Axial growth after discontinuing soft multifocal contact lens wear in the Bifocal Lenses In Nearsighted Kids 2 (BLINK2) Study

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Abstract Number: 424

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Purpose
The BLINK Study was a 3-year randomized clinical trial that found +2.50 add center-distance multifocal contact lenses (MFCLs) slowed eye growth and myopia progression compared to single vision contact lenses (SVCLs) and +1.50 MFCLs. In BLINK2, all children wore +2.50 MFCLs for two years then SVCLs for one year. This analysis explores whether there was a rebound in eye growth and progression after discontinuing MFCLs.

Methods
Myopic children (n = 248; 59% female) in the BLINK2 Study were included (mean ± SD age at start of BLINK2 = 14.9 ± 1.4 years; 11-17 years old). Axial length (AL) was measured every 6 months using optical biometry and spherical equivalent refraction (SER) was measured annually by cycloplegic autorefraction; right and left eye measurements were averaged. AL and SER were each modelled as a function of time controlling for original BLINK Study treatment group (SVCL, +1.50 MFCL, or +2.50 MFCL), baseline age, sex, race and site. Each model had two linear time predictors for the change in either AL or SER, one when wearing MFCLs (baseline to Year 2) and one when wearing SVCLs (Year 2-3).

Results
At the start of BLINK2, mean ± SD AL and SER were 25.2 ± 0.9 mm and -3.40 ± 1.40 D, respectively. After all participants switched from MFCLs to SVCLs at Year 2, there was an increase in AL growth of 0.04 mm/year (95% CI: 0.01 to 0.06; $p = 0.003$) that did not depend on the original BLINK treatment assignment ($p = 0.81$). For SER, there was also an increase in myopia progression after switching from MFCLs to SVCLs at Year 2 of -0.16 D/year (95% CI: -0.11 to -0.21; $p < 0.001$) that also did not depend on the original BLINK treatment assignment ($p = 0.57$). There continued to be a difference in AL and SER throughout BLINK2 based on the BLINK Study treatment assignment with the original +2.50 MFCL group from BLINK having shorter eyes and lower myopia than the +1.50 MFCL and SVCL groups (both $p < 0.001$).

Conclusions
While there was a statistically significant increase in eye growth and myopia progression after discontinuing MFCL wear, the increases were small and not clinically meaningful (on average, 0.04 mm/year and -0.16 D/year). These minimal increases did not depend on the length of previous MFCL wear and do not suggest a loss of treatment effect after discontinuation of MFCLs in this age group.

Hyperopic Reserve as a Treatment Indicator for Low-Concentration Atropine to Delay Myopia Onset in Children (LAMP 2 Study)

Abstract Number: 425

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DisclosureBlock: Xiu Juan Zhang, None; Yuzhou Zhang, None; Ka Wai Kam, None; Clement C. Tham, None; Li Jia Chen, None; Calvin C P Pang, None; Jason C.S. Yam, None;

Purpose
Low-concentration atropine eye drops can delay myopia onset. Identifying whom to consider for treatment is important. This study aimed to evaluate the associated factors affecting the effectiveness of low-concentration atropine eyedrops for delaying the onset of myopia.

Methods
Secondary analysis from a randomized, placebo-controlled, double-masked trial. (LAMP 2 study). A total of 353 non-myopic children aged 4–9 years with cycloplegic spherical equivalent between +1.00 D to 0.00 D and astigmatism less than -1.00 D, were randomly assigned to the 0.05% atropine (n=116), 0.01% atropine (n=122), and placebo (n=125) groups who completed 2 years of LAMP 2 trial. Factors associated with myopia onset, fast myopic shift, spherical equivalent and axial length changes over 2 years, and the interactions of these factors with atropine treatment concentration were assessed.

Results
Less baseline hyperopic reserve and higher level of parental myopia were the risk factors for myopia onset (OR=0.02, P<0.001 and OR=2.29, P=0.003 respectively), fast myopic shift (OR=0.16, P<0.001 and OR=1.87, P=0.01 respectively), spherical equivalent myopic shift (β=0.45, P<0.001 and β=-0.22, P=0.003 respectively) and AL elongation (β=-0.22, P<0.001 and β= 0.08, P=0.01 respectively). There was positive interaction between treatment of 0.05% and baseline hyperopic reserve (P=0.02), but not parental myopia (P=0.94). In the placebo group, the myopic shift over 2 years was highly influenced by the hyperopic reserve, the lesser hyperopic reserve the faster progression (-0.74D for the subgroup between +1.0D and 0.75D, increased to -1.42D for the subgroup between +0.00 to +0.25D, P-trend <0.001). The same trends were observed in 0.01% group (P<0.001). In contrast, in 0.05% atropine group, myopic shift was stable, from 0.44 to 0.48D, in various hyperopic reserve groups (P=0.99). Similar trends were observed in AL elongation in various hyperopic reserve groups over 2 years.

Conclusions
Reduced baseline hyperopic reserve and higher level of parental myopia were two significant risk factors for both myopia onset and myopic shift in non-myopic children, and therefore should be considered for preventive treatment. Hyperopic reserve could be an indicator for treatment, implying that children may benefit more from early intervention with 0.05% atropine when their hyperopic reserve remains relatively preserved.

Association of Myopia with Higher Risk of Incident Visual Impairment in a Multi-ethnic Asian Population: the Singapore Epidemiology of Eye Diseases Study

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Abstract Number: 423

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DisclosureBlock: Faye Yu Ci Ng, None; Zhi Wei Lim, None; Miao Li Chee, None; Hengtong Li, None; Charumathi Sabanayagam, None; Ching-Yu Cheng, None; Yih Chung Tham, None;

Purpose
To examine the association between baseline myopia status with 6-year incident visual impairment. Myopia is the most common type of refractive error with significant morbidity on visual function. The disease has been associated with higher risk of developing myopic macular degeneration, choroidal neovascularisation, cataract and glaucoma.

Methods
We conducted a population-based prospective cohort study on participants from the Singapore Epidemiology of Eye Diseases (SEED) Study. Adults aged ≥40 years with no VI at baseline were recruited and followed up at the 6-year mark for incident VI. VI was defined as best-corrected visual acuity <20/40 determined by subjective refraction, consisting of low vision between <20/40 and ≥20/200 and blindness of <20/200. Myopia was defined as SE <-0.5 D. We performed multivariable Poisson regression with robust variance to evaluate the association between baseline myopia status and incident VI, adjusting for age, gender, ethnicity, alcohol intake, smoking, BMI, diabetes mellitus, hypertension, hyperlipidaemia, cardiovascular disease, chronic kidney disease, housing, education, and income. Generalized estimating equation (GEE) with exchangeable correlation structure was applied to account for correlation between pairs of eyes.

Results
A total of 6,077 participants (11,559 eyes) with no baseline VI were included in the analysis (2,385 Chinese, 1,722 Malay, and 1,970 Indian individuals). Subjects included in the final analysis had a mean age of 56.0 ± 8.6 years and 2,955 (48.6%) were male. Compared to eyes with no myopia (n=7860), eyes with low myopia (n=2359) (-3D<SE≤-0.5; RR=1.33; 95%CI, 1.09-1.63; P=0.006) and high myopia (n=367) (SE≤-6D; RR=3.34; 95%CI, 2.09-5.33; P<0.001) had increased risk of incident VI. Eyes with axial length >26mm were 2.8 times more likely to develop VI (95%CI, 1.83-4.27; P<0.001) compared to those with AL≤23mm. Primary causes of incident VI were cataracts (71.0%), age-related macular degeneration (6.93%), posterior capsular opacification, and maculopathy (Table 1).

Conclusions
In this multiethnic population-based cohort study, myopia, in particular high myopia, was associated with higher incident risk of best-corrected VI. Our findings provide further impetus for close monitoring and screening of individuals with high myopia for incident vision loss.

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.
Myopia, in particular high myopia, was associated with higher incident risk of best-corrected visual

impairment. Our findings provide further impetus for close monitoring and screening of individuals with high myopia for incident vision loss.

Table 1. Primary Causes of Incident Best-Corrected Visual Impairment over 6 years

Causes of VI*	Incident Best-corrected VI*		
	Low Vision* (n=217)	Blindness* (n=14)	Total* (n=231)
Under-Corrected Refractive Error	N/A	N/A	N/A
Cataracts	155 (71.4%)	9 (64.3%)	164 (71.0%)
Diabetic Retinopathy	13 (6.0%)	0 (0.0%)	13 (5.63%)
Posterior Capsular Opacification	8 (3.7%)	2 (14.3%)	10 (4.33%)
Age-Related Macular Degeneration	16 (7.4%)	0 (0.0%)	15 (6.93%)
Maculopathy	10 (4.6%)	0 (0.0%)	10 (4.33%)
Myopia Maculopathy	2 (0.9%)	0 (0.0%)	2 (0.87%)
Glaucoma	5 (2.3%)	1 (7.1%)	6 (2.60%)
Amblyopia	2 (0.9%)	0 (0.0%)	2 (0.87%)
Corneal Diseases	2 (0.9%)	0 (0.0%)	2 (0.87%)
Retinal Vein Occlusion	0 (0.0%)	0 (0.0%)	0
Pterygium	0 (0.0%)	1 (7.1%)	1 (0.43%)
Others	4 (1.8%)	1 (7.1%)	5 (2.16%)

VI= Visual Impairment; N/A= Not Applicable

Data presented as number (percentage)

*Based on US definition – VI was defined as VA <20/40, low vision was defined as between <20/40 and ≥20/200; blindness was defined as <20/200, based on better-seeing eye

Repeated Low-Level Red-Light Therapy Combined with Orthokeratology to Achieve “Glasses-off” in Daytime and Full Control of Myopia Progression: A Multicenter Randomized Controlled Trial

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Abstract Number: 429

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DisclosureBlock: Mingguang He, Code P (Patent) Eyerising Ltd, Code O (Owner) Eyerising International Pty Ltd, Eyerising Ltd, Ruilin Xiong, None; Wei Wang, None; Xiao Yang, None;

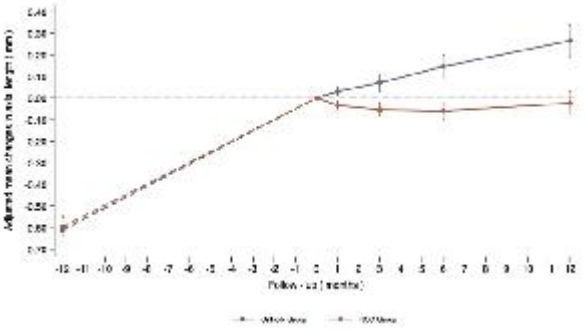
Purpose
Orthokeratology (Ortho-k) is currently the only solution that achieves “glasses-off” vision (free from spectacles and contact lenses) during the daytime, and repeated low-level red-light (RLRL) therapy has demonstrated strong efficacy in controlling myopia progression. This study aims to investigate the efficacy and safety of combining these two solutions among school-aged children.

Methods
In this multicenter, randomized, parallel-group, single-blind clinical trial, children aged 8-13 years with a cycloplegic spherical equivalent refraction of -1.00 to -5.00 diopters (D), astigmatism of 1.50 D or less, and anisometropia of 1.50 D or less in the initial Ortho-k fitting examination, and who had poorly controlled myopia despite using Ortho-k for 1 year (annual axial length [AL] elongation ≥ 0.50 mm), were randomly assigned to the RLRL combined with Ortho-k (RCO) group or the Ortho-k group in a 2:1 ratio. The Ortho-k group wore Ortho-k lenses at night for at least 8 hours per day only, while the RCO group additionally received daily RLRL therapy twice a day for 3 minutes, with sessions spaced at least 4 hours apart. The primary outcome was the change in AL measured at 12 months relative to baseline, based on the modified intention-to-treat principle (ClinicalTrials.gov, NCT04722874).

Results
A total of 47 (97.9%) children were included in the analysis (30 in the RCO group and 17 in the Ortho-k group). The mean axial elongation rate before the trial was 0.597 mm/year in the RCO group and 0.612 mm/year in the Ortho-k group. After 12 months following the intended intervention, the adjusted mean AL changes were -0.024 mm (95% CI: -0.078 to 0.030 mm) in the RCO group and 0.265 mm (0.191-0.338 mm) in the Ortho-k group. The adjusted mean difference in AL changes was 0.288 mm (0.137-0.440 mm) between the RCO and Ortho-k groups. No serious adverse events, ocular damage, or increased incidence of contact lens-related adverse events were observed following RLRL therapy.

Conclusions
Combined therapy with RLRL and Ortho-k is likely to offer the advantages of “glasses-off” vision during daytime and full control of myopia progression.

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.
A combination of RLRL and Ortho-K is a unique solution achieving both 'glasses-off' in daytime and full control of myopia progression.



Five-Year Clinical Trial of Low-concentration Atropine for Myopia Progression (LAMP) Study: Phase 4 Report

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Abstract Number: 426

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Purpose
To evaluate (1) the long-term efficacy of low-concentration atropine over 5 years, (2) the proportion of children requiring retreatment and associated factors (3) the efficacy of *pro re nata* (PRN) retreatment using 0.05% atropine from year 3 to 5.

Methods
This is a randomized, double-masked extended trial. Children aged 4–12 years originally from the Low-Concentration Atropine for Myopia Progression study were followed up for 5 years. During the third year, children in each group originally on 0.05%, 0.025%, and 0.01% atropine were randomized to continued treatment and treatment cessation. During years 4 and 5, all continued treatment subgroups were switched to 0.05% atropine for continued treatment, while all treatment cessation subgroups followed a PRN retreatment protocol to resume 0.05% atropine for children with myopic progressions of 0.5D or more over one year. Cycloplegic spherical equivalent (SE) refraction and axial length (AL) were measured at 6-month intervals. The main outcomes include (1) Changes in SE and AL over 5 years in different concentration atropine groups over 5 years; (2) Proportion of children who needed retreatment; (3) Changes in SE and AL in continued treatment and PRN retreatment groups from years 3 to 5.

Results
269 (82.5%) of 326 children from the third year completed 5 years of follow-up. Over 5 years, the cumulative mean SE progressions were –1.34±1.40D, –1.97±1.03D, and –2.34±1.71D for the continued treatment groups with initial 0.05%, 0.025%, and 0.01% atropine respectively (P=0.02). Similar trends were observed in AL elongation (P=0.01). Among the PRN retreatment group, 87.9% (94/107) of children needed retreatment. The proportion of retreatment across all studied concentrations is similar (P=0.76). The SE progressions for continued treatment and PRN retreatment groups from years 3 to 5 were – 0.97D±0.82D, and –1.00±0.74D (P=0.55), and the AL elongations were 0.51±0.34 mm, and 0.49±0.32 mm (P=0.84), respectively.

Conclusions
Over 5 years, the continued 0.05% atropine treatment demonstrated good efficacy for myopia control. The majority of children needed to restart treatment after atropine cessation at year 3. Restarted treatment with 0.05% atropine achieved similar efficacy as continued treatment. Therefore, children should be considered for retreatment of atropine if myopia progresses after treatment cessation.

The MOSAIC Study: Year 3 results of 0.01% and 0.05% Atropine treatment in a European Population

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Abstract Number: 427

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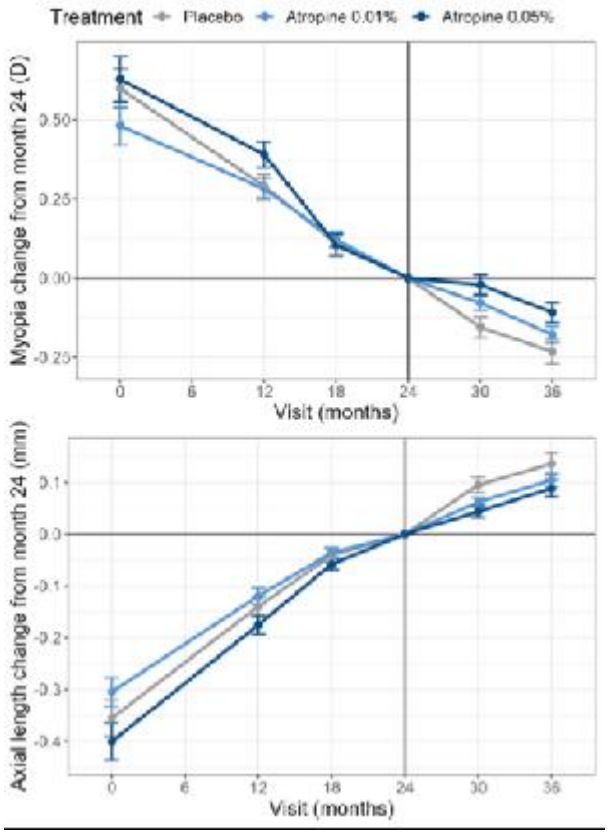
DisclosureBlock: James Loughman, Code C (Consultant/Contractor) Dopavision,EssilorLuxottica, Code F (Financial Support) Coopervision,Ocumension,EssilorLuxottica,Dopavision,Vyluma, Code I (Personal Financial Interest) Ocumetra, Code P (Patent) Ocumetra, Code O (Owner) Ocumetra, Gareth Lingham, Code E (Employment) Ocumetra, Ernest Kyei Nkansah, None; Emmanuel Kobia-Acquah, None; Ian Flitcroft, Code C (Consultant/Contractor) Johnson & Johnson,Coopervision, EssilorLuxottica,Thea,Vyluma,Dopavision, Code F (Financial Support) Ocumension,Vyluma,Coopervision,Essilorluxottica,Dopavision, Code O (Owner) Ocumetra, Code P (Patent) Ocumetra, Code I (Personal Financial Interest) Ocumetra

Purpose
Phase 1 of the Myopia Outcome Study of Atropine in Children found a modest myopia control effect of atropine 0.01% at 24 months. To explore the impact of (i) sudden versus gradual 0.01% atropine cessation on myopia progression (rebound) and (ii) the safety and efficacy of atropine 0.05% eye drops in a European population, a follow-on crossover phase was conducted over an additional 12-month period.

Methods
Of the 204 subjects who completed Phase 1, 199 consented to participate in the crossover phase. Participants using atropine 0.01% eye drops in Phase 1 were re-randomized to receive placebo eye drops nightly, placebo eye drops in a tapering regimen, or atropine 0.01% eye drops in a tapering regimen (1:1:2 ratio). Participants originally allocated to placebo were re-randomized to 0.05% atropine treatment. Linear mixed models were used to model change in refraction and axial length from the 24- to 36-month visit.

Results
No significant differences were present in key characteristics of the 0.01%, 0.05% atropine and placebo groups at the 24-month visit ($p>0.05$ for all). 182 participants completed the 36-month study visit [67 (36.8%) 0.01% atropine group, 61 (33.5%) 0.05% atropine, 54 (29.7%) placebo]. The atropine 0.05% group had significantly less myopia progression compared to placebo (difference=+0.13 D, $p=0.01$), and significantly less eye growth compared to both placebo (difference=-0.05mm, $p=0.008$) and atropine 0.01% (difference=-0.04, $p=0.04$) groups, after adjusting for age, sex and other variables. No obvious rebound effect was noted in either sudden or tapered cessation groups. Adverse events potentially related to the study treatment occurred in 1/60 (1.7%), 2/73 (2.7%) and 12/66 (18.2%) of placebo, atropine 0.01% and atropine 0.05% group participants, respectively ($p=0.001$), no serious adverse events were reported. Compliance was similar across all groups ($p=0.81$).

Conclusions
This is the first RCT of 0.05% atropine eye drops for the management of myopia progression in a predominantly White, European population. While treatment-related adverse events were more common in this group, the higher concentration was well tolerated, with no participants discontinuing treatment due to adverse events and only 5% requiring varifocal lenses to manage symptoms. A dose-response effect was observed, with significantly greater myopia control achieved with the higher concentration atropine.


Treatment
Placebo
Atropine 0.01%
Atropine 0.05%
Myopia change from month 24 (D)
0.50
0.25
0.00
-0.25
0
6
12
18
24
30
36
Visit (months)
Axial length change from month 24 (mm)
0.1
0.0
-0.1
-0.2
-0.3
-0.4
0
6
12
18
24
30
36
Visit (months)

NVK002 low-dose atropine 0.01% maintains myopia control during a fourth year of dosing and discontinuation does not cause rebound myopia progression

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Abstract Number: 428

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DisclosureBlock: Karla Zadnik, Code C (Consultant/Contractor) Vyluma, Houman Hemmati, Code E (Employment) Vyluma, Tung Fong, Code E (Employment) Vyluma, Simon Chandler, Code E (Employment) Vyluma

Purpose
The CHAMP phase 3 trial demonstrated that NVK002 atropine 0.01% significantly increased the proportion of myopic children who progressed less than 0.50 D in spherical equivalent refraction (SER) over 36 months of nightly dosing (responders). Stage 2 of CHAMP assessed the impact of continued dosing of NVK002 on myopia control and the occurrence of myopia rebound upon cessation of NVK002 dosing over an additional 12 months.

Methods
116 of the 164 participants aged 3 to 16 years (intent-to-treat set) at baseline in the EU and US with SER between −0.50 D to −6.00 D who were randomized to receive nightly NVK002 0.01% eye drop for 36 months in Stage 1 continued to Stage 2. Among those participants, 38 were re-randomized to continue treatment with NVK002 0.01% for 12 months, for a total of 48 months dosing, while 39 were re-randomized to placebo for 12 months to assess rebound of myopia. Cycloplegic SER and axial length (AL) were measured at 48 months.

Results
Among the 38 participants who continued 12 additional months of dosing with NVK002 0.01%, mean SER changed -0.95 D (SD 0.82 D) from study baseline, and mean AL changed 0.61 mm (SD 0.62 mm) from study baseline. Among the 39 participants re-randomized from NVK002 0.01% to 12 months of placebo, mean SER changed -1.12 D (SD 0.78 D), and mean AL changed 0.78 mm (SD 0.42 mm). The between-group least square mean difference (0.01% to 0.01% – 0.01% to placebo) in SER change from study baseline at Month 48 was 0.17 D (95% CI [-0.23, 0.57], p=0.4). There were no serious ocular treatment-emergent adverse events (TEAE). The most common ocular TEAE was dry eye (NVK002 0.01%: 7.5%; Placebo: 2%;).

Conclusions
These findings from Stage 2 of the CHAMP phase 3 trial suggest that NVK002 low-dose atropine 0.01% continues to be both effective and safe in treating pediatric myopia progression following four years of nightly dosing. Moreover, after switching to placebo drops for one year following three years of dosing with NVK002 0.01%, there was no meaningful rebound effect. These data support NVK002 0.01% as a potential long-term treatment for pediatric myopia.

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.
We showed that once nightly dosing with NVK002 0.01% eye drops, a new formulation of low-dose atropine drops, when taken for four years, can meaningfully show the progression of nearsightedness in children with myopia. Additionally, we demonstrated that myopia progression does not rebound or occur more

quickly once a child stops taking NVK002 0.01% eye drops after having taken the drops for three years.