Continuous Wear Non-Invasive Device for Sustained Ocular Drug Delivery

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Purpose

Safety, awareness, positioning and retention of a large Topical Ophthalmic Drug Delivery Device (TODDD™) were evaluated in normal human subjects during four weeks of uninterrupted continuous wear. The TODDD™ is designed to continually deliver drug 24/7 while being worn on the superior sclera under the eyelid. In this design validation human study, a vehicle (non-drug containing) device was worn by human subjects in an open label study conducted with the New England College of Optometry at two sites.

Methods

Each subject, randomized to unilateral right or left eye treatment, received 1 topically applied study device on Day 0 (Visit 1). Qualified subjects (24 of 31) with acceptable fit and comfort then kept the device on eye to wear in their own environments continuously for four weeks without removing the device. Follow up consisted of a telephone interview on Day 1, and examinations were performed at Weeks 1, 2 and 4, as shown in Table 1. Slit-lamp findings demonstrated soon after the device was removed. Site 1: The four subjects who did not complete the study had suboptimal stability that became more pronounced by the first night of wear; three of these exited within the first 24 hr. The fourth subject continued wear for another week, but noticed instability during vigorous sports, leading to redness (grade 3) from repeated manipulation of the device, that cleared soon after the device was removed. Site 2: This older group appeared to tolerate the device well, with 10 of 11 who tried it being dispensed. Two of these had suboptimal stability at Visit 1 but elected to continue, and were exited between weeks 1 and 2.

Results

24 (16 female and 8 male, two age groups, 24-29, avg. 24.4, Site 1, and 54-70, avg. 66.0, Site 2) of 31 screened subjects were dispensed the device and 16 have completed the study to date, with 2 now at 2 weeks and ongoing. In all completed subjects, the device positioned on the superior sclera without excess rotation, under the lid, with good stability and movement. Subjects reported good tolerability and comfort.

Study Design:

Table 1

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Visit 1 (Day 0)</th>
<th>Visit 2 (Day 1-3)</th>
<th>Visit 3 (Week 1-2)</th>
<th>Visit 4 (Week 2-3)</th>
<th>Visit 5 (Visit 5+ 24/7)</th>
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Questionnaire Results:

- Comfort -
  - 0 = Normal comfort, no awareness of device
  - 1 = Normal comfort, intermittent awareness
  - 2 = Mildly decreased comfort

- Tolerance -
  - 0 = Comfortable all or virtually all the time
  - 1 = Comfortable most of the time
  - 2 = Moderately comfortable
  - 1 subject failed to report

- Stability/Retention during 28 days of wear – All Visits
  - 4 subjects recorded 7 total instances of the device coming out of their eye over 450 patient days. In all cases, it was replaced immediately by the subject.

- Vision during 28 days of wear – All Visits
  - Same with or without the device
  - Comparison to contact lens wear -
    - Comparable to contact lens
    - Easier to use than contact lens
    - More difficult to use than contact lens
    - Inadequate experience to answer

TODDD™ Safety

All Subjects Dispensed (n=24)

Adverse Events:
- 2 instances of conjunctival redness, one with reported blurry vision that all resolved without treatment the same day
- 1 report of lid swelling in non-device eye

- Visual Acuity Changes:
  - All subjects maintained entering best-corrected Snellen acuity

- Keratometry Changes:
  - No changes ±0.25D, no mire distortions

- Slit Lamp Exam:
  - No significant changes in any parameter, with the following exceptions:
    - Grade 2 bulb redness in 1 subject with poor stability that existed at visit 4
    - Grade 2 lid redness and/or roughness in 4 subjects which exited at visit 2

- Drug Depot TODDD
  - Material with drug is placed in distinct pockets or chambers
  - TODDD acts as the depot carrier

TODDD™ Platform Options:
- Matrix TODDD – non-erodible
  - Proprietary platform technology with customized formulation for each drug
  - Formulation for each drug
    - Drug is mixed with polymers prior to molding
    - Drug molecule unaffected by polymerization
    - Drug depot cleared soon after the device was removed.

Advantages of TODDD™ Platform

- Eliminates prevalent eye drop insertion and dosing issues
- Incorporates the drugs and combinations of drugs currently prescribed as eye drops
- Fewer compliance issues. Continuous, 90+ day 24/7 release of drug, eliminating patient dosing regimen
- Preservative free
- Tolerated well and presence easily confirmed
- Simple replacement in less than a minute
- Fewer, perhaps elimination of, systemic side-effects from excess drug in eye drops
- Can incorporate less soluble drugs not suitable for aqueous formulations