#481 – D0100

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 were graded according to the Brien Holden Vision Institute and NEI Grading Scales.

Study Design:

Procedure	Visit 1 (Day 0)	Visit 2 (Day 1 + 1 Day)	Visit 3 (Week 1 ± 2 Days)	Visit 4 (Week 2 ± 3 Days)	Visit 5 (Week 4 ± 3 Days)
	Qualification	Safety/ Efficacy	Safety/ Efficacy	Safety/ Efficacy	Safety/ Efficacy
Informed Consent	X				
Demographics	X				
Inclusion/Exclusion	X				
Medical/Meds History	X	X	X	X	X
Visual Acuity	X	X	X	X	X
Keratometry	X				X
External exam	X	X	X	X	X
Slit-Lamp Exam	X	X	X	X	X
Insert Evaluation	X[1]	X	X	X	X
Fluorescein Staining	X	X	X	X	X
Lissamine Staining	X	X	X	X	X
Ocular Comfort Questionnaire	X	X	X	X	X
Placement of Device	X	X[2]	X[2]	X[2]	
Photography	X				X
Ocular Comfort Questionnaire	X	X	X	X	X
Placement of Device	X	X[2]	X[2]	X[2]	
Insertion/removal lesson	X	X[3]	X[3]	X[3]	
Study Devices Dispensed	X	X[2]	X[2]	X[2]	
Study Devices Collection					X
Exit Study					X

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.

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.

TODDD™ - Topical Ophthalmic Drug Delivery Device

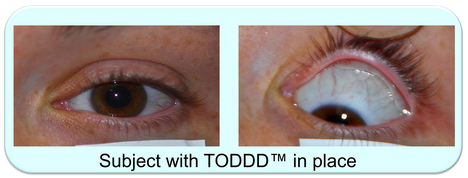
Designed for uninterrupted (24/7) drug delivery for 7 – 90+ days

Device design – Utilizes modified contact lens design features and new elements to fit the eye under the eyelid, to provide sustained comfort, retention, stability and capacity.

- •Central curvature
- •Peripheral curves
- •Edge apex contours
- •Edge lift
- •Corneal relief curve
- •Elevated lobes

Inserted and completely concealed under the eyelid
•No intrusion onto the cornea or into the visual field
•No inter-blink surface drying or deposits

TODDD™ Positioning and Stability



Subject with TODDD™ in place

Photo credit: R. Gutner, O.D.

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 bulbar redness in 1 subject with poor stability that exited at visit 4
- Grade 2 lid redness and/or roughness in 4 subjects which exited at visit 2

Questionnaire Results:

completed subjects

Comfort -	Visit 1	Visit 5
0 = Normal comfort, no awareness of device	3	7
1 = Normal comfort, intermittent awareness	12	9
2 = Mildly decreased comfort	1	0

Tolerability -	Visit 4*	Visit 5*
0 = Comfortable all or virtually all the time	5	9
1 = Comfortable most of the time	9	6
2 = Moderately comfortable	1	0

*one subject failed to report

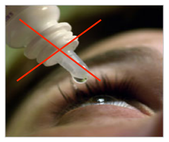
Stability/Retention during 28 days of wear – All Visits
4 subjects recorded 7 total instances of the device coming out of their eye over 450 patient days. In all cases, it was replaced immediately by the subject.

Vision during 28 days of wear –	All Visits
Same with or without the device	16

Comparison to contact lens wear -	Visit 5
Comparable to contact lens	6
Easier to use than contact lens	3
More difficult to use than contact lens	1
Inadequate experience to answer	6

Conclusions

Results in this human subject population indicate that this large device is well-tolerated under the lid during continuous wear. Retention and comfort were demonstrated in 75% of subjects using only a single device size, with success being predictable based on comfort and stability during the first 24 hr. The device produced no safety concerns after 4 weeks of continuous wear. Older subjects, more representative of a glaucoma patient population, tolerated the device as well or better than the younger group, with 8 of 10 who had the device inserted continuing in the study.



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

TODDD Platform Options:

Matrix TODDD – non-erodible

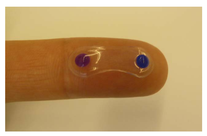
- •Proprietary platform technology with customized formulation for each drug
- •Comfort and biocompatibility emphasized in polymer selection
- •Drug is mixed with polymers prior to molding polymerization
- •Drug molecule unaffected by polymerization process

Drug Depot TODDD

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

Combination TODDD

- •A matrix TODDD with drug depots



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