A Phase 2 Multicenter, Randomized, Vehicle-Controlled Study to Evaluate the Safety and Efficacy of CBT-001 for Pterygia

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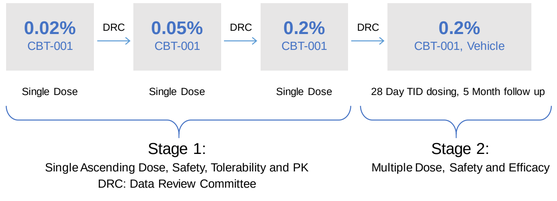
Purpose

- A pterygium is a commonly occurring, benign fibrovascular growth onto the cornea that can impair vision
- There are no FDA-approved drugs for pterygia and treatment often involves surgery[1]
- The purpose of this study is to evaluate the safety and efficacy of CBT-001, a topical multi-kinase inhibitor nintedanib eyedrop, for pterygia

https://clinicaltrials.gov/ct2/show/NCT03049852

Methods, Study Design

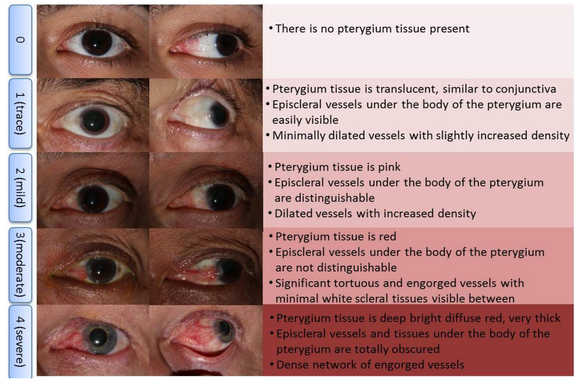
- CBT-001 evaluated in a Phase 2 clinical trial in two stages
  - Stage 1: single center, open-labeled, vehicle-controlled study, 24 eyes of 24 patients received one drop of CBT-001 in a dose escalation fashion to determine maximally tolerated dose
  - Stage 2: multicenter, randomized, double-masked, vehicle-controlled, parallel-group clinical trial. Patients with primary or recurrent pterygia were randomly assigned to receive the maximally tolerated dose of CBT-001 or vehicle dosed TID for 4 weeks with a 20 week follow up
- The study was conducted under IND # 131092 in accordance with the ethical principles of the Declaration of Helsinki and in compliance with Good Clinical Practice. All patients were provided with an IRB-approved written informed consent at the Screening Visit and were required to sign prior to study entry



Methods: Stage 2 Endpoints

- Primary efficacy endpoint was lesion vascularity based on masked grading of color primary gaze photographs on a validated scale (0: absent - 4: severe) by an independent reading center
- Secondary Endpoints
  - Pterygia lesion size (measured based on photographs analyzed using ImageJ software)
  - Hyperemia
  - Safety

Pterygia Vascularity Grading Scale



Huang P, Huang J, Tepelus T, Maram J, Sadda S, Lee OL. Validity of a new comprehensive pterygia grading scale for use in clinical research and clinical trial. Int Ophthalmol. 2018 Dec;38(6):2303-2311.

Stage 1 Results: Safety and Systemic Drug Exposure

Table 1. Safety and Efficacy

Cohort	Treatment	Observations	Pterygia vascularity at 8 h post dosing
Cohort 1 (0.02%)	Vehicle eye	Mild itching in 1/8	No change
	Drug eye	Conjunctiva follicle +3 in 1/8	No change
Cohort 2 (0.05%)	Vehicle eye	No findings	No change
	Drug eye	No findings	No change
Cohort 3 (0.2%)	Vehicle eye	Mild burning in 1/8	No change
	Drug eye	Mild foreign body sensation in 1/8, mild burning in 3/8,	One grade reduction in 3/8

Table 2. Pharmacokinetics

Dosing Route	C_{max} (ng/ml)	AUC (ng.hr/ml)
Approved Oral Capsule (150 mg, BID)	34.8	342
Ocular CBT-001 0.02%	<0.01	<0.24
Ocular CBT-001 0.05%	<0.01	<0.24
Ocular CBT-001 0.2%	0.01	0.24
Safety Margin (Oral/Ocular)	3480	1425

Table 3. Stage 2 Baseline Data

Safety Population			
		CBT-001 0.2% (n=26)	Vehicle (n=25)
Age mean (n)		52.0 (26)	49.4 (25)
Gender male [n(%)]		12 (46.2)	14 (56.0)
Gender female [n(%)]		14 (53.8)	11 (44.0)
Race [n(%)]	Asian	1 (3.8)	0 (0.0)
	White	24 (92.3)	21 (84.0)
	Other	1 (3.8)	4 (16.0)
Modified Intent-to-Treat Population			
		CBT-001 0.2% (n=25)	Vehicle (n=23)
Baseline pterygia vascularity grade mean (SD)		2.9 (0.7)	3.0 (0.8)
Baseline global hyperemia grade mean (SD)		2.8 (0.6)	2.7 (0.7)
Corneal Pterygium Lesion Length mean mm (SD)		2.27 (0.98)	2.68 (1.36)

Stage 2 Results

- Baseline demographic characteristics were similar between patients receiving CBT-001 (n=25) and vehicle (n=23).
- After 4 weeks of dosing, mean vascularity scores were significantly decreased in patients receiving CBT-001 (-0.8) compared to vehicle (0.0) ($p<0.001$).
- Vascularity remained significantly decreased at weeks 8 and 16, but not at week 24.
- CBT-001 group showed significantly greater mean reductions in lesion length at weeks 4 and 8 ($p<0.05$).
- The most commonly reported adverse events associated with CBT-001 were ocular, mild in severity, resolved after therapy, and did not result in discontinuation.

Figure 1. Pterygia vascularity mean grade change from baseline (Statistically significant drug vs vehicle p-values are shown)

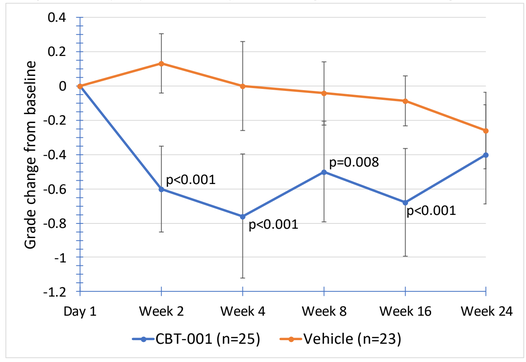


Figure 2. A representative eye treated with CBT-001 showing reduced pterygia vascularity at Week 4.

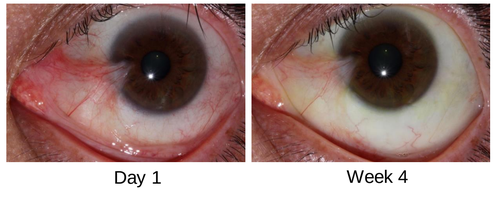


Figure 3. Global hyperemia mean grade change from baseline (Statistically significant drug vs vehicle p-values are shown)

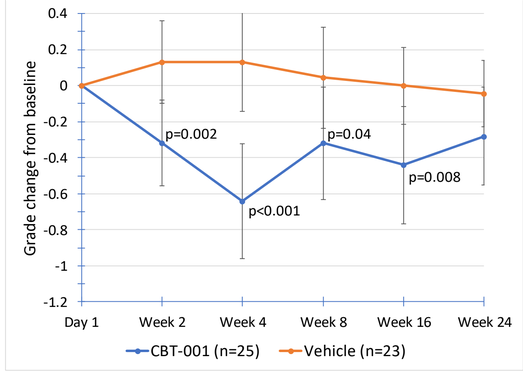


Figure 4. Pterygia lesion length mean change from baseline (Statistically significant drug vs vehicle p-values are shown)

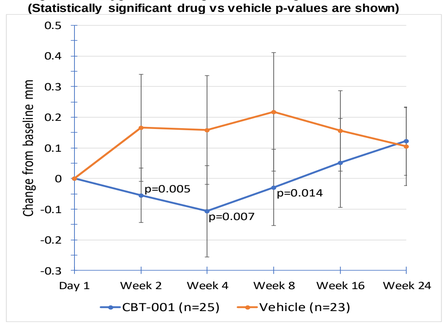


Table 4. Incidence of treatment emergent adverse events (TEAE) that occurred more than once by preferred term, safety population

	Ocular			
	CBT-001 0.2% (n=26)		Vehicle (n=25)	
Preferred Term	Study Eye n (%)	Non-study Eye n (%)	Study Eye n (%)	Non-study Eye n (%)
Conjunctival Discoloration	14 (53.8)	0	0	0
Foreign Body Sensation in Eyes	2 (7.7)	0	0	0
Lacrimation Increased	2 (7.7)	1 (3.8)	0	0
Non-ocular				
Preferred Term	**CBT-001 0.2% (n=26)**		**Vehicle (n=25)**	
Dysgeusia	2 (7.7)		0	
Influenza A Virus Test	0		2 (8.0)	

Note:

- All TEAEs were mild except one moderate conjunctival discoloration and one moderate lacrimation increased
- All TEAEs resolved without therapy
- No discontinuation resulted from TEAEs

Conclusions

- CBT-001 effectively decreased pterygia vascularity after 4 weeks of dosing with a prolonged effect
- Lesion length was reduced at Weeks 2, 4 and 8
- CBT-001 was well tolerated with minimal systemic exposure and no discontinuations for adverse events
- Additional trials are needed to assess the safety and efficacy with treatment greater than 4 weeks

References

1. Detorakis ET and Spandidos EA. Pathogenetic Mechanisms and Treatment Options for Ophthalmic Pterygium: Trends and Perspectives. Int J Mol Med. 2009;23:439-447.
2. Huang P, Huang J, Tepelus T, Maram J, Sadda S, Lee OL. Validity of a new comprehensive pterygia grading scale for use in clinical research and clinical trial. Int Ophthalmol. 2018 Dec;38(6):2303-2311.

Disclosures

Scott M. Whitcup, Cloudbreak Therapeutics Code C (Consultant) , Cloudbreak Therapeutics Code I (Personal Financial Interest) , Kenneth N. Sall, Cloudbreak Therapeutics Code F (Financial Support) , Cloudbreak Therapeutics Code C (Consultant) , Allergan Code F (Financial Support) , John A. Hovanesian, Cloudbreak Therapeutics Code F (Financial Support) , Allergan Code F (Financial Support) , Allergan Code C (Consultant) , Allergan Code I (Personal Financial Interest) , IOP/Katena Code C (Consultant) , IOP/Katena Code S (Non-remunerative) , IOP/Katena Code F (Financial Support) , Harvard Eye Associates Code I (Personal Financial Interest) , Damien F. Goldberg, Cloudbreak Therapeutics Code R (Recipient) , Allergan Code C (Consultant) , Allergan Code R (Recipient) , Paula Bernstein, Cloudbreak Therapeutics Code C (Consultant) , Allergan Code C (Consultant) , Glaukos Code E (Employment) , Olivia L. Lee, Cloudbreak Therapeutics Code F (Financial Support) , Allergan Code C (Consultant) , Allergan Code F (Financial Support)

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