Clinical Assessment of a New Multi-Purpose Disinfecting Solution in Asymptomatic and Symptomatic Patients

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ABSTRACT

Purpose: Clinically assess a new multi-purpose disinfecting solution (MPDS) with a variety of lens materials in asymptomatic and symptomatic subjects.

Methods: Five randomized, double-masked studies conducted at 66 sites evaluated the clinical performance of a new MPDS with traditional and silicone hydrogel (SiH) soft contact lenses. Regimen 1 (OPTI-FREE® RepleniSH® MPDS) was compared with Regimens 2 (ReNu® MultiPlus® MPS), 3 (ReNu® with MoistureLoc®) and 4 (Complete® MoisturePLUS™). Corneal staining was evaluated by investigators. Subjects recorded rewetting drop use, as well as subjective comfort and symptoms using visual analog scales and Likert-style questionnaires. At a subset of sites, worn lenses were collected for total residual lens lysozyme and lens wettability analyses.

Results: Residual lysozyme of Group IV lenses was significantly lower for Regimen 1 (564.5 and 677.9 µg) compared with Regimens 2 (1062.8 µg) and 3 (959.2 µg, p<0.0001). There was significantly less severe corneal staining with Regimen 1 compared to Regimen 2 in SiH lens wearers (p=0.0019) and compared to Regimen 3 in symptomatic Group IV lens wearers (p=0.0038). Group I and IV soft contact lenses cared for with Regimen 1 (58.0° and 5.8°) had significantly lower contact angles (better wettability) than those using Regimen 2 (76.2° and 90.5°; p<0.002). Group IV wettability was also significantly better with Regimen 1 (5.3°) compared to Regimen 3 (91.3°; p<0.0001). Rewetting drop use was significantly higher in SiH lens wearers using Regimen 4 compared to Regimen 1 (p<0.004). Many indices of comfort were significantly higher for those subjects using Regimen 1, particularly for symptomatic subjects who reported significantly better comfort on all 12 of the Likert statements (p<0.05).

Conclusions: A new MPDS was shown to have clinical benefits with traditional and SiH lenses when compared with three MPS. This group of studies shows that the choice of lens care regimen can influence ocular health and patient comfort.

INTRODUCTION

With the new lens materials continuously introduced to the market, developing solutions with properties that are beneficial for all soft lenses is an increasing challenge for manufacturers of contact lens care solutions. Solutions need to be able to effectively clean, condition and disinfect lenses, while providing a comfortable lens wearing experience and without causing any negative interactions with the ocular surface. A new multi-purpose disinfecting solution (OPTI-FREE® RepleniSH® MPDS, Alcon) that reconditions the lens surface for enhanced comfort has been developed and recently marketed. The solution contains the proprietary reconditioning system, TearGlyde™, a combination of the surface active agent TETRONIC® 1304 (registered trademark of BASF Corporation) and a novel surface-active wetting agent, C9-ED3A (nonanoyl ethylenediaminetriaceticacid). These components work synergistically with each patient's own natural tears to keep the lens surface moist throughout the day. The new MPDS solution contains the proven disinfecting agents, POLYQUAD® (polyquaternium – 1) and ALDOX® (myristamidopropyl dimethylamine), which have high antibacterial and antifungal activity. The solution also contains propylene glycol, a demulcent and osmolality agent intended to enhance lens wetting, lubrication and comfort. An extensive clinical effort was undertaken in order to evaluate the safety and efficacy of the new solution. Studies examined the product with various lens materials, including Groups I and IV and silicone hydrogel materials, with both asymptomatic and symptomatic subjects, and compared to several multi-purpose solutions.

OBJECTIVE

The purpose of these studies was to clinically assess the safety and efficacy of a new multi-purpose disinfecting solution with a variety of lens materials in both asymptomatic and symptomatic contact lens wearers compared to several lens care regimens.

METHODS

Table 1
Study Summary

Study Description	# Sites	# Subjects	Duration/ Visits	Contact Lenses	Comparator(s)
Study 1 FDA "Core"	12	252	3 months (Days 0, 14, 30, 60, 90)	I and IV[a]	Regimen 2 (ReNu® MultiPlus®)
Study 2 Silicone Hydrogel	12	233	1 Month (Days 0, 7, 14, 30)	Silicone Hydrogel	Regimens 2 & 4 (ReNu® MultiPlus® and Complete® MoisturePLUS™)
Study 3 Symptomatic	19	362	1 Month (Days 0, 14, 28)	IV[b]	Regimen 2 (ReNu® MultiPlus®)
Study 4 Long Term Wettability	1	80	1 Month (Days 0, 1, 14, 30)	I and IV[a]	Regimen 2 (ReNu® MultiPlus®)
Study 5 Symptomatic	22	357	1 Month (Days 0, 14, 28)	IV[b]	Regimen 3 (ReNu® with MoistureLoc®)

[a]Optima® 38, Hydrasoft® XW; [b]Acuvue® Advance® and Night & Day® (Group II; [b]Various Brands; [b]Biomedics® 38, Acuvue® 2

Table 2
Formulation Comparison

	Cleaners	Antimicrobials	Buffers	Lubricant/Wetting Agents
Regimen 1 (OPTI-FREE® RepleniSH®)	Sodium Citrate Tetronic 1304 C_9ED3A	POLYQUAD® ALDOX®	Sodium Citrate Sodium Chloride Sodium Borate	Propylene Glycol Tetronic® 1304 C_9ED3A
Regimen 2 (ReNu® MultiPlus®)	HYDRANATE® (Hydroxyalkyl phosphonates), Poloxamine EDTA	DYMED® [Polyaminopropyl Biguanide (PHMB)]	Sodium Chloride Boric Acid Sodium Borate	Poloxamine, Tetronic® 1107
Regimen 3 (ReNu® with MoistureLoc®)	HYDRANATE® (Hydroxyalkyl phosphonates), Poloxamine	Alexidine	Boric Acid Sodium Chloride Sodium Phosphate	MoistureLoc® (poloxamer, polyquaternium-10)
Regimen 4 (Complete® MoisturePLUS™)	Poloxamer 237 EDTA	Polyhexamethylene Biguanide (PHMB)	Phosphate Taurine Sodium Chloride Potassium Chloride	HPMC (hydroxypropyl methylcellulose) Propylene Glycol

Table 3
Safety and Efficacy Variables

Variable	Method	Study	Visit Days Assessed
Comfort/ Acceptability/ Symptoms	**Likert Questionnaire** (1 = strongly disagree to 5 = strongly agree) **Visual Analog Scales** (0-100)	1, 2, 3, 5	All
Corneal Staining (Severity/Area)	**Severity** (5 Corneal Regions, 0-4) **Area** (5 Corneal Regions, 0 – 100%)	2, 3, 5	All
Wettability	**Ex Vivo Contact Lens Angle Measurement**	4, 5	Days 1& 30 (Study 4) and Day 28 (Study 5)
Lens Cleanliness	**Residual Lens Lysozyme** (High Performance Liquid Chromatography (HPLC)) **Modified Rutko** (Investigator-rated lens cleanliness)	1, 5	Day 28 (Study 5) and Day 90 (Study 1)
Rewetting Drop Use	**Average Number of Times per Day**	1 – 5	All
Average Lens Wearing Time	**Average Number of Hours per Day**	1 – 5	All
Visual Acuity	**Snellen**	1 – 5	All
Slit-Lamp Findings	**Investigator assessed** – corneal edema, neovascularization and infiltrates, injection, tarsal abnormalities, other complications	1 – 5	All
Adverse Events	**Reported by subjects or observed by investigator**	1 – 5	Post Day 0

RESULTS

Comfort/Acceptability/Symptoms

Figure 1 - Subject Likert Questionnaire
Significant Statistical Differences in favor of Regimen 1
Study 3

Statement	Day 14	Day 28
Enhances lens comfort	0.09*	<0.01
Comfortable end of day	X	<0.01
Long lasting comfort	0.05	<0.01
Feel clean	X	0.03
Feel moist	X	0.01
Not feel dry end of the day	X	0.03
Gentle	0.08*	0.02
Not sting	0.02	0.03
Vision clear end of day	0.02	<0.01
Eyes free from redness	0.07*	0.03
Eyes red end of day	X	0.01
Eyes bright end of day	X	<0.01

Figure 2 - Subject Likert Questionnaire
"This solution gives my lenses long lasting comfort"
Study 2

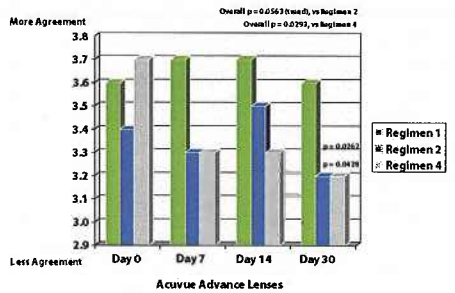


Figure 3 - Subject Likert Questionnaire
"This solution enhances my comfort"
Study 3

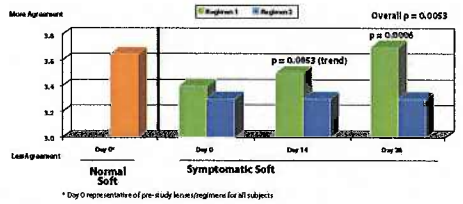
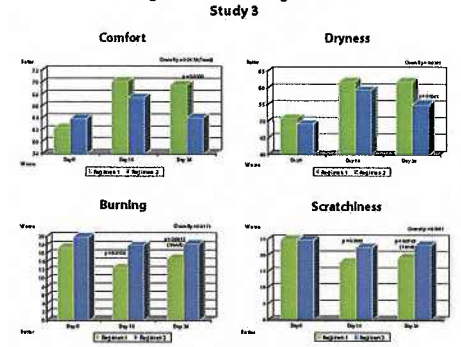


Figure 4 - Visual Analog Scales
Study 3



Comfort differences were consistently in favor of Regimen 1, particularly with symptomatic subjects (Studies 3 & 5) and in patients wearing silicone hydrogel lenses (Study 2).

RESULTS - Continued

Corneal Staining

Figure 5 - Corneal Staining Severity
Study 2

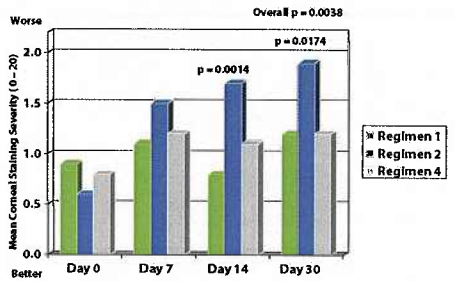
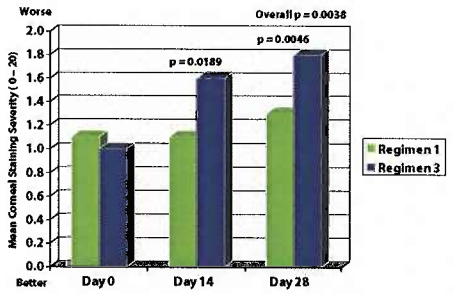


Figure 6 - Corneal Staining Severity
Study 5



Corneal staining severity was significantly greater for Regimens 2 (Study 2) and 3 (Study 5) when compared with Regimen 1. Corneal staining area was also greater with Regimen 2 than with Regimen 1 (data not shown, Study 2, p = 0.006).

Wettability

Figure 7 - Acute (1-day, 14 hours) & Long Term (30-days, 14 hours) Wetting Angle Measurements
Study 4

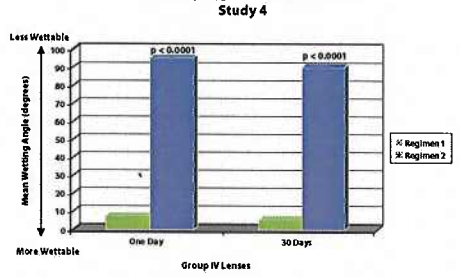


Figure 8 - Mean Wetting Angle
(29 Days, 14 hours)
Study 5

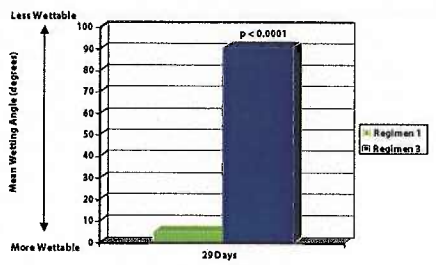
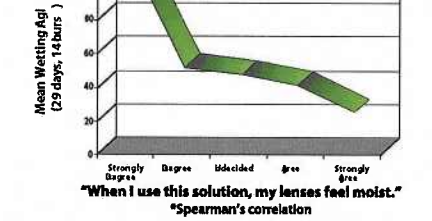


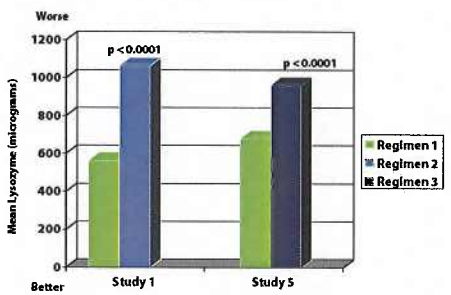
Figure 9 - Correlation* Between Wetting Angle and Subjective Lens Moistness
Study 5



Mean wetting angle measurements of Group I (data not shown) and IV lenses were significantly lower (indicating better wettability) with Regimen 1 than with Regimen 2 (Study 4) or Regimen 3 (Study 5). In addition, a moderate correlation was found between mean wetting angle and a subjective feeling of lens moisture (Study 5, r = -0.426).

Lens Cleanliness

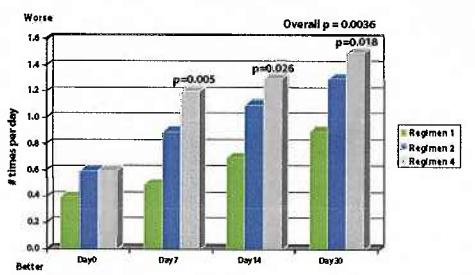
Figure 10 - Mean Residual Lysozyme
Study 1 and Study 5



Residual lens lysozyme on Group IV lenses was significantly lower for Regimen 1 compared with Regimen 2 (Study 1, p < 0.0001) and Regimen 3 (Study 5, p < 0.0001). In addition, the investigator-rated percent area of crystalline deposits in Group IV lenses was significantly lower for Regimen 1 compared with Regimen 2 at Day 90 (data not shown, Study 1, p = 0.0224).

Rewetting Drop Use

Figure 11 - Rewetting Drop Use
Study 2



Daily rewetting drop use was significantly lower for Regimen 1 compared with Regimen 4 (Study 2, p = 0.0036).

Other Variables

- Average daily lens wear time ranged from 12.2 to 14.7 hours over the course of the five studies. No significant regimen differences were observed for average daily lens wear time.
- No clinically relevant changes from baseline in best-corrected Snellen visual acuity were observed.
- No clinically relevant differences in slit-lamp findings were observed between regimens during the studies.
- Adverse events related to any regimen were nonserious, mild or moderate in intensity, and resolved with or without treatment.

CONCLUSIONS

- Subjective comfort and regimen acceptability were consistently higher for Regimen 1 when compared with Regimens 2, 3, and 4, particularly in symptomatic subjects. Better comfort and acceptability could potentially lead to fewer contact lens dropouts.
- Corneal staining, both severity and area, was significantly greater for Regimens 2 and 3 when compared with Regimen 1. An uncompromised corneal epithelium is paramount to healthy lens wear.
- Contact lens wettability, assessed by ex-vivo contact lens angle measurements, was significantly better for Regimen 1 compared with Regimens 2 and 3. Additionally, a moderate correlation between wettability and a subject feeling of lens moisture was found.
- Residual lens lysozyme was significantly lower for Regimen 1 than for Regimens 2 and 3. Investigator-rated lens cleanliness was significantly better for subjects using Regimen 1 than for those using Regimen 2.
- Subjects using Regimen 2 or Regimen 4 used significantly more rewetting drops than those randomized to Regimen 1. The increased use of rewetting drops over the course of the study for some regimens might have diminished the abilty to show comfort differences among the regimens in some instances.

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