outcomes

In patients treated with SCS-TA, there was rapid improvement in BCVA (mean change of 9.6 ETDRS letters at the week 4 assessment) that continued throughout the study (mean change

Table 1 Demographics and baseline characteristics

Characteristic	SCS-TA (n = 95)	Control (n = 60)
Age, years		
Mean (SD)	50.3 (14.3)	50.7 (14.4)
Median (range)	52.0 (18–92)	50.5 (22–85)
Sex, n (%)		
Male	41 (43.2)	29 (48.3)
Female	54 (56.8)	31 (51.7)
Race, n (%)		
Asian	40 (42.1)	26 (43.3)
Black/African American	13 (13.7)	10 (16.7)
White	41 (43.2)	24 (40.0)
Other	1 (1.1)	0 (0)
Uveitis anatomic location, n (%)		
Anterior	29 (30.5)	13 (21.7)
Intermediate	34 (35.8)	23 (38.3)
Posterior	20 (21.1)	12 (20.0)
Panuveitis	30 (31.6)	22 (36.7)
Time since uveitis diagnosis, months		
Mean (SD)	40.2 (53.0)	26.1 (31.5)
Median (range)	15.6 (0–290)	16.0 (0–149)
Duration of uveitis, n (%)		
Limited, $\leq$ 3 months	15 (15.8)	7 (11.7)
Persistent, $>$ 3 months	78 (82.1)	53 (88.3)
Unavailable	2 (2.1)	0 (0)
Course of uveitis, n (%)		
Acute	4 (4.2)	5 (8.3)
Recurrent	30 (31.6)	16 (26.7)
Chronic	59 (62.1)	39 (65.0)
Unavailable	2 (2.1)	0 (0)
BCVA, study eye, ETDRS letters		
Mean (SE)	53.2 (14.3)	52.3 (12.4)
Median (range)	57.0 (9–70)	53.5 (12–70)
CST, study eye, μm		
Mean (SD)	488.7 (148.1)	536.7 (155.0)
Median (range)	456.0 (303–857)	533.0 (303–971)

BCVA best-corrected visual acuity, *CST* central subfield thickness, *ETDRS* Early Treatment Diabetic Retinopathy Study, *SCS-TA* triamcinolone acetonide injectable suspension, for suprachoroidal use

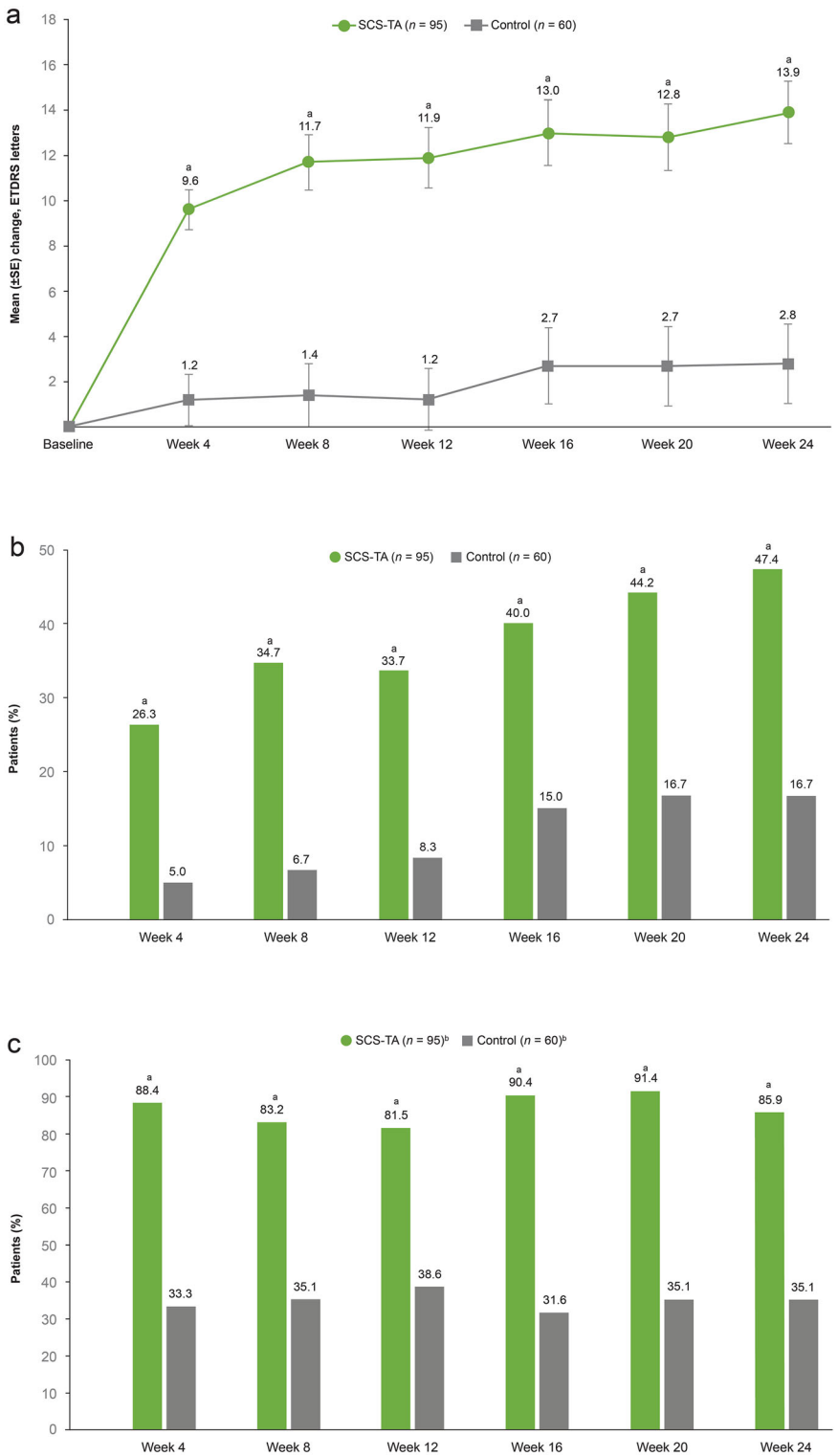

Fig. 2 Improvement in BCVA shown as **a** mean change from baseline in ETDRS letters, **b** percentage of patients with gain of $\geq$ 15 ETDRS and **c** percentage of patients with BCVA of 20/40 or better at each assessment. [a]$P < 0.001$ versus control. *BCVA* best-corrected visual acuity, *ETDRS* Early Treatment Diabetic Retinopathy Study, *SCS-TA* triamcinolone acetonide injectable suspension for suprachoroidal use

of 13.9 letters at week 24). Mean improvement in ETDRS letters was statistically significantly greater in the active treatment group compared with the control group at every assessment (Fig. 2A), with a mean between-group difference of 10.7 letters at week 24 (95% confidence interval, 6.3, 15.0; $P < 0.001$). There was a gain of $\geq$ 15 ETDRS letters from baseline at week 24 in 47.4% of patients in the SCS-TA group compared with 16.7% of patients in the control group ($P < 0.001$; Fig. 2B). At week 24, BCVA was 20/40 or better ($\geq$ 70 ETDRS letters) in 51.6% of the SCS-TA group versus 18.3% of the control group ($P < 0.001$; Fig. 2C); BCVA was 20/200 or worse ($\leq$ 35 ETDRS letters) in 4.2% of the SCS-TA group versus 13.3% of the control group ($P = 0.038$).

Macular Edema Outcomes

Mean CST was rapidly reduced in patients who received SCS-TA (mean change of − 158.4 μm at week 4), with a sustained reduction throughout the study (mean change of − 163.9 μm at week 24). Small mean reductions of CST (< 28 μm) were observed in the control group, and the between-group differences were statistically significant at every assessment (Fig. 3A). At week 24, excess retinal thickness was reduced by $\geq$ 20% from baseline in 85.9% of patients treated with SCS-TA versus 35.1% of patients in the control group ($P < 0.001$; Fig. 3B). CST measured at week 24 was < 300 μm in 57.6% of the SCS-TA group and 12.3% of the control group ($P < 0.001$; Fig. 3C). Supplementary Fig. 2 depicts representative SD-OCT images from three SCS-TA patients, all of whom demonstrated a gain of $\geq$ 15 ETDRS letters from baseline at week 24.

Anterior Chamber and Vitreous Inflammation

A substantial proportion of patients had additional signs of uveitic inflammation at baseline. Specifically, AC cells, AC flare and vitreous haze were reported for 56.8% and 36.7%, 40.0% and 33.3%, and 78.9% and 70.0% of patients in the SCS-TA group and control group, respectively. Among those patients with signs of inflammation at baseline, 72.2%, 71.1% and 72.0% of patients treated with SCS-TA experienced resolution (score of 0) of AC cells, AC flare and vitreous haze, respectively, at week 24, compared with $\leq$ 20% of patients in the control group (Fig. 4).

Rescue Therapy

Twelve patients (12.6%) in the SCS-TA group and 44 patients (73.3%) in the control group received rescue therapy at any time during the study based on predefined BCVA, CST and signs of uveitis criteria or the investigator's medical judgment (Supplementary Table); 5 (5.3%) and 30 (50.0%) patients, respectively, received rescue therapy before the scheduled second dose of SCS-TA or sham. Of the 44 patients in the control group who received rescue therapy, intravitreal or periocular corticosteroid injections were administered to 35 patients, with the remainder receiving nonsteroidal anti-inflammatory drugs, topical corticosteroids and/or oral steroids. The Kaplan-Meier estimate of median time to rescue was not estimable for SCS-TA, as < 50% of patients were rescued, and was 84.0 days for the control group.

Safety

Adverse events in the study eye were experienced by 51.6% of patients in the SCS-TA group (122 total AEs) and 56.7% of patients in the control group (49 total AEs; Table 2). The majority of study eye AEs were mild (SCS-TA: 75.4%; control: 55.1%) or moderate (SCS-TA: 22.1%; control: 42.9%) in intensity. The most commonly reported ocular AEs were related to elevated IOP, eye pain and cataract development. The only serious AE in the study eye (retinal detachment in a patient in the SCS-TA group) occurred approximately 8 weeks after the second suprachoroidal injection procedure and in a different quadrant [19]. This AE was considered by the masked investigator as not related to study treatment, resolved following surgical correction and did not result in study discontinuation.

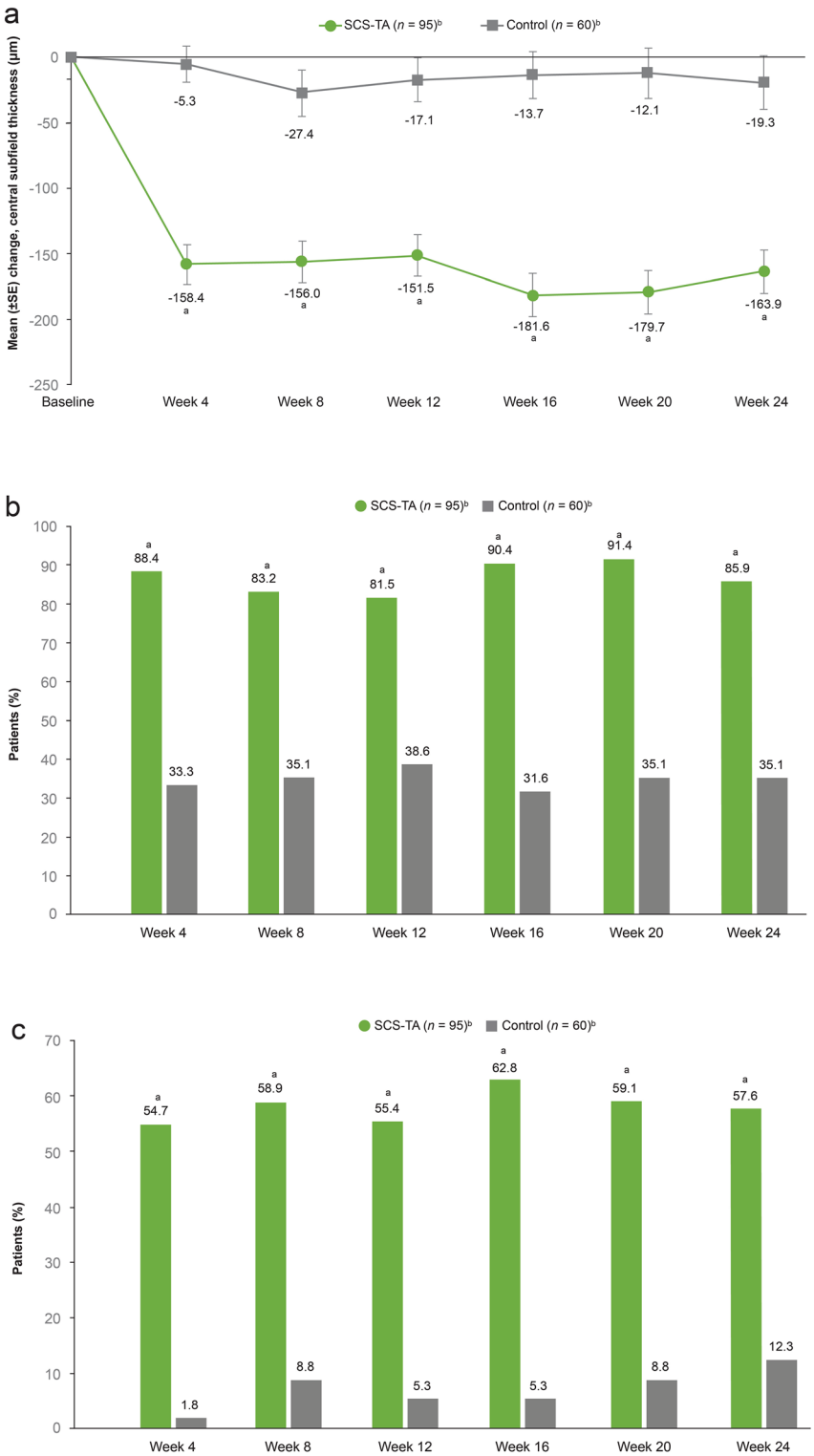

Fig. 3 Improvement in macular edema shown as **a** mean change from baseline in central subfield thickness, **b** percentage of patients with ≥ 20% reduction in excess CST and **c** percentage of patients with CST < 300 µm at each assessment. [a]$P < 0.001$ for SCS-TA versus control. [b]Sample sizes vary slightly by visit based on data availability. *SCS-TA* triamcinolone acetonide injectable suspension for suprachoroidal use

Adverse events led to treatment discontinuation in 4 patients (4.2%) in the SCS-TA group (1 patient each with visual acuity reduced [26 BCVA letter loss], steroid-induced elevated IOP, vitreous hemorrhage and worsening of uveitis) and 4 patients (6.7%) in the control group (2 patients with worsening uveitis, 1 patient with worsening uveitis and IOP increased and 1 patient with iridocyclitis). All eight patients were followed through the end of the study, and none of the AEs led to study discontinuation.

Adverse events pertaining to cataract formation/worsening in the study eye (Table 2) were considered by the investigator to be treatment related in 4 patients (4.2%) treated with SCS-TA and 0 (0.0%) patients in the control group. There were no surgeries for cataract in the study eye. Vitreous detachment was deemed treatment related in 1 patient (1.1%) receiving SCS-TA.

Adverse events pertaining to elevated IOP (i.e., IOP increased, ocular hypertension, open angle glaucoma), excluding AEs incurred on the day of treatment (which are generally considered to be injection volume related), occurred in 12 of 95 patients (12.6%) in the SCS-TA group and 9 of 60 patients (15.0%) in the control group. All nine control group patients received intravitreal or periocular corticosteroid injections as rescue therapy. Thus, IOP-related AEs were reported in 9 of 35 control group patients (25.7%) who received rescue therapy with intravitreal or periocular corticosteroid injections. A small mean increase in IOP was observed after each injection in patients who received SCS-TA (Supplemental Fig. 3). An increase in IOP of $\geq$ 10 mmHg from baseline at any post-baseline visit was observed in 14 of 94 patients (14.9%) who received SCS-TA and 10 of 60 patients (16.7%) in the control group; an increase of $\geq$ 30 mmHg was reported in 7 of 94 patients (7.4%) and 4 of 60 patients (6.7%), respectively. The proportion of patients who required one or more additional IOP-lowering medications was 10.4% in the SCS-TA group and 9.4% in the control group.

DISCUSSION

The efficacy and safety of SCS-TA in the treatment of patients with ME secondary to NIU were demonstrated in a randomized, double-masked, sham-controlled, phase 3 clinical trial (PEACHTREE) [19] with additional safety information provided by an open-label safety study (AZALEA) in patients with NIU with or without ME [20]. This integrated analysis of data from the PEACHTREE and AZALEA trials evaluated the combined results exclusively in patients with active ME at both screening and baseline from these two studies, highlighting the efficacy and safety of SCS-TA in patients with ME associated with NIU and further showing the objective improvements in anterior chamber and vitreous inflammation for these patients. In the PEACHTREE study, patient eligibility for study enrollment was established during the screening period; however, some patients who met criteria for ME and visual acuity impairment at screening no longer met one or both criteria at study baseline [19]. In the AZALEA study, which focused on safety, enrolled patients were not required to have visual impairment, ME or active uveitis at baseline [20]. Stringent inclusion criteria employed in this integrated analysis, which included only data from patients with confirmed ME (CST $\geq$ 300 μm) and visual acuity impairment ($\geq$ 5 and $\leq$ 70 ETDRS letter) at both screening and baseline, provided a more rigorous evaluation of SCS-TA.

In this integrated analysis, vision was significantly improved in patients who received SCS-TA, with mean visual acuity benefit of 14 ETDRS letters and visual acuity gains of $\geq$ 15 ETDRS letters ($\geq$ 3 lines) in almost 50% of patients. Improvement in vision was accompanied by significant reductions in ME, and other signs of uveitic inflammation (AC cells, AC flare, vitreous haze) were resolved by week 24 in most patients who exhibited these signs at baseline. The most frequently occurring ocular AEs were related to elevated IOP, eye pain and cataract development; there were no treatment-related serious AEs.

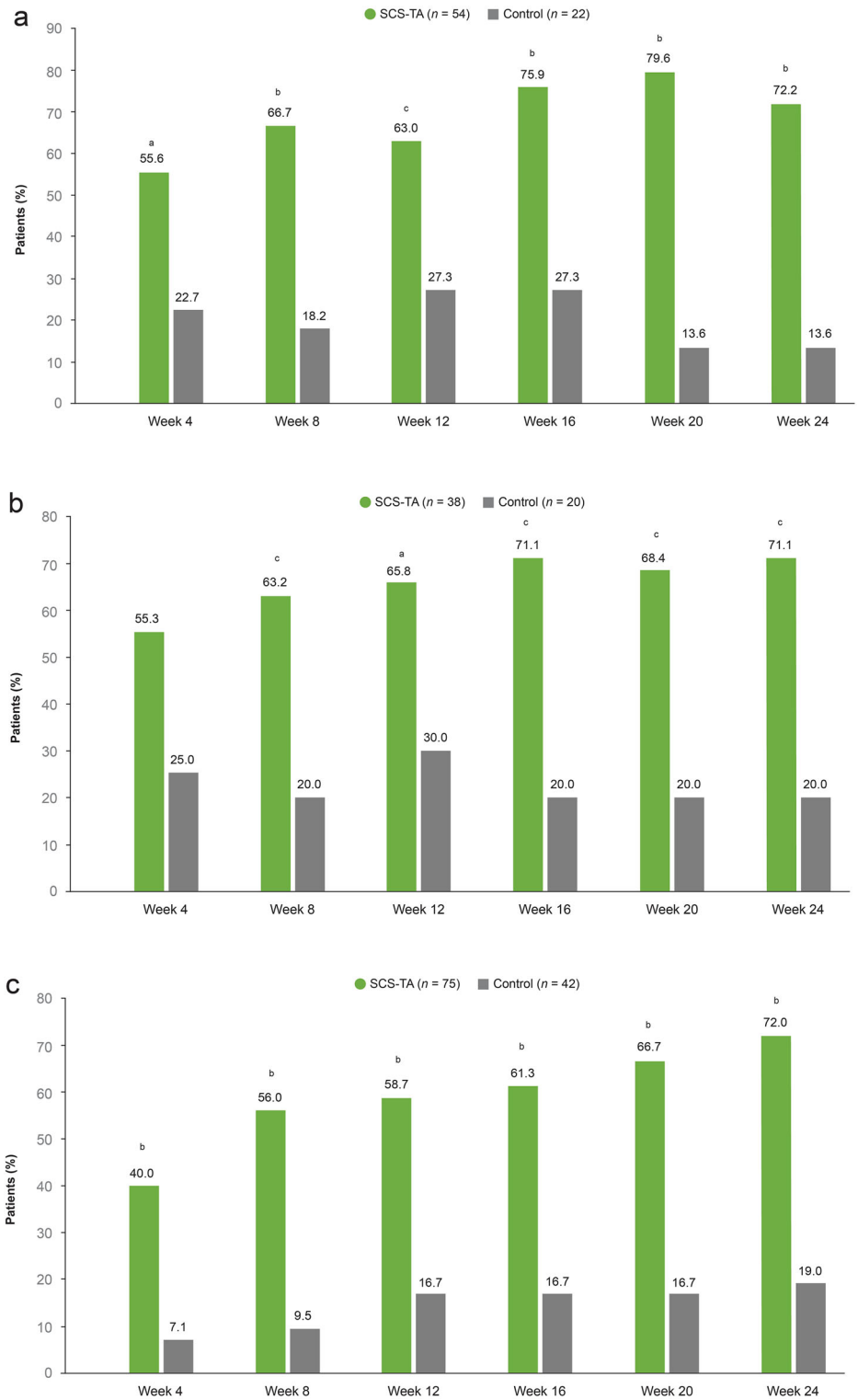

Fig. 4 Percentage of patients with resolution of **a** anterior chamber cells, **b** anterior chamber flare and **c** vitreous haze at each assessment among patients with baseline inflammation (i.e., Standardization of Uveitis Nomenclature criteria grade > 0) for each sign. [a]$P < 0.05$ for SCS-TA versus control. [b]$P < 0.001$ for SCS-TA versus control. [c]$P < 0.01$ for SCS-TA versus control. *SCS-TA* triamcinolone acetonide injectable suspension for suprachoroidal use

Drug delivery to the SCS has the potential to address unmet needs in the treatment of ocular diseases [11, 12, 24]. The SCS is a potential space, located between the sclera and choroid, that expands when fluid is introduced [10, 11, 25]. Suprachoroidal drug delivery has potential advantages in terms of efficacy (by targeting and providing sustained drug levels in the affected chorioretinal tissues) and safety (by sparing the anterior segment and the vitreous chamber) [24].

Clinical studies have shown that suprachoroidal injection of SCS-TA, via the SCS Microinjector, causes a temporary expansion of the SCS with no detrimental lasting effects on SCS anatomy [26, 27]. The safety of the SCS Microinjector has been demonstrated in studies across multiple ocular diseases (e.g., ME secondary to retinal vein occlusion, diabetic ME) [26, 27]. Proof of concept for suprachoroidal injection of SCS-TA to reduce ocular inflammation was established using a porcine animal model [28]; a small open-label study of patients with NIU (with or without ME) [29] and a phase 2, randomized, masked clinical trial of patients with ME secondary to NIU [18] provided preliminary efficacy and safety data.

The studies included in this integrated analysis (PEACHTREE, AZALEA) demonstrated the efficacy and safety of two suprachoroidal injections of SCS-TA 4.0 mg, with a 12-week interval between doses, through follow-up at week 24 [19, 20]. While there is only moderate correlation between CST and BCVA [30], a recent post hoc analysis of PEACHTREE and AZALEA showed that improvements in CST in SCS-TA-treated eyes preceded improvements in BCVA, based on longitudinal modeling [31]. In addition, SCS-TA-treated eyes that showed an early CST response (reduction from baseline of $\geq$ 50 µm at 4 weeks) experienced a greater 24-week improvement in BCVA compared to those without such an early response [31].

Another post hoc analysis of the PEACHTREE study found that SCS-TA provided meaningful benefits in patients with uveitic ME regardless of concurrent usage of systemic medications (corticosteroids and/or steroid-sparing therapy) [32]. In a separate post hoc analysis of PEACHTREE data, patients treated only with SCS-TA (no rescue therapy) showed consistent trends of greater improvements in visual acuity, greater reductions in CST and lower rates of IOP-related safety issues than patients randomized to the control group who subsequently received rescue

Table 2 Summary of adverse events in the study eye

Study eye, *n* (%)	SCS-TA (*n* = 95)	Control (*n* = 60)
Any AE	49 (51.6)	34 (56.7)
AE related to study treatment	28 (29.5)	7 (11.7)
Serious AE	1 (1.1)	0 (0)
Serious AE related to study treatment	0 (0)	0 (0)
AE leading to treatment discontinuation	4 (4.2)	4 (6.7)
AE leading to study discontinuation	0 (0)	0 (0)
Most common AEs[a]		
Eye pain[b]: day of procedure	10 (10.5)	2 (3.3)
Eye pain[b]: other than day of procedure[c]	6 (6.3)	0 (0)
Elevated IOP[d]: day of procedure	7 (7.4)	0 (0)
Elevated IOP[d]: other than day of procedure[c]	12 (12.6)	9 (15.0)
Cataract[e]	7 (7.4)	4 (6.7)
Vitreous detachment	5 (5.3)	1 (1.7)
Uveitis	1 (1.1)	6 (10.0)

AE adverse event, *IOP* intraocular pressure, *SCS-TA* triamcinolone acetonide injectable suspension for suprachoroidal use

[a]Incidence $\geq$ 5% in either group

[b]Includes the preferred terms (1) eye pain, (2) injection site discomfort and (3) injection site pain

[c]Includes all events that did not occur on the day of the procedure

[d]Includes the preferred terms (1) IOP increased, (2) ocular hypertension and (3) open-angle glaucoma

[e]Includes the preferred terms (1) cataract, (2) cataract cortical, (3) cataract nuclear and (4) cataract subcapsular

therapy (most commonly intravitreal or periocular corticosteroids) [33].

Longer-term outcomes of SCS-TA were evaluated in an observation-only extension study that enrolled 33 patients from PEACHTREE (n = 28 SCS-TA, n = 5 control) who completed that study without the need for rescue medication [34]. Among the 14 SCS-TA-treated patients (50.0%) who did not require rescue therapy during 6 months of follow-up after the completion of PEACHTREE, mean change in BCVA and CST observed in PEACHTREE were retained through the extension study with a gain of 12.1 ETDRS letters and a reduction in CST of 174.5 μm at week 48 [34]. In the extension study population, an IOP increase ≥ 10 mmHg was observed during 48 weeks of follow-up in 4 patients (14.3%) treated with SCS-TA; AEs related to cataract formation were noted in 7 patients (25.0%) [34].

Limitations of the studies included in this analysis include the lack of a direct comparison with other locally administered corticosteroid treatments and the duration of follow-up (6 months). The efficacy and safety of other corticosteroid formulations (i.e., periocular TA injection, intravitreal TA injection and intravitreal dexamethasone implant) have been evaluated in a randomized clinical trial of patients with uveitic ME [35]. Although cross-trial comparisons have limitations, at week 24, the proportion of eyes with ≥ 20% reduction in CST was 61% for periocular TA, 73% for intravitreal TA and 74% for dexamethasone (compared with 67% of SCS-TA patients in the present analysis); mean gain in BCVA (ETDRS letters) was 4.1 letters, 9.6 letters and 9.2 letters, respectively (compared with 13.9 letters in this analysis). The proportion of eyes with IOP increase of ≥ 10 mmHg during the 24-week study period was 12% for periocular TA, 22% for intravitreal TA and 31% for dexamethasone (compared with 15% for SCS-TA in the present analysis).

CONCLUSION

This integrated analysis demonstrated that SCS-TA was effective in the treatment of uveitic ME in patients for whom ME and visual acuity impairment were observed at two separate assessments prior to treatment initiation. Overall, the safety profile of SCS-TA was favorable, with a low incidence of known risks associated with corticosteroid treatment (e.g., IOP elevation, cataract formation) that were manageable with appropriate monitoring and treatment. Suprachoroidal drug delivery was effectively applied to the treatment of uveitic ME and is a promising alternative delivery platform to advance the treatment of ocular diseases.

ACKNOWLEDGEMENTS

We thank the participants of the studies on which this analysis is based.

Funding. The studies used in this analysis were sponsored by Clearside Biomedical, Inc., Alpharetta, GA. The sponsor participated in designing the study; conducting the study; collecting, managing, analyzing and interpreting the data; and preparing and reviewing the manuscript. The journal's Rapid Service Fees were funded by Bausch + Lomb.

Medical Writing, Editorial and Other Assistance. Editorial and medical writing assistance was provided under the direction of the authors by Nancy Holland, PhD, Synchrony Medical Communications, LLC, West Chester, PA, USA, and funded by Bausch + Lomb.

Authorship. All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. Steven Yeh contributed to study conception and design, collection and interpretation of data, and manuscript preparation. Christopher R. Henry contributed to collection and interpretation of data and manuscript preparation. Barry Kapik

contributed to analysis and interpretation of data and manuscript preparation. Thomas A. Ciulla contributed to interpretation of data and manuscript preparation. All authors reviewed and approved the manuscript.

Prior Presentation. Portions of the paper were presented at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting; Denver, CO; May 1–4, 2022 (virtual, May 11–12, 2022), and the American Society of Retina Specialists (ASRS) Annual Meeting; New York, NY; July 13–16, 2022.

Disclosures. Steven Yeh reports serving as a consultant to Clearside Biomedical and Santen and receiving research grants from Clearside Biomedical. Christopher R. Henry reports serving as a consultant to Clearside Biomedical, Bausch + Lomb, and EyePoint Pharmaceuticals. Barry Kapik and Thomas A. Ciulla are employees of Clearside Biomedical.

Compliance With Ethics Guidelines. This study is an integrated analysis of data from two phase 3 clinical trials that have been reported previously. The two trials from which this analysis was constructed adhered to the tenets of the Declaration of Helsinki, were performed in accordance with the Health Insurance Portability and Accountability Act (HIPAA) and were approved by each site's institutional review board. All patients provided written informed consent to participate in the initial studies.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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