ALTASCIENCES
CLINICAL SERVICES

OPHTHALMOLOGY CLINICAL RESEARCH SERVICES

With **over 40 clinical trials** conducted in the area of ophthalmology, Altasciences combines depth of knowledge and expert capabilities to offer you a full range of early ophthalmic clinical development. In-house ophthalmic specialists with access to a variety of patients at our three North American inpatient units, combined with numerous partnerships with key opinion leaders and renowned research sites, sets the foundation for the success of your opthalmology trials.

Ophthalmic Clinical Development Highlights

Altasciences conducts Phase I to Phase II trials in the following indications:

- Open-angle glaucoma
- Ocular hypertension
- Dry eye disease
- Corneal disorders
- Myopia
- Presbyopia
- Uveitis

Altasciences' strategically located clinical sites provide access to an ethnically diverse population of ophthalmology patients, particularly for ethnobridging and proof-of-concept trials. Additionally, we have built a database of over 400,000 participants, both healthy normal and patient populations. With 500 beds, we conduct various ophthalmic procedures and assessments in-house, including best corrected visual acuity (BCVA), slit lamp examination, lens opacification, intraocular pressure (IOP) measurement, gonioscopy, and specular microscopy.

Sample Experience List

Phase	Indication	Study Population	Study Design Elements
I	Corneal injuries	Healthy normal volunteers	Bioavailability, double masked, first in human, multiple ascending doses, pharmacodynamics, pharmacokinetics, placebo controlled, randomized, safety and tolerability
I	Ocular inflammation	Healthy normal volunteers	Double masked, single dose, multiple doses, pharmacokinetics, placebo controlled, safety and tolerability
I	Glaucoma	Bilateral OHT or chronic open-angle glaucoma	Double masked, pharmacodynamics, pharmacokinetics, placebo controlled, safety and tolerability, single ascending dose.
II	Acute anterior uveitis	Non-infectious acute anterior uveitis	Double masked, randomized, safety and efficacy
II	Corneal epithelial disorders	Moderate-to-severe corneal epithelial disorders	Double masked, parallel group, placebo controlled, randomized, safety and efficacy
II	Presbyopia	Presbyopia	Double masked, parallel group, pharmacokinetics, randomized, safety and efficacy
II	Reduction of lower lid steatoblepharon	Moderate-to-severe, bilateral lower eyelid steatoblepharon	Double masked, placebo controlled, randomized

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CASE STUDY 1

A Phase II, Single-Masked, Randomized, Crossover Study of the 24-Hour Intraocular Pressure (IOP) Lowering and Systemic Exposure of PF-04217329

- Alone and in combination with Latanoprost

Population

32 patients with glaucoma or ocular hypertension

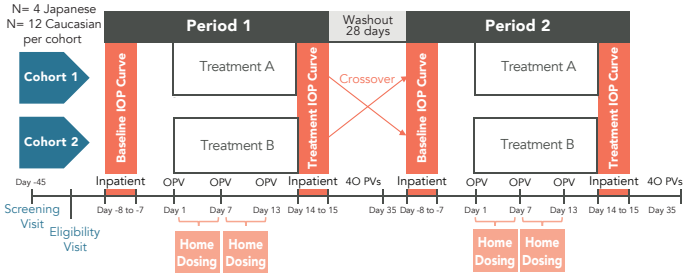
- Caucasian: 24
- Japanese: 8

Enrollment Period

45 days

Study Design

- Screening period of up to 45 days prior to the dosing day
- Eligibility visit three to 28 days after the screening visit
- Period 1:
  - Two 24-hour inpatient visits for baseline and IOP curve at Altasciences
  - Eight outpatient visits (OPVs) at ophthalmologist's office
  - Total 10 days of home dosing (self-administration)
- Period 2:
  - Two 24-hour inpatient visits for baseline and treatment IOP curve at Altasciences
  - Eight OPVs at ophthalmologist's office
  - Total 10 days of home dosing (self-administration)



Procedures Performed

- Manifest refraction
- BCVA
- Visual field
- Hyperemia assessment
- Biomicroscopy
- Corneal staining
- Ophthalmoscopy
- Confocal microscopy
- Sitting and supine IOP measurements
  - (Serial to compare baseline and on-treatment curves)
- Gonioscopy
- Pachymetry
- Serial pharmacokinetic blood sampling

Challenges

- Added layer of Japanese ethnicity requirement to subset of patients, while maintaining IOP eligibility requirements for the glaucoma or ocular hypertension criteria
- Robust data collection: diurnal IOP at Period 1 compared to Period 2; crossover PK and safety data; ethnic-sensitivity data

Results

- Study conducted with two ophthalmology sites enrolling patients and centralized inpatient visits conducted at Altasciences' clinical facility in Los Angeles

CASE STUDY 2

A Phase I, Double-Masked, Vehicle-Controlled Study to Assess Safety, Tolerability, and Pharmacokinetics of Ascending Doses of Palovarotene Ophthalmic Solution in Healthy Adults

Purpose

- To determine the ocular and systemic safety, tolerability, and pharmacokinetics of ascending doses of palovarotene (POS) in healthy adults
- An ophthalmic solution formulation of POS, a selective retinoic acid receptor agonist, is under investigation for the treatment of dry eye disease (DED)

Methods

- Single-center, randomized, double-masked, vehicle-controlled Phase I study in healthy adults
- Participants were randomized 3:1 to receive either POS (at 0.025, 0.05, or 0.10 mg/mL) or vehicle (placebo-to-match POS)
- Six cohorts of eight participants
  - Six participants in the POS group and two in the vehicle group
  - Three cohorts were each administered treatment once daily (QD) or twice daily (BID) for seven consecutive days
- Escalation to the next dose required review committee approval
- Eligibility: healthy adults, 18 to 55 years of age
  - Safety assessments: physical examinations, vital signs, ECGs, clinical laboratory parameters, ocular assessments, adverse events (AEs), and treatment emergent ocular adverse events (TEOAEs)
  - Blood sample collection for PK assessments of POS: prior to and following dose administration

Results

- 36 participants were randomized to POS and 12 to vehicle
- 89 TEOAEs were reported by 22 participants (61%) receiving POS
- 10 TEOAEs were reported by five participants (42%) receiving vehicle
- Most common TEOAEs in participants receiving POS: Erythema, irritation, and skin dryness of the eyelid
- Incidence of TEOAEs and eyelid-related findings in participants treated with POS increased with ascending dose and frequency compared with participants treated with vehicle
- All TEOAEs were mild (96.6%) or moderate (3.4%)
  - Resolved without sequelae
- No serious AEs
- Similar PK profiles were observed for the QD and BID regimens following multiple ascending doses of POS
- No meaningful difference was observed between the pharmacokinetic profile of POS following the a.m. and p.m. doses during BID treatment

Conclusion

- The administration of POS was generally well tolerated at doses up to and including 0.10 mg/mL BID. These data support further investigation of the safety and efficacy of POS in patients with DED

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