PROGRAM #:
527-B0082

DEVELOPMENT AND CLINICAL EXPERIENCE WITH SUPRACHOROIDAL INJECTION OF TRIAMCINOLONE ACETONIDE (CLS-TA) AS A LOCAL TREATMENT FOR NONINFECTIOUS UVEITIS

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PURPOSE

To review the efforts involved with suprachoroidal injection of CLS-TA in development of a potential local treatment for Non-infectious Uveitis from preclinical studies through early clinical development including Phase 1/2 and Phase 2 trials.

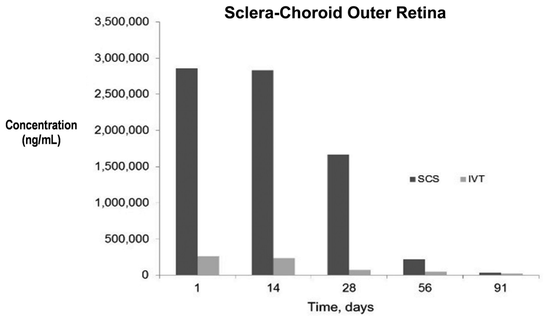
METHODS

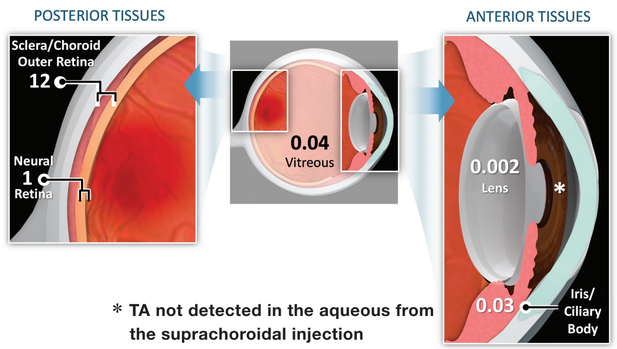
Animal pharmacokinetic and pharmacodynamic data along with efficacy results from phase 1/2 and phase 2 clinical trials will be presented. In each of these human trials, a single suprachoroidal injection of triamcinolone acetonide (TA) (4.0mg/100 µL) was administered and a total of 25 subjects (phase 1/2 = 8 subjects, phase 2 = 17 subjects) were followed for 6 months and 2 months respectively.

PRECLINICAL RESULTS

Pharmacokinetics

- Preclinical data from a three-month ocular distribution study in rabbits has shown higher amounts of drug accumulating in the choroid and retina following suprachoroidal injection (by 1200%) compared to an intravitreal injection.
- The same study has shown relative sparing of the vitreous and anterior segment including lens (ranging from below quantification levels in the anterior chamber to 4% in the vitreous) when compared to drug distribution levels following an intravitreal injection.





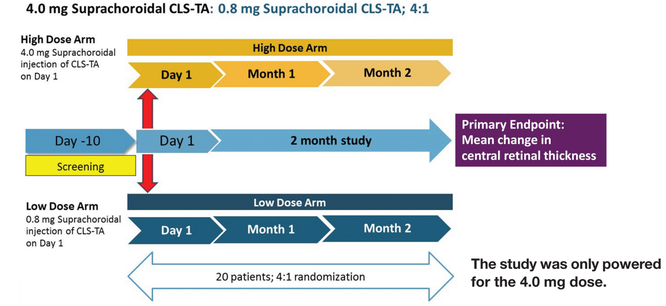
* TA not detected in the aqueous from the suprachoroidal injection

Pharmacodynamics

Animal efficacy experiments in preclinical models of Uveitis have shown that the 2 mg (50 µL) and 0.2 mg (50 µL) doses are both equally effective when TA is injected suprachoroidally.

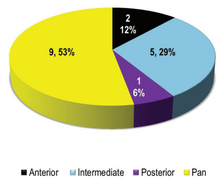
STUDY DESIGN

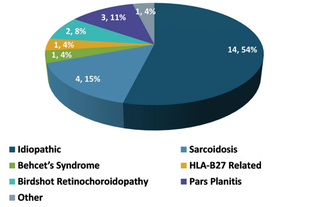
Phase 2 Study Design



- Twenty-two (22) patients were randomized into high and low dose arms
- 17 patients received 4.0 mg (High Dose Arm) and 5 patients received 0.8 mg (Low Dose Arm)
- All patients completed the study; No patients discontinued

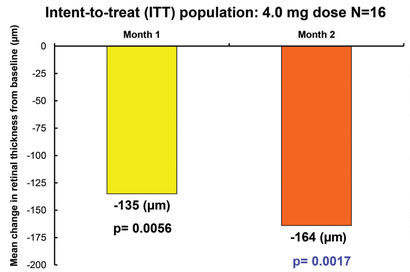
	CLS-TA 4.0 mg N=17	CLS-TA 0.8 mg N=5	TOTAL N=22
AGE (YEAR)			
MEAN	52.2	51.8	52.1
MEDIAN	50.0	53.0	53.0
MIN, MAX	20, 83	24, 69	20, 83

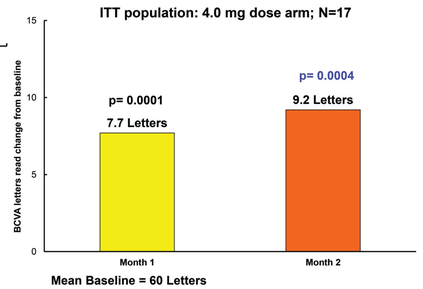




PHASE TWO RESULTS

- Mean reduction from baseline in macular edema (ME) was 164 µm (p=0.0017) at month 2.
- Mean improvement from baseline in visual acuity (VA)was 9.2 letters (p=0.0004) at month 2.
- Mean twenty percent (20%) reduction is 105 microns.

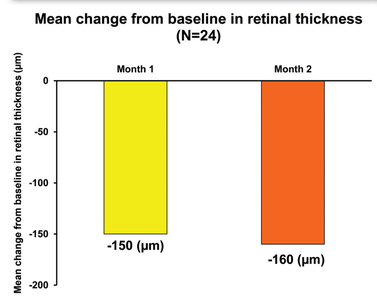


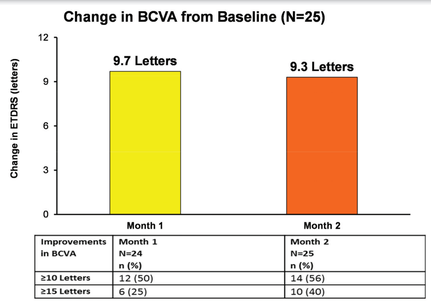


Visit	CST information	4.0 mg (N = 16)
Month 2	Subjects with ≥ 20% reduction in CST	11
	Subjects with CST <310 microns	9

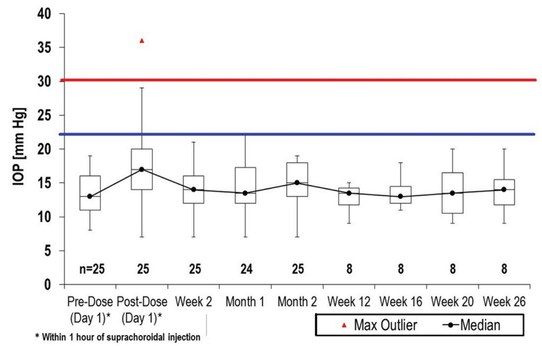
- In the open-label phase 1/2 study conducted prior to this phase 2, eight patients were dosed with a single suprachoroidal injection of TA and followed for 6 months
- Four of 8 patients did not receive any additional treatment through the 6-month study. Mean improvements were similar to those seen in the phase 2 trial with >10 letters in BCVA and 154 µm reduction in CST by OCT

COMBINED EFFICACY RESULTS (P1/2 & P2)





Improvements in BCVA	Month 1 N=24 n (%)	Month 2 N=25 n (%)
≥10 Letters	12 (50)	14 (56)
≥15 Letters	6 (25)	10 (40)



IOP measurements following a single 4 mg dose of TA in subjects with uveitis: *combined P1/2 and P2 data*

- No patients showed steroid related increases in intraocular pressure(IOP)
- No IOP lowering medication was required or used
- No drug related serious adverse events (SAE) were reported in the study
- No patients dosed with TA suprachoroidally showed cataract development over 6 months

CONCLUSIONS

- Suprachoroidal injection of CLS-TA as a potential treatment of noninfectious uveitis appears to show promise for further development on account of the selective distribution of the drug, along with the potential for improved efficacy and safety relative to other periocular and intraocular administration routes.
- A phase 3 randomized, masked, controlled trial is currently underway as part of continued developmental efforts.