CBI
DRY EYE MODELS

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COMPARATIVE BIOSCIENCES, INC.
A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH

COMPARATIVE BIOSCIENCES, INC.

Premier Preclinical Contract Research Organization

- **19 years** of experience
- Conveniently **located in the heart of Silicon Valley,** amidst many biotech companies
- **State of the art, purpose-built facility**
- Approximately **35 employees**
- **Highly experienced staff**
- **GLP, OECD, FDA, USDA, OLAW**
- **AAALAC Accreditation**

DRY EYE MODELS

Dry eye is an unmet medical need with an immunologic component as well as direct effects on the cornea itself.

- **Mouse Scopolamine**
  - Mice are administered scopolamine for at least 7 days and place in an air blower to ablate tear production and induce secondary immune mediated condition on the cornea.
- **Rabbit ConA**
  - Lacrimal glands injected with Concanavalin to ablate tear production and induce immune mediated condition on cornea
- **Mouse Botulinum**
  - Lacrimal glands injected with botulinum toxin to ablate tear production and induce immune mediated condition on cornea

TYPICAL STUDY DESIGN

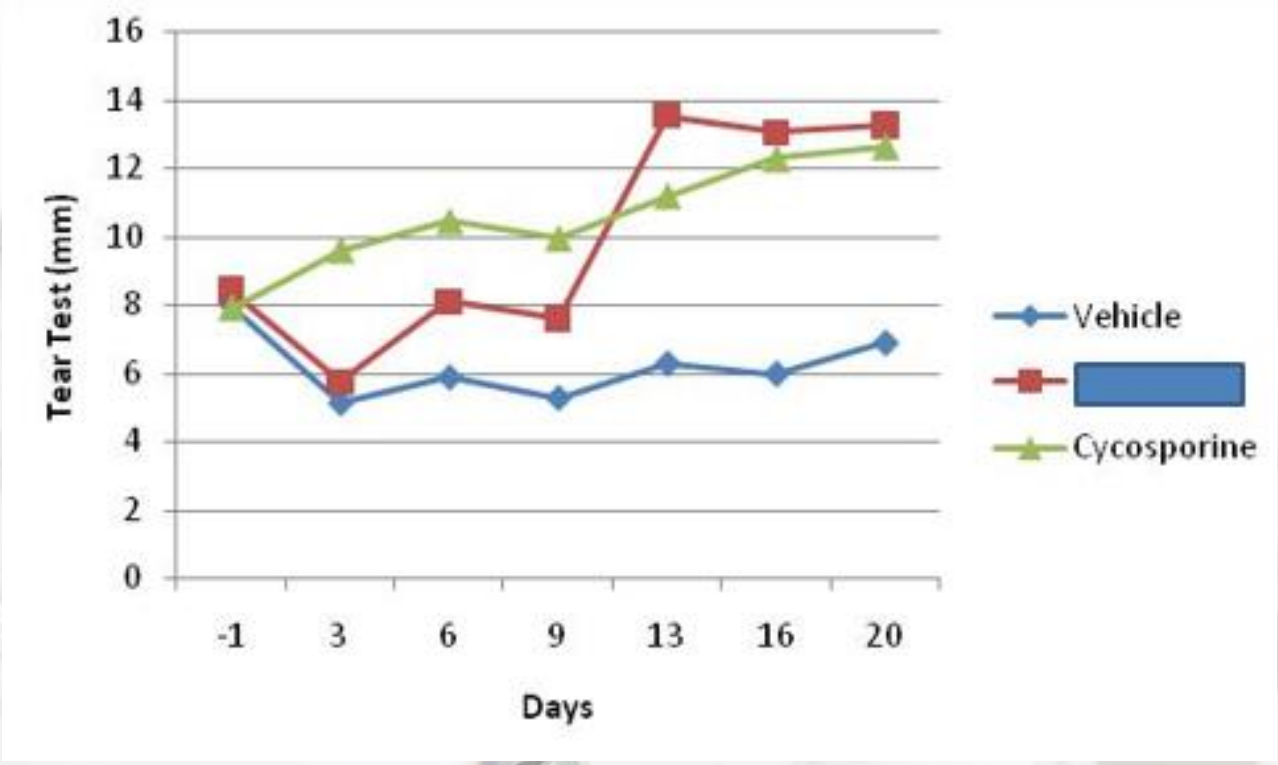
- SV129 Mice, 10-12 per group: Vehicle, positive control (Dexamethasone and/or cyclosporine, test article at various dose levels)
- Induction with 3-4x day subcutaneous dosing with scopolamine or botulinum to induce dry eye and dry blower environment
- Treatment period is 2-3 weeks
- TBUT 3x weekly
- Phenol red thread test 3x weekly
- Fluorescein and SLE examination of cornea 3x weekly
- Weekly body weights and daily clinical observations
- Histology on eye
- Cytokine analysis-optional

VALIDATION DATA

- Both topical dexamethasone and topical cyclosporine will induce a statistically significant increase in the two main parameters of tear break up test and phenol red thread test.

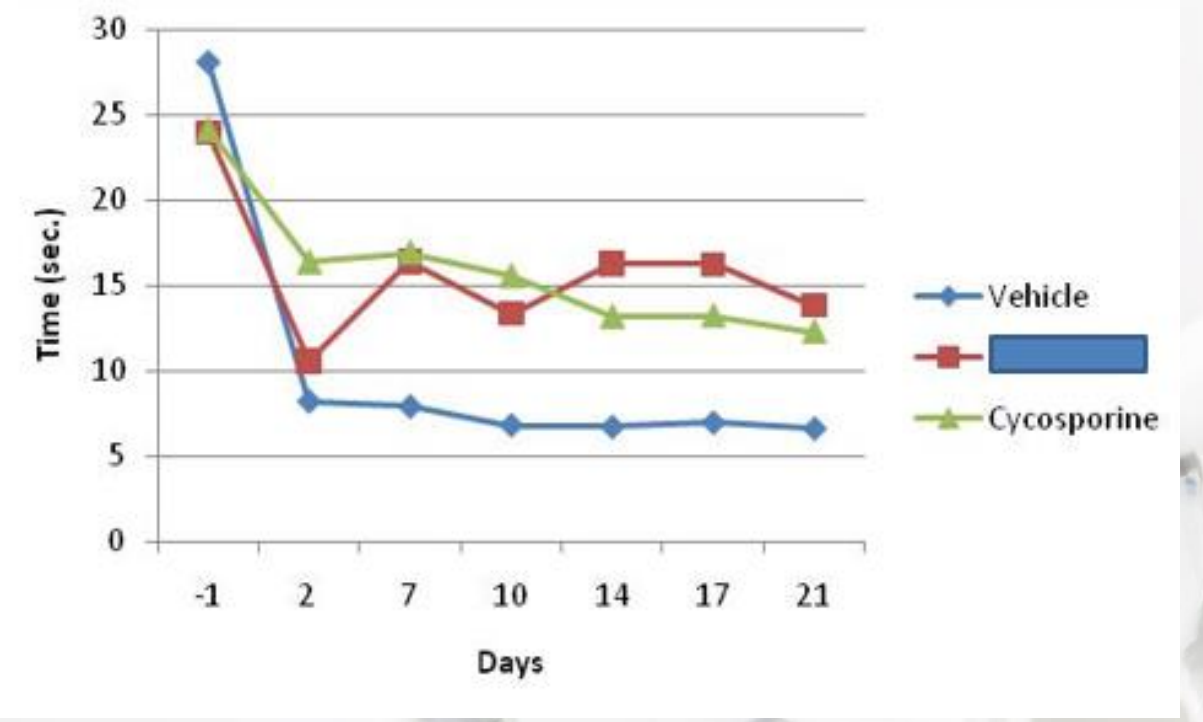
- Histology: Improvement in ocular inflammation and corneal integrity

PHENOL RED THREAD TEST



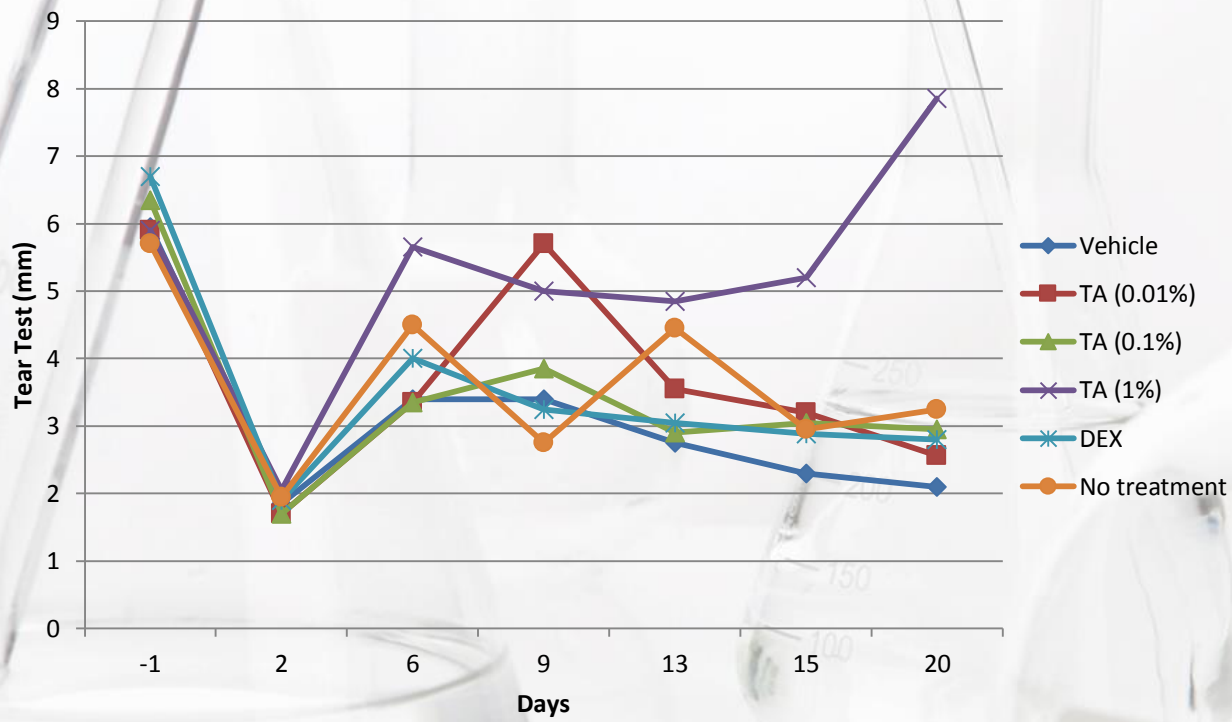
Cyclosporine administration induces a normalization of tear production as per the phenol red thread test as per the vehicle

TEAR BREAK UP TEST



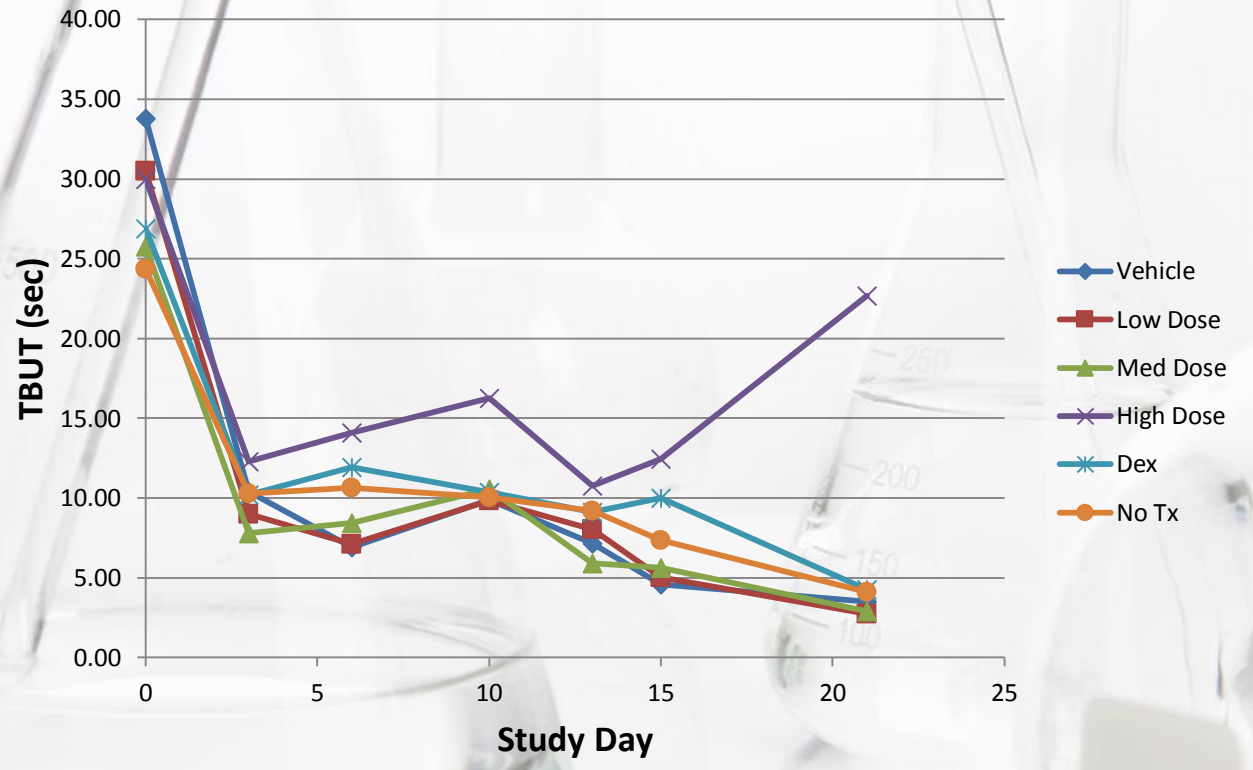
Cyclosporine administration induces a normalization of tear break up test as per the vehicle

PHENOL RED THREAD TEST



Dexamethasone administration induces a normalization of phenol red threat test as per the vehicle

TEAR BREAK UP TEST



Dexamethasone administration induces a normalization of tear break up test as per the vehicle

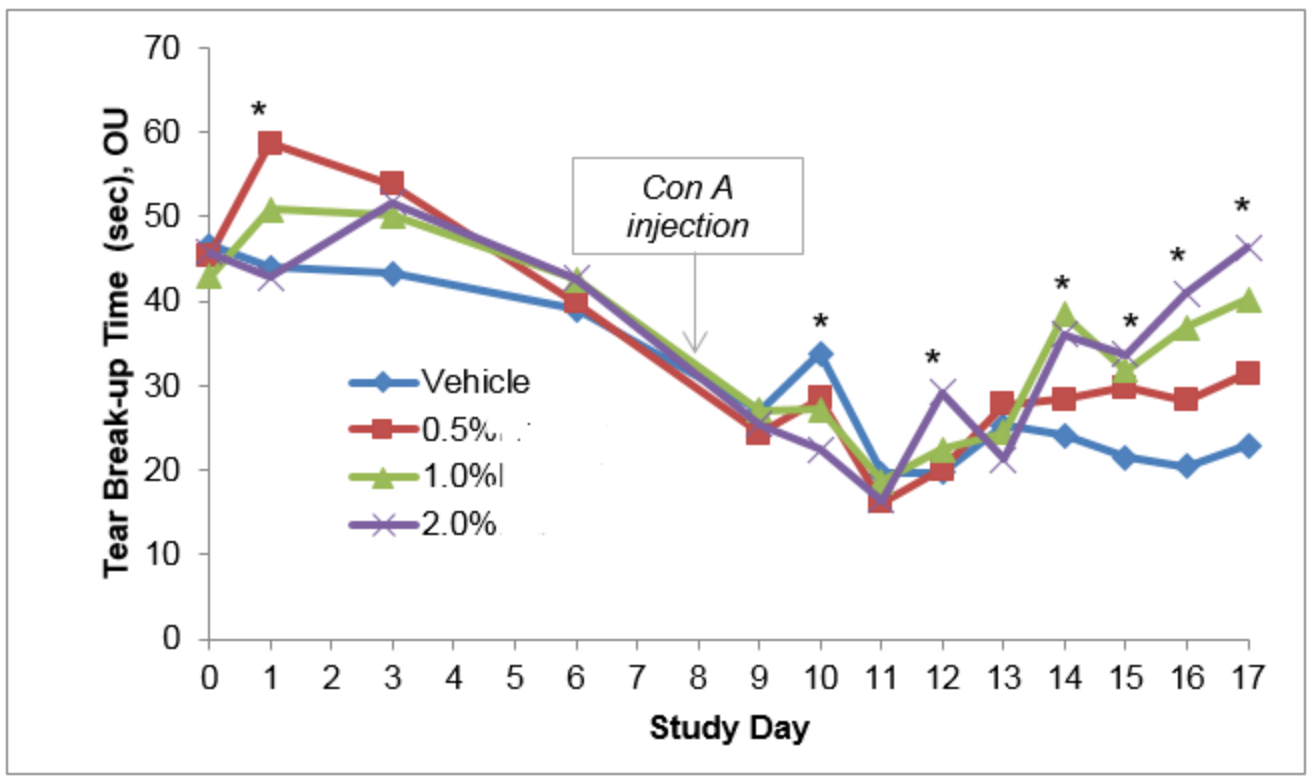
CON A INDUCED DRY EYE

Typical study Design

- NZW Rabbits with n = 6-8 per group
- Single Con A injection bilaterally into lacrimal glands
- Prophylactic dosing or Therapeutic dosing depending on MOA of Test Article
- Daily Tear production assessment by Schirmer Tear Test and Tear Break Up Time (TBUT)
- 14 to 21 days duration typically
- Histology of lacrimal glands by H&E
- Optional Cytokine analysis

CON A INDUCED DRY EYE

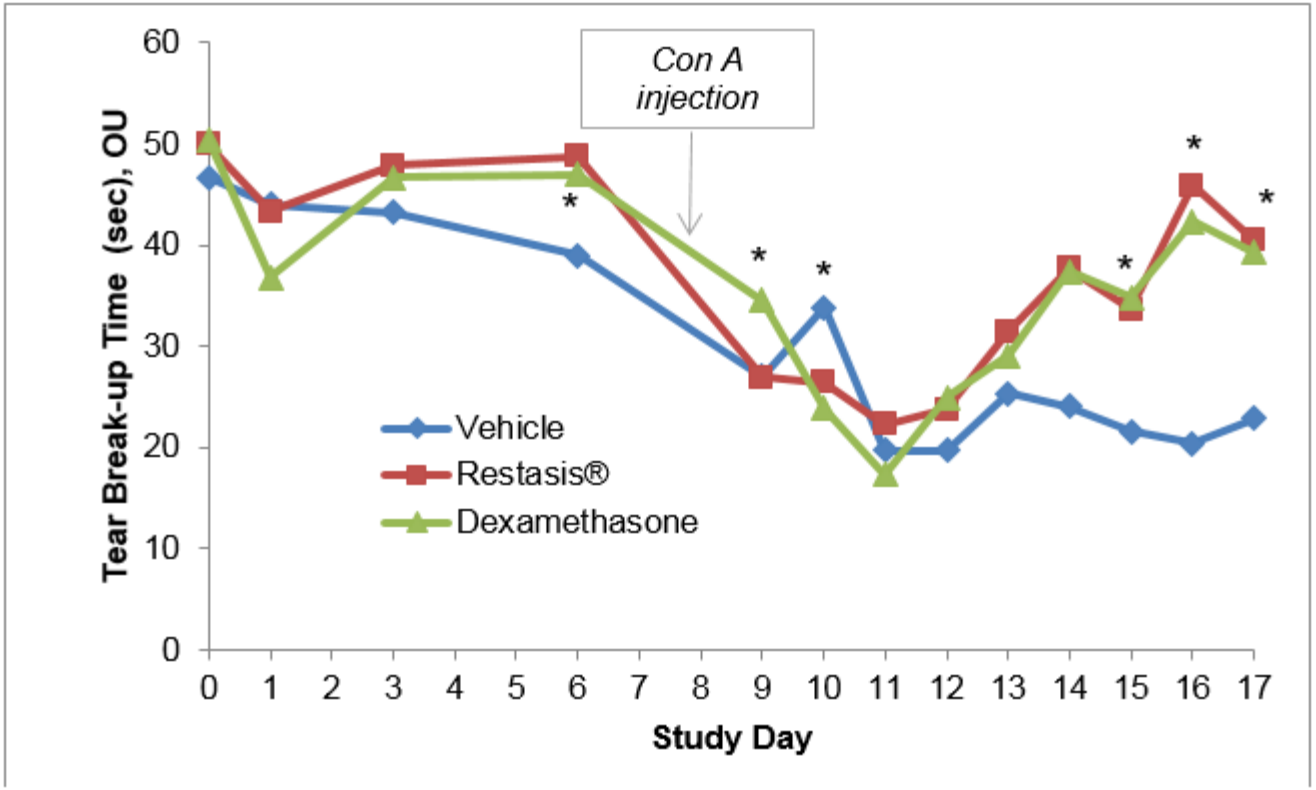
TBUT Sample Data



*=statistically significant for a treatment group vs. vehicle
Test Article was administered from Day 0 to Day 16

CON A INDUCED DRY EYE

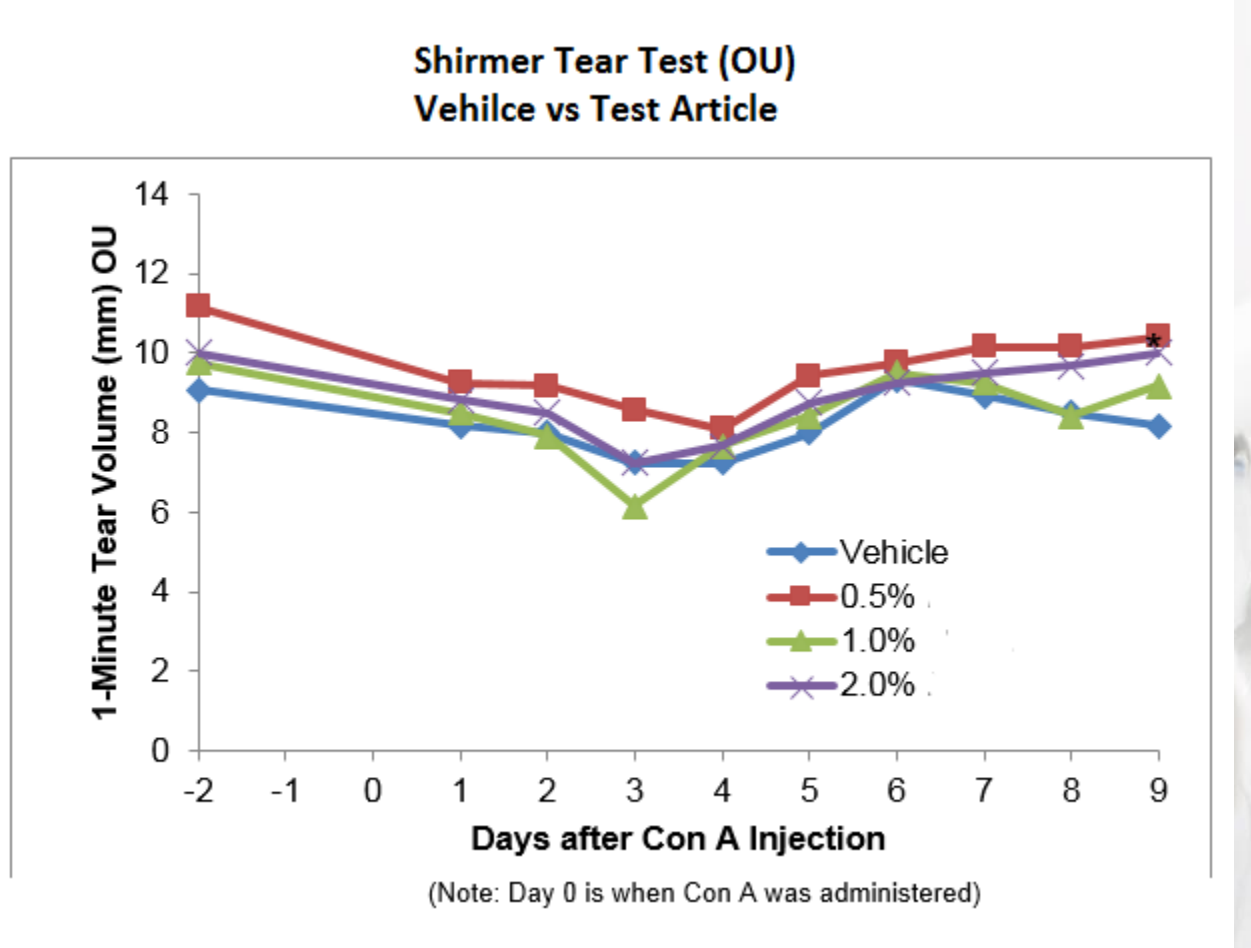
TBUT Sample Data



*=statistically significant for a treatment group vs. vehicle (see Sec. 4.6)
Restasis® administered Days 0-16, Dexamethasone administered Days 9-16

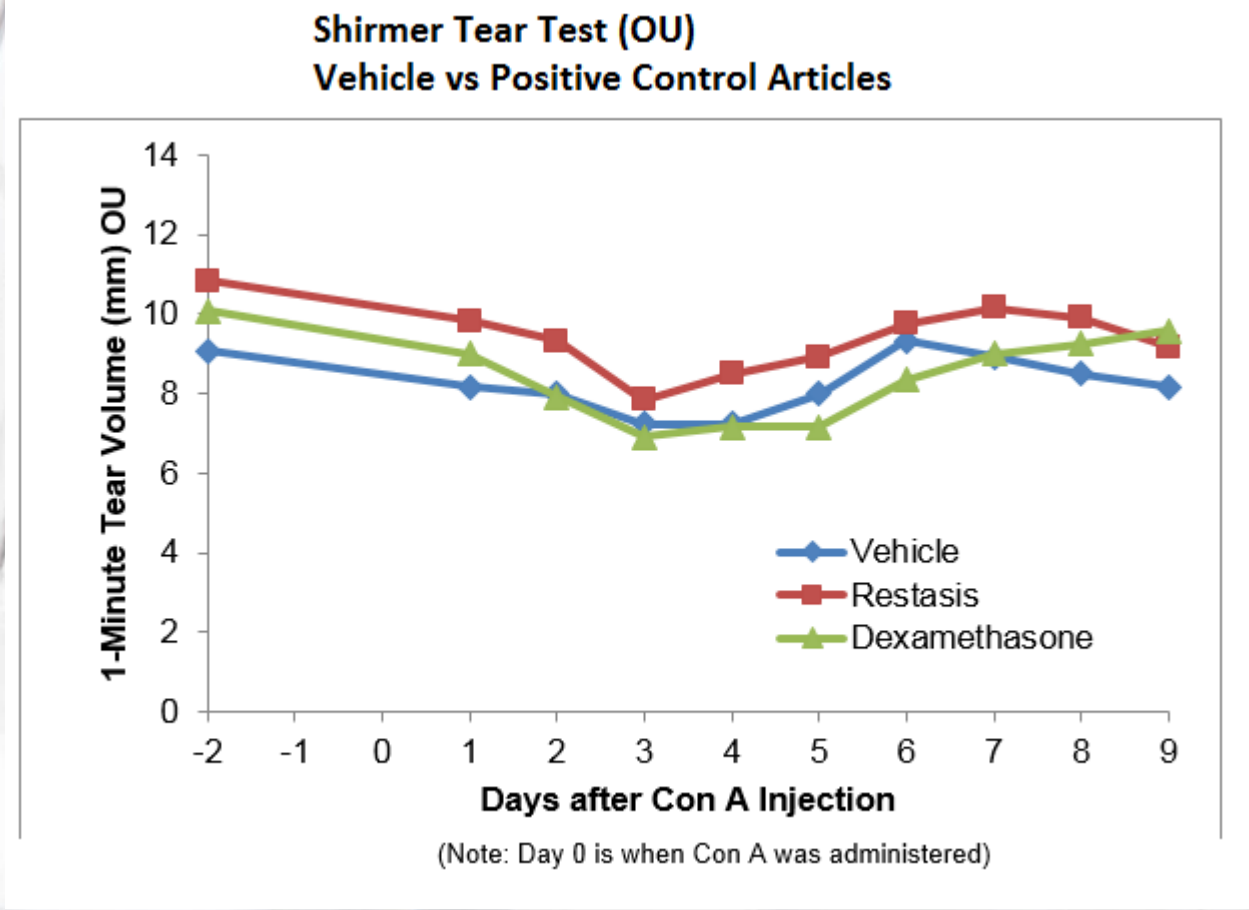
CON A INDUCED DRY EYE

Schirmer Tear Test Sample Data



CON A INDUCED DRY EYE

Schirmer Tear Test Sample Data



Service and Quality

- ***Thoroughness in planning and execution is key to a successful study***. All protocols are vetted and approved by multiple personnel. Our QAU has a rigorous training program. All non-GLP studies are conducted in the spirit of GLP.
- ***We believe in sound science.*** Our ratio of scientists to non-scientists is one of the highest in the industry. Every study director is a PhD-level scientist.
- ***We believe in communication.*** Timely responses to your inquiries and frequent updates on your study are mandatory.
- ***We welcome visitors.*** You are always welcome at CBI to meet the staff, tour the laboratory and discuss the progress and results of your study.