Learnings of managing myopic children using catenary power profile multifocal soft contact lenses from the PROTECT Randomized Controlled Trial

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PURPOSE:

To evaluate the overall impact of using a catenary curve power profile multifocal soft contact lens design (NVMF) **, with up to 8D relative plus, on managing myopic children at 1-year visit.

Optical designs for myopia progression control (MPC) typically provide around 2D of relative plus; we hypothesize that the catenary lens will be effective and, despite a higher-than-usual magnitude of relative plus, will not adversely impact the wearer's vision and comfort.

PROgressive Myopia Treatment Evaluation for NaturalVue Multifocal Contact Lens Trial (PROTECT) [NCT05159765] is a 3-year multinational, double-masked, randomized controlled trial (RCT) evaluating the effectiveness and safety of these lenses for MPC in children.

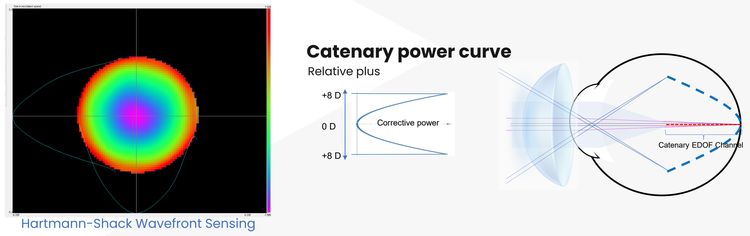

Figure 1. NVMF power profile. Left: Wavefront measurement of NVMF and decomposed to power profile; 8 D of relative plus at 6mm diameter Right: Schematic of the light rays passing through NVMF optic into the eye.

METHODS:

The PROTECT study recruited children from age 7 to <13 years with cycloplegic autorefraction (CSER) between -0.75 D and -5.00 D from 8 clinical sites. Participants were randomized into two treatment groups (both etafilcon A):

- **Control**: NaturalVue Sphere; **Treatment**: NaturalVue Multifocal
- Control: Treatment 1:2 with Control group cross-over after 24-months.
- Outcome measures: Change of CSER and Change of axial length (AXL)
- Exploratory outcomes: vision performances and Patient Reported Outcomes.
- PREP2 is a validated questionnaire for comparing vision-specific quality of life measurements between children wearing multifocal and single vision contact lenses for Myopia Progression Control, and was previously validated for this purpose in the BLINK study [doi.org/10.1111/opo.13216] evaluating myopia progression control in a single-vision contact lens versus the Biofinity Multifocal. PREP2 was administered at BL, 1M and yearly.
- Accommodative accuracy uses MEM at Baseline under best corrected spectacle and with contact lenses at 1M and yearly.
- Pupil size measured using slitlamp reticle and under minimal retro-illumination at Baseline and yearly.
- Linear Mix Model adjustment is a standard procedure of RCT analysis. It uses a type of multivariate regression analysis to take into account the impacts of covariates (age, sex, sites, pupil sizes, etc.) in order to better represent the treatment effects.

RESULTS:

- 145 subjects from Canada, the US, Hong Kong, and Singapore with the average age of 9.9±1.5 and CSER of -2.4±1.3 at enrollment.
- No statistical difference between the two groups for age, gender, or race.
- At 1 year, there were 131 active subjects (including 3% drop-outs).
- Significant covariates identified being: age, sex, site and pupil size.
- Adjusted values from Linear Mixed Models were computed by incorporating the covariates to remove their potential impacts, thus the Adjusted results are a better representation of the actual effect of the intervention being studied.
- Planned subgroup analysis to match common enrollment criteria to allow better meta-analysis in the future. Subgroup ages 8 to <13; CSER -0.75 to -4.00 D.
- Nonetheless, 7-year-olds showed a similar treatment effect; the same goes for myopia stronger than -4.00 D.

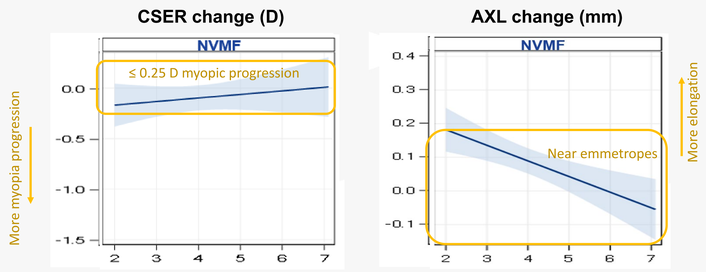

Figure 2: PROTECT's Significant Covariate, Pupil size
CSER: full range within ≤ 0.25 myopic shift; larger pupils associated with less progression

AXL: large majority within the age-matched emmetropic axial elongation; larger pupils associated with less elongation

CSER (D)	Unadjusted Mean ± SD	p-value*	Adjusted Mean ± SD	p-value*
Planned Subgroup				
SVCL	-0.58 ± 0.06	<0.001	-0.54 ± 0.09	<0.001
NVMF	-0.17 ± 0.04	<0.001	-0.06 ± 0.07	0.435
SVCL - NVMF	-0.42 ± 0.08	<0.001	-0.48 ± 0.09	<0.001

AXL (mm)	Unadjusted Mean ± SD	p-value*	Adjusted Mean ± SD	p-value*
Planned Subgroup				
SVCL	0.29 ± 0.02	<0.001	0.30 ± 0.03	<0.001
NVMF	0.12 ± 0.01	<0.001	0.13 ± 0.02	<0.001
SVCL - NVMF	0.17 ± 0.03	<0.001	0.17 ± 0.03	<0.001

Table 1: PROTECT Efficacy Results
Unadjusted and Adjusted CSER & AXL Change (Planned Subgroup)
Adjusted numbers from the Mixed Linear Model (see **METHODS**); NVMF had no statistically significant change of CSER from baseline, whereas SVCL was.

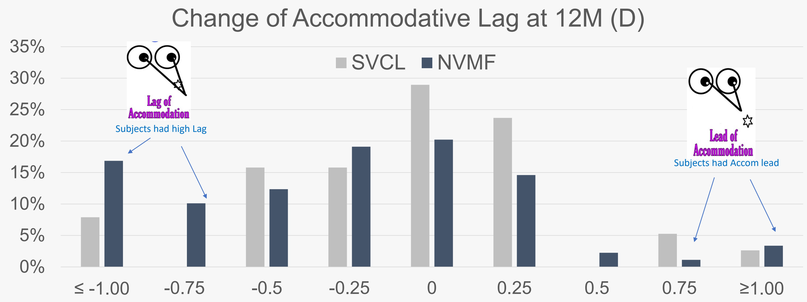

Figure 3. Frequency Distribution of Change in Accommodative Accuracy (ITT)

- **Baseline:** similar accommodative lag (SVCL 1.07±0.75D), NVMF (1.04±0.84D).
- **SVCL:** similar to BL at 1M (1.12±0.82D, p=0.573) & 12M (0.99±0.71D, p=0.286).
- **NVMF:** had a significant reduction of accommodative lag from BL at 1M (0.63±1.02D, p<0.001) and at 12M (0.76 ± 0.67D, p<0.001).
- The peak of change of the NVMF arm centered around zero, which signals that the average reduction of accommodative lag is not due to measurement bias coming from the multifocality of the multifocal optic.
- Subjects with reduced accommodative lag >0.50D at the 12M visit were the ones who had a large magnitude of lag at BL (+2.00D or more).
- Three subjects from the NVMF arm increased more than 0.50 D in accommodative lag at 12M compared to their BL values; all three had accommodative lead (-0.50 to -2.50D) at BL, and their accommodative lag measurements were between +0.50 to +0.75D at 12M.
- There was also no correlation between accommodative accuracy at BL/12M and the magnitude of axial elongation or myopia progression at 12M (R^2=0.03 to 0.10).

Study Group (Mean±SD)	Dist HCVA OU	Dist LCVA OU	Near HCVA OU
BL Spec (n = 41)	-0.04 ± 0.05	0.11 ± 0.14	-0.04 ± 0.06
SVCL (n = 41)	-0.04 ± 0.08	0.11 ± 0.14	-0.03 ± 0.05
p-value (Spec vs CL)	0.946	0.987	0.506
BL Spec (n = 93)	-0.05 ± 0.06	0.09 ± 0.11	-0.03 ± 0.06
NVMF (n = 93)	-0.04 ± 0.07	0.17 ± 0.15	-0.02 ± 0.04
p-value (Spec vs CL)	0.723	<0.001	0.106
p-value (SVCL vs NVMF)	0.883	0.024	0.248

Table 2. High Contrast and Low Contrast Visual Acuity in logMAR (0.00=20/20; -0.10=20/16), ITT

Study Group (Mean±SD)	Vision	Symptoms (Comfort)	Activities	Overall
Baseline (n = 41)	42.45 ± 11.82	52.26 ± 15.0	40.32 ± 22.13	44.36 ± 20.18
SVCL (n = 41)	68.06 ± 11.51	57.06 ± 19.5	79.34 ± 14.42	78.36 ± 11.95
Paired p-value	<0.001	0.172	<0.001	<0.001
Baseline (n = 93)	46.27 ± 12.45	51.88 ± 11.95	40.59 ± 20.10	44.79 ± 19.09
NVMF (n = 93)	70.17 ± 12.53	61.79 ± 18.01	77.78 ± 15.86	78.06 ± 14.24
Paired p-value	<0.001	<0.001	<0.001	<0.001
P-value (SVCL vs NVMF)	0.345	0.189	0.577	0.898

Table 3. Patient-reported outcomes
Based on subjective assessment using the *PREP2* validated survey (All available data/ITT) during the Baseline visit and 12M visit.

RESULTS:

- Children from both groups reported significant improvement in Quality of Life (QoL) after wearing contact lenses.
- At both the Baseline and the 12-month visit, the NVMF group had similar PREP2 subscale scores compared to the SVCL group.
- In the BLINK study, the PREP2 questionnaire was able to differentiate the magnitude of impact between the groups wearing +1.50D and +2.50D add. The average score of the +2.50 group had a 3.2 points reduction in Vision Subscale compared to the +1.50D group and 4 points reduction in Vision score compared to the SVCL group.
- Compared with the BLINK data, the PROTECT data was within a similar range of variability on the Subscale scores. No reduction in scores were observed from the NVMF group as compared to the SVCL group for any Subscore, indicating NVMF's multifocal optics did not cause noticeable negative impacts on the vision, comfort and vision-related quality of life measurements compared to children wearing single vision contact lenses.
- The mean wearing time of SVCL arm was 81.3±12.6 hrs/wk and 80.9±11.4 hrs/wk for the NVMF arm with no statistical difference between groups (P=0.84).
- The similar wearing times aligning with the similar PREP2 scores reported by each group.
- NVMF's multifocal optics did not adversely impact the wearers' vision-related clinical outcomes, which enabled them to achieve sufficient wearing time.

CONCLUSIONS:

- In the population of 8 to<13-year-olds, baseline CSER between -0.75D to -4.00D, compared with SV control, NVMF had adjusted value of:
- **0.48 D (89%)** reduction of myopia progression
- **0.17 mm (58%)** reduction of axial length elongation
- The catenary multifocal contact lens is **effective for a large range of pupil sizes** but the larger the pupil, the larger the treatment effect.
- The high magnitude of relative plus does not negatively impact Patient Reported Outcomes, **NVMF wearers are as satisfied as SVCL wearers** when it comes to Vision, Comfort, daily activities and overall satisfaction.
- Objective outcomes (vision and wearing time) corroborate with PRO.
- The potential impact of both vision-related QoL attributes with multifocal optics and the optics' sensitivity to small pupils are critical considerations when evaluating a treatment option to maximize the chance of success.
- PROTECT is an ongoing clinical trial.

**US: NaturalVue® (etafilcon A) Multifocal 1 Day™ Disposable Soft Contact Lenses are indicated for daily wear for the correction of refractive ametropia (myopia and hyperopia), and/or presbyopia in normal eyes. OUS: indicated for daily wear for the correction of refractive ametropia (myopia and hyperopia), and/or presbyopia, and myopia progression control in normal eyes.