Clinical Investigation Plan

Study Title: Comparison of clinical performance and subjective preference out of three cosmetic contact lenses (limbal ring-enhancing lenses, LRE lenses)

SPONSOR: CooperVision Korea, Inc.

CLINICAL SITE: School of Optometry & Vision Science, Catholic University of Daegu, Korea (Rep)

PROTOCOL DATE: October 21, 2016

PROPOSED START DATE: Dec, 2016

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Comparison of clinical performance and subjective preference out of three cosmetic contact lenses (limbal ring-enhancing lenses, LRE lenses)

SPONSOR COMPANY: COOPERVISION KOREA, INC.

DOCUMENT TYPE: PROTOCOL

PRINCIPAL INVESTIGATOR:

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DOCUMENT PREPARED BY:

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DOCUMENT REVEIWED AND APPROVED BY:

[redacted]

Study summary

This bilateral subject-masked, randomized, crossover dispensing study will investigate the clinical performance [redacted] of the Hydron 1-day cosmetic contact lens (Hydron Inc.), when compared to the 1-day Acuve Define (Johnson & Johnson Vision Care Inc.) and Claren 1-day Iris (Interrozzo Inc). Sixty subjects will be enrolled into this three-week study, where they will wear each lens type for one week. The order of lens wear will be randomized so that the effects related to order are minimized. The outcome measures will divided into subjective and objective measure. Primary subjective measure [redacted] comfort, [redacted]

Table 1: Study summary

Section 1. Overview

1.1 Background

Contact lenses markets has been steadily increased. One of driving factors for growing market is a cosmetic contact lenses which is designed to change the appearance of their eye in addition to correction of refractive error. With its popularity, there are many cosmetic contact lenses available in market and personnel preference are all different. Therefore, this study aims to evaluate the performance of a new daily disposable limbal ring lens, Hydron-1day (Hydron Inc), compared to the existing daily disposable limbal ring lens, 1.Day ACUVUE® Define™ (Johnson & Johnson Vision Care Inc) and Claren 1-day Iris (Interrozzo Inc). Limbal ring lenses are cosmetic lenses which enlarge and define the wearer's iris and are particularly popular in East Asian countries.

1.2 Personnel

This work will be conducted at [redacted]

1.3 Study Objectives

The purpose of this study is to evaluate the clinical performance [redacted] out of three LRE lens types; 1-day Acuve Define, Claren 1-day Iris and Hydron 1-day cosmetic contact lenses. Clinical performance measures will include comfort, [redacted]

[redacted]

1.4 Study Design

This will be a subject-masked if possible, bilateral, randomized, crossover dispensing study to compare clinical performance and subjective preference out of three lens types. Sixty subjects will be assigned into three groups and each group will wear the test and control lenses as matched pairs for one week each in random order. Lenses will be worn on a daily wear, daily disposable schedule.

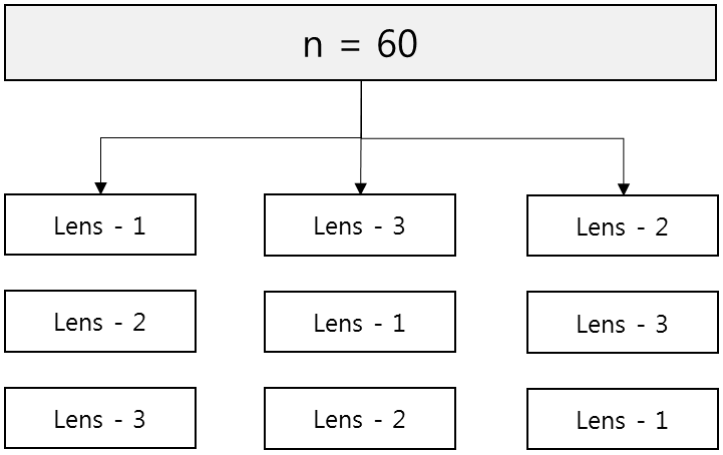

Figure 1. Grouping and lens randomization order

1.5 Statistical considerations

The prinicpal null hypothesis is that the [redacted] comfort for the three lens types are equal. Prior to statistical analysis, normality of data will be assessed. Ordinal measure such as lens fit, biomicroscopy [redacted] Deviations from this statistical plan will be discussed in the final report.

1.5.1 Power analysis

Study sample size was estimated a priori for the principal outcome measure, the subject's preference with respect to attractiveness. We are testing the null hypothesis that there is no difference in the subject's preference with respect to attractiveness between the three lens types. The sample size was estimated using G* Power, to detect a small effect size of 0.20, α=0.05 for one group, three repetitions and an assumed correlation of 0.5 amongst the repeated measures with a power of 0.90. The total sample size was estimated at 55. To allow for discontinuations, 60 participants will be recruited.

1.6 Risk analysis

There are no expected risks in this study other than wearing contact lenses. Also all subjects enrolled in this study will be existing contact lens wearers, therefore all subjects are very familiar with handling contact lenses.

1.7 Ethics Review and statement of compliance

Ethical approval will be sought from the Institutional Review Board Catholic University of Daegu (hereafter referred to as CU IRB, Phone Number: +82-53-850-2653, e-mail address: swji@cu.ac.kr). The work where practical will be conducted in accordance with the ICH Good Clinical Practice Guidelines and the international standard BS EN ISO 14155:2011 'Clinical investigation of medical devices for human subjects'. This study will be registered with clinicaltrials.gov in accordance with section 801 of the Food and Drug Administration (FDA) Act which mandates the registration of certain clinical trials of drugs and medical devices.

Section 2. Resources

2.1 Subject selection

Sixty subjects who are currently existing contact lenses wearers will be enrolled. Out of 60 subjects, twenty subjects will be recruited from the current wearers of 1.Day ACUVUE® Define™ (Johnson & Johnson Vision Care Inc) and another twenty subjects will be current wearers of Claren 1-day Iris (Interrozzo Inc). Rest twenty subjects will be no previous wearer of any study lenses. All subjects will go through the screening procedure to ensure they satisfy the inclusion criteria. At the screening visit, a detailed Participant Information Sheet explaining the nature of the study will be provided to potential subjects along with a Participant Instruction Sheet, which includes study-specific instructions as well as general lens wear precautions. Once subject agrees to participate, then will be asked to sign a written consent form to confirm their agreement to participate the study.

2.1.1 Subject withdrawal and replacement

Subject's participation in this study is voluntary. Subjects have the right to withdraw from participation at any time during the study without comment or penalty. Withdrawal from the study will not impact upon current or future relationship with the School of Optometry & Vision Science, Catholic University of Daegu. Subjects who have agreed to enroll the study, but have not completed the dispensing visit will be replaced.

2.1.2 Subject recruitment

Subjects will be recruited by one or more of following means:

1. Posting study details on the notice board of the optometry clinic in the Catholic University of Daegu.
2. Advertising through the optometry clinic around the Catholic University of Daegu

2.1.3 Inclusion criteria

Subjects will be only eligible for the study if they meeting the following inclusion criteria:

1. Age of 18 years and above and has full legal capacity as a volunteer
2. Understand the rights as a research subject and willing and able sign a statement of informed consent.
2. Existing soft contact lens wearers or previous experience of contact lens wear
3. Being able to wear the study lenses for at least eight hours a day
4. At least 6/9 visual acuity in each eye with the study lenses
5. Astigmatism less than 1.50 D in both eyes
5. Agreed to follow the protocol and not to participate in other clinical research for the duration of this study.

2.1.4 Exclusion criteria

Subjects will not be eligible to take part in the study if they:

1. Have an ocular disorder which would normally contraindicate contact lens wear.
2. Have a systemic disorder or any infectious diseases which would normally contraindicate contact lens wear.
3. Have previously had any ocular surgery such as corneal refractive surgery
4. Have less than 6/9 visual acuity in each eye with the study lenses
5. Are currently using any topical medication such as eye drops or ointment.
6. Have any corneal distortion resulting from previous rigid lens wear or have keratoconus.
7. Are currently pregnant or lactating.
8. No previous contact lens wear

2.2 Subject discontinuation

All subjects have the right to discontinue the study at any time. Also subjects will be discontinued if a serious adverse event occurs or non-compliance of study protocol.

2.3 Safety parameters, adverse events and concurrent illnesses

Any adverse events either the study lens related or non-study lens related will be described as anticipated condition. These adverse event are classified as ‘serious’, ‘significant’, or ‘non-significant’ by clinical assessment. Any adverse events occurring during the study period must be recorded. The clinical course of each event should be followed until resolution.

2.3.1 Investigator obligations

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to subject participation in the investigation will be reported to the Principal Investigator and to the designated medical monitor of the sponsor within 24 hours of the investigator becoming aware of the event. The Principal Investigator will report the event to the EC/IRB as soon as possible (by fax, mail/delivery, phone, or email), but within 10 business days of becoming aware of the problem. All fatal or life threatening events will be reported immediately to the IRB. Significant and Non-Significant Adverse Events will be reported to the sponsor and the study coordinator as soon as possible, but no later than 5 working days after the occurrence. Sponsor medical monitor contact details are:

2.4 Study termination

If study needs to terminate earlier than planned due to any reason, the Industrial Contact Person will notify the Principal Investigator who will end the study with the cooperation of other staff members. CU IRB will be informed.

2.5 Protocol deviations

If there is any protocol deviation, these will be recorded and reported to the Industrial Contact Person. CU IRB will be informed as necessary.

2.5.1 Protocol amendments

Any amendments will be agreed between the Industrial Contact Person and the Principal Investigator with the cooperation of other staff members. Amendments will be recorded, identified and distributed. Approval from CU IRB will be obtained as necessary.

2.6 Study resources

Study products will be stored according to the manufacturer's product instructions.

2.6.1 Lenses

Details of the study lenses are provided in Table 2.

	1-day Acuve Define	**Claren 1-day Iris**	**Hydron 1-day**
Manufacturer	Johnson&Johnson	Interozzo	Coopervision
Replacement	1-day	1-day	1-day
Material	Etafilcon A	Methafilcon A	Methafilcon A
Water Content (%)	59%	55%	55%
Base curve (mm)	8.5mm	8.6mm	?
Lens diameter (mm)	14.2	14.2	?
Power (D)	0.00, -0.50 ~ -6.00(0.25steps) -6.50 ~ -9.00(0.50steps)	0.00, -0.50 ~ -6.00(0.25steps) -6.50 ~ -10.00(0.50steps)	?
Wearing schedule	Daily disposable	Daily disposable	Daily disposable

Table 2: Study contact lens parameters

2.6.1.1 Use of lenses

The lenses in this study will be all daily disposable lenses, therefore it will be only worn on a daily wear with a minimum of eight hours per day, five days a week.

2.6.2 Care regimens

No care regimen will be required, as the lenses are to be worn on a daily disposable basis

2.6.3 Inventory control

All lenses will be supplied by CooperVision Inc. All worn lenses will be discarded.

2.6.4 Clinical equipment

Clinical equipment such as [redacted] is regularly maintained and calibrated as required. Standard operating procedures and international standards are used where appropriate.

2.7 Study control

The study design is controlled crossover comparison design. The order to wear the lenses will be pseudo-randomized to minimize the impact of order. The lenses will be masked if possible by covering name of contact lens brand.

2.8 Documentation

Documents related to this work that require archiving will be kept by the School of Optometry & Vision Science for a period of 5 years after completion of the final report, before being destroyed.

2.9 Data collection and analysis

Data collected in this work will be recorded on a spreadsheet format. This spreadsheet will be exported into a statistical package for analysis.

2.10 Study completion

The study is complete when all subjects have signed the exit statement.

2.11 fidentiality

All matters and responses are anonymous and will be treated confidentially. The name of individual persons are not required in any of the responses and subjects will only be referred by their unique identity number in the study report. No individual will be identified in any presentation or publication.

2.12 Study monitoring

In order to provide quality control and quality assurance as part of this work, the study monitor will:

1. Liaise closely with the Principal Investigator.
2. Monitor and ensure the safety of the subjects.
3. Ensure that the investigation is being conducted according to the protocol.
4. Monitor and review (or oversee review of) the study records to ensure accuracy.
5. Document their observations in the monitoring report for the study and make them available to relevant authorised parties (e.g. CU IRB).

Section 3. Subject management

3.1 Visit scheduling

Subjects will be required to attend for up to four visits –an initial dispensing visit, and three follow-up visits. Acceptable date ranges are shown in Table 3.

Visit	Target day to visit	Allowable range
Initial dispensing	NA	NA
One week	7 days from dispensing visit.	5-10 days from dispensing visit
Two week	7 days from dispensing visit.	5-10 days from dispensing visit
Three week	7 days from dispensing visit.	5-10 days from dispensing visit

3.1.1 Unscheduled visits

If any subjects experience any discomfort or problem with the study lenses, they will be asked to return to the clinic to be examined. This visit will be classified as 'unscheduled'. All necessary documentation such as the reason for the visit, clinical findings and action taken will be recorded on the clinical study database.

3.1.2 Missed visits

If any subjects are not attending, investigator will attempt all reasonable means to encourage to attend the study. However, any subjects not attending for two consecutive study visits are missed.

3.2 Visit conduct

3.2.1 Initial dispensing visit

The subject will receive a study summary form prior to enrolment and will then be required

to sign an informed consent form. When the subject has signed the consent form, they are considered to be enrolled on the study.

Subjects will be instructed on the following:

1. Lens handling, application and removal, where necessary.
2. Specific study instructions, such as the importance of not using any other contact lens products.
3. General contact lens information such as the management of red eyes.

The following procedures will be performed:

1. Details of the ocular history and contact lens wearing history of the subject.
2. Refraction and distance monocular logMAR visual acuity
3. Auto-keratometry measures using the Keratoraph 5M (Oculus, Germany)
4. Slit lamp biomicroscopy will be carried out for the signs of any abnormality using Efron Grading Scales.
5. The investigator will confirm that the subject satisfies all the inclusion and exclusion criteria. Subjects who fail to meet all the criteria at this time will be discontinued and replaced.
6. The study lenses will be fitted according to the randomisation order and allowed to settle for five minutes. The subject will be masked from the lens type.
7. Monocular logMAR visual acuity will be recorded before performing an over-refraction, and then monocular logMAR visual acuity will be carried out with the over-refraction in place.
8. Lens fit will then be assessed using the following evaluations: horizontal and vertical centration, corneal coverage and movement. Normally, for an acceptable fit, centration and movement will fall within currently accepted clinical criteria
9. The subject will then be discharged and asked to return for the one-week follow-up visit wearing the study lenses for a minimum of two hours. Subjects should be asked to wear their lenses for a minimum of eight hours per day, five days per week.

3.2.2 One-week follow-up visit

Subjects should attend wearing the study lenses which should have been in situ for at least

two hours. Subjects who attend without lenses in situ for at least two hours will usually be rescheduled. The following procedures will be performed (any ocular measurement procedures outlined below will be carried out on each eye):

1. Lens wearing times since the previous visit will be recorded.
2. Lens wearing time on study visit day.
3. Monocular logMAR visual acuity (high contrast) with the study lens.
4. The subject will be asked to score the following qualities using a visual analog scale for:

Comfort after insertion

Comfort before removal

[redacted]

Overall comfort

[redacted]

7. The lenses will then be removed and discarded.
8. The investigator will then conduct a complete biomicroscopic examination of the clinical signs
9. The second pair of lenses will be applied
10. . Visual acuity & lens fit will be assessed with second pair of lenses worn

3.2.3 Two and Three-week visit

Subjects should attend wearing the study lenses which should have been in situ for at least two hours. Subjects who attend without lenses in situ for at least two hours will usually be rescheduled. The following procedures will be performed (any ocular measurement procedures outlined below will be carried out on each eye):

1. The same procedures as the 1-week visit (3.2.2) sections 1-10 will be carried out.
2. Additionally, subjects will be asked to rank the lens in order of preference.
3. At the final visit (or when the subject is discontinued at an earlier visit) the subject will sign a study exit statement acknowledging that the work is complete, although they may have been asked by the investigator to attend a post-study follow-up visit, and that they should continue to use their lenses and solutions as advised, and seek aftercare for their contact lenses. A copy of this signed form will be issued to the subject.

3.2.4 Post-study follow-up visit

In the case of a subject who exits the study with significant clinical signs or symptoms, the investigator must undertake to examine the subject at intervals he/she determines to be clinically appropriate until the sign or symptom has resolved or returned to a level that is considered to be clinically acceptable. Details from these visits will be recorded on a post study follow-up visit form.

3.3 Monitoring subject compliance

Subjects are required to adhere to the instructions provided during this clinical investigation. This will be confirmed at the study visits by verbal questioning of the subject by the

investigator.

3.4 Missing, unused and spurious data

The absence of any data will be carefully and critically considered. If appropriate, partial datasets will be included in the final analysis. Any data missing from a subject visit will be outlined in the report by indicating the number of subjects included for each analysis. Data that are unused or considered to be spurious will be detailed and discussed in the report.

Section 4. Study co-ordination

4.1 Document processing

All case report forms will be processed and evaluated by the School of Optometry & Vision Science, Catholic University of Daegu, who will produce the final report with full statistical analysis. A draft report will be sent to the Industrial Contact Person in order to make comments and ask for re-drafts. If no comments are received from the Industrial Contact Person within eight weeks, a final report will be released with a separate document control page (in duplicate), requesting the Industrial Contact Person to sign both copies, one to keep and the other to be returned to the School of Optometry & Vision Science, Catholic University of Daegu.

4.2 Disclosure

All matters relating to this clinical study are confidential and should only be disclosed to relevant authorized parties. More precise details relating to disclosure are outlined in the Research Agreement. None of the investigators involved in this work owns equity in the funding company.

[redacted]

Personnel

[redacted]

[redacted]

Participant Information for Research Project

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