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Efficacy and safety of a lipid-containing artificial tear compared with a non-lipid containing tear: a randomized clinical trial

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Abstract

Background Dry eye disease (DED) is a prevalent condition affecting over 16 million patients in the USA. DED and the symptoms of ocular discomfort are debilitating and a significant burden on patients. If left untreated, DED can progress to cause severe pathology. Treatment is often initiated by patients without consulting a healthcare professional. This study investigated the safety and efficacy of a novel lipid-containing eye drop (BTC), which might better mimic the components of natural tears.

Methods This was a multicenter, randomized, double-masked, active control, two arm, parallel group study of eye drops in adult subjects with self-reported DED. Subjects were randomly assigned to BTC or control (commercially available non-lipid eye drops; NLED) arm and were followed for 30 days. Assessments using visual analog scale and patient-reported outcomes (PRO) questionnaires, non-invasive tear break up time, slit-lamp examination, and subject-reported ocular symptoms were conducted at baseline and at days 7 and 30. The primary endpoint was change in overall ocular comfort score from baseline to day 30.

Results 158 subjects were randomized, of whom 130 completed the study per protocol (PP). Mean (SD) age was 47.8 (14.14) years. The mean (95% CI) change in overall comfort scores at the 30-day follow-up in the PP population was 21.4 (15.1, 27.7) for the test drop and 10.0 (3.9, 16.1) for the comparator. The mean (95% CI) treatment difference was 11.3 (2.6, 20.1); this met the pre-defined requirements for non-inferiority. There was no significant difference in the proportion of eyes with reported ocular symptoms between the groups. At day 7, the OR (95% CI) was 0.967 (0.528, 1.770) and at day 30 was 1.160 (0.610, 2.203). There were no Grade 3 or higher corneal edema, corneal neovascularization, corneal staining, conjunctival injection, tarsal abnormalities or any other biomicroscopy findings, and no corneal infiltrates observed during the study.

Conclusions The investigational lipid eye drop BTC was noninferior to the commercially available non-lipid comparator in all parameters measured and has the potential to provide an effective therapy for subjects with symptoms of dry eye who would benefit from a lipid-based artificial tear.

Trial Registration NCT03995355 (http://www.clinicaltrials.gov), registered June 24, 2019.

Keywords Dry eye, Artificial tear, Lipid eye drop, Ocular surface disease

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Background

Dry eye disease (DED) is a multifactorial disease [1, 2], defined by a clinical consensus as being " characterized by a persistently unstable and/or deficient tear film causing discomfort and/or visual impairment, accompanied by variable degrees of ocular surface epitheliopathy, inflammation and neurosensory abnormalities" [2]. Presentation and symptoms are heterogeneous, with estimates of ~ 14% of DED resulting from reduced tear production (aqueous-deficient dry eye, ADDE), ~ 50% having increased evaporation (evaporative dry eye, EDE), often caused by meibomian gland dysfunction, or a combination of both ADDE and EDE [3]. Because dry eye and DED represent a spectrum of a progressive disease one type of dry eye can exhibit features of the other [4]. The prevalence of DED ranges from ~ 10% to > 50%; greater prevalence has been reported in women and DED increases in prevalence with age [5, 6]. The highest prevalence estimates are from studies in South East Asia [5]. In the USA, over 16 million adults are estimated to have diagnosed DED [7].

Subjects with dry eye suffer from discomfort and effects on vision that affect normal activities of daily life. DED is typically diagnosed after patients experience persistent symptoms of dryness, often with the sensation of grittiness or foreign bodies in the eyes, burning and itchiness, leading to visual disturbances including blurred vision or sensitivity to light [5, 8, 9]. DED is a chronic disease and the reduction in quality of vision and overall quality of life is perceived by patients to be as serious as angina [10].

Left untreated, the underlying pathologies of dry eye and DED – tear film instability, epithelial damage and inflammation, along with nerve damage and functional lid changes – can result in progressive worsening of the pathologies and symptoms [11, 12], including conjunctival scarring and corneal ulcers, and the potential for vision loss [13, 14]. The progression of dry eye and DED is described as a 'vicious cycle,' driven by inflammation, in which the pathologies further exacerbate symptoms and pathology [11, 15]. Therefore, early intervention – at the presentation of ocular discomfort – is essential to break the cycle and prevent subsequent worsening of disease and damage.

Although there are multiple approaches to treating dry eye, including systemic treatments, topical and nasal applications to stimulate tear production, prevention of tear drainage, dietary approaches, topical or local antibiotics, or physical interventions [9], the first-line treatment option is typically over-the-counter artificial tears [14, 16]. Artificial tears may prevent further damage to the eyes but their effects are temporary, requiring frequent use. Improvements in artificial tear formulations, such as the inclusion of lipids to reduce the speed of evaporation, have been made in an attempt to better mimic natural tears. The aim of these formulations is to reduce evaporation and tear break up, thereby improving their effectiveness and reducing required frequency of use [17, 18].

The objective of this study was to evaluate the safety and efficacy of an investigational lipid eye drop (BTC) in comparison with a commercially available non-lipid-based eye drop (NLED).

Methods

This was a multicenter, randomized, double-masked, active control, two arm, parallel group study of eye drops in adult subjects with self-reported dry eye (NCT03995355)[19]. It was conducted at seven centers in the USA.

This study was performed in accordance with the ethical principles of the Declaration of Helsinki [20] and Good Clinical Practice (GCP) [21], including the archiving of essential documents. The study was approved by Sterling IRB (Atlanta, GA, USA).

Participants

Subjects aged 18–69 years were eligible for enrolment if they were not contact lens wearers and had self-reported symptoms of ocular dryness or irritation, or who had used lubricating eye drops in the prior three months. Subjects must have read, understood and signed the informed consent statement.

Subjects were excluded if they were pregnant or breastfeeding; had diabetes, a systemic disease, an autoimmune disease, an infectious disease, or a contagious immunosuppressive disease; were using a medication that, in the opinion of the investigator, might interfere with the study; had any ocular abnormalities or condition that might interfere with the study; had a history of ocular or corneal surgery; had participated in a clinical trial in the 30 days prior to enrolment; had a history of binocular vision abnormality or strabismus; were habitual wearers of soft contact lenses in the preceding month or rigid gas permeable lens within the preceding 3 months; were users of prescription medicine to treat dry eye or ocular discomfort, ocular steroids, or any medication (whether prescribed or over-the-counter) that might interfere with the clinical study, except artificial tears (at the discretion of the investigator); or were employees or family members of employees of an investigational clinic involved in the study.

Subjects were randomly assigned to either the test or control group based on a computer-generated randomization schedule prepared before the start of the study. The randomization was stratified by investigational site.

Subjects were randomized after informed consent, once all inclusion and exclusion criteria were met, and subject history and baseline characteristics were collected.

Study interventions

The investigational product in this study was a lipid eye drop (Blink® Triple Care [BTC] Bausch + Lomb, Inc., Bridgewater, NJ, USA); the comparator non-lipid eye drop (NLED) was Blink® Tears (Bausch + Lomb, Inc.), a non-lipid-containing commercially available formulation (Appendix A).

Study design and outcomes

This was a 30-day study, during which subjects attended three scheduled visits. At visit 1 (baseline), screening and baseline evaluations were recorded before subjects were randomly assigned to receive BTC or NLED. The subjects instilled one drop per eye; drops were allowed to settle for 5 min before assessments were conducted. Sufficient study drops were dispensed for use until the subsequent visit (at least one drop per eye, twice daily).

Visit 2 occurred 7 ± 1 days after the baseline visit. Follow-up evaluations were conducted and eligible subjects were dispensed study drops for use until the final visit. Visit 3 was 28–32 days after visit 1, during which assessments and final evaluations were carried out. Remaining study drops were collected from subjects.

At each visit, the following assessments were conducted: visual analog scale (VAS) questionnaires; patient-reported outcomes (PRO) questionnaires; non-invasive tear break up time (NIBUT); slit-lamp examination; and subject-reported ocular symptoms (SROS). The VAS, PRO and SROS questionnaires were healthcare-professional guided assessments (Appendix B).

The primary endpoint was the change in overall ocular comfort score from baseline at the 30-day follow-up visit, using a VAS from 0 (extremely uncomfortable) to 100 (extremely comfortable). The primary hypothesis was that BTC would be non-inferior to NLED with respect to change in ocular comfort, from baseline to 30-day follow-up, based on a non-inferiority margin of -20 points on the VAS.

The secondary endpoints were corneal staining (grade 2 or higher, using the FDA scale), change in overall vision quality (using a VAS) from baseline to the day-7 and day-30 visits, SROS (yes / no), and change in overall ocular comfort (using a VAS) at day 7. The secondary hypotheses were that there would be no difference between BTC and NLED groups for corneal staining, vision quality, ocular symptoms, or ocular comfort at day 7 (using a non-inferiority margin of -20 points ocular comfort on the VAS scale).

Additional endpoints were NIBUT, slit lamp findings (FDA scale), end of day ocular comfort, Snellen best corrected distance visual acuity, subjective evaluation of symptoms of dryness, adverse events (AEs), and number of and reasons for discontinuation.

Statistical analysis

Approximately 150 eligible subjects (with a minimum of 60 per arm) were planned to be enrolled with the target of 112 (56 per arm) subjects to complete the study. The sample size was calculated to test for non-inferiority of BTC relative to NLED control with respect to the ocular comfort score using VAS with a minimum power of 85% and a 2-sided type I error of 0.05.

All data summaries and statistical analyses were performed using the SAS software Version 9.4 (SAS Institute, Cary, NC, USA) or higher. Summary tables (descriptive statistics and/or frequency tables) were provided for all baseline variables, efficacy variables, and safety variables as appropriate. Continuous variables were summarized with descriptive statistics (n, mean, SD, median, minimum and maximum). Frequency count and percentage of subjects or eyes within each category were provided for categorical data.

The safety population consisted of any subject who administered a study eye drop. The intent-to-treat (ITT) population consisted of all randomized subjects regardless of treatment or subsequent deviation from protocol. The per-protocol (PP) population consisted of all subjects who completed all visits and did not substantially deviate from the protocol, and constituted the primary analysis population.

The hypothesis testing of non-inferiority for the primary endpoint was based on the least square (LS) mean difference in change from baseline and its corresponding 95% confidence interval (CI) from the final model. The lower bound of the 95% CI was compared with the non-inferiority margin of -20; if the lower bound was greater than -20, the null hypothesis was rejected and the test was considered non-inferior to the control. The primary analysis was conducted on the PP population and the sensitivity analysis conducted on the ITT population.

Hypothesis testing of corneal staining analysis was conducted on the safety population and was based on no difference in the proportion of subjects with corneal staining Grade 2 or higher between the test and control groups. It was conducted based on the estimated odds ratio (OR) and its corresponding 95% CI from the Fisher's Exact test. The null hypothesis was rejected in favor of the alternative if 1 fell within the 95% CI of OR.

Testing of the overall quality of vision analysis was conducted on the PP population. The hypothesis test for the difference between the test and control groups from

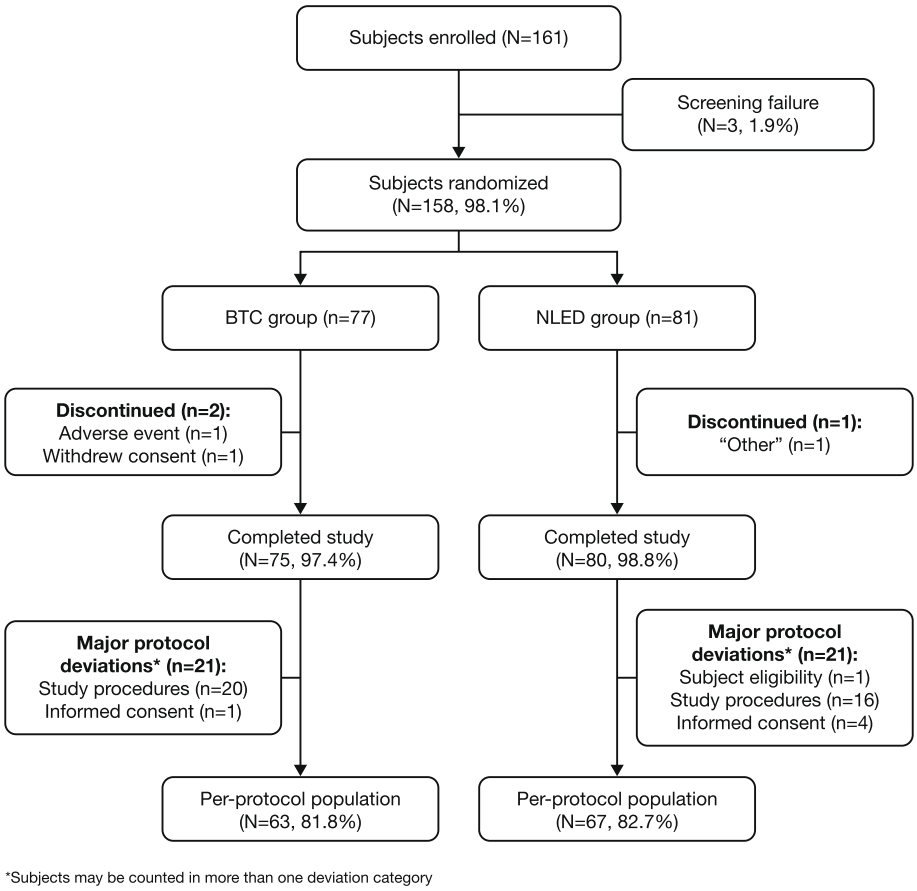

Fig. 1 Subject disposition

baseline at each follow-up was conducted using 95% CI constructed for the LS mean difference (test minus control). No difference between the test and control was established if 0 was contained in the 95% CI.

Hypothesis testing for no difference in presence of ocular symptoms between the test and control groups was conducted on the safety population and based on the estimated OR and its corresponding 95% CI from the final model. The null hypothesis was rejected in favor of the alternative if 1 fell within the 95% CI of OR.

Results

A total of 161 subjects were enrolled, of whom 158 (98.1%) were randomly assigned to one of the two treatment arms (77 BTC; 81 NLED) and had treatment administered (comprising both the safety and ITT populations). The per-protocol populations, of subjects who completed the study without a major protocol violation, comprised 63 and 67 subjects in the BTC and NLED groups, respectively (Fig. 1). Of the 158 subjects who received study treatment, 114 (72%) were female, 133 (83%) were white and the mean age was 48 years (Table 1).

At 30 days, there was a LS mean (95% CI) difference for overall comfort score from baseline of 21.4 (15.1, 27.7) for BTC and 10.0 (3.9, 16.1) for NLED in the PP population; the LS mean difference was 11.3 (2.6, 20.1) (Fig. 2). Therefore, the primary endpoint (noninferiority of test versus control, based on the lower 95% CI being greater than -20) was met. The LS mean (95% CI) differences for the ITT population with and without imputation, respectively, were 7.6 (-0.1, 15.3) and 7.5 (-0.3, 15.2). For the secondary endpoint of overall comfort score from baseline to day 7, the LS mean difference was also statistically significant in the PP population: BTC LS mean (95% CI), 14.3 (8.6, 19.9); NLED, 11.7 (6,2, 17.2); LS means difference, 2.6 (-5.3, 10.4), therefore the lower 95% CI was greater than the prespecified noninferiority level of -20. The LS means difference in the ITT population at day 7 was also statistically significant, at 0.5 (-6.4, 7.4).

Because there was a low rate of corneal staining Grade 2 or higher, subject-level data combining all visits were used for the analysis rather than using eye-level data.

Table 1 Patient demographics

	BTC (*N* = 77)	NLED (*N* = 81)	Total (safety / ITT population) (*N* = 158)	Total (PP population) (*N* = 130)
Age				
Mean (SD)	46.8 (14.51)	48.8 (13.80)	47.8 (14.14)	47.1 (12.24)
Median	48.0	51.0	49.5	49.0
Range	18–68	19–69	18–69	18–69
Sex, n (%)				
Female	58 (75.3)	56 (69.1)	114 (72.2)	92 (70.8)
Male	19 (24.7)	25 (30.9)	44 (27.8)	38 (29.2)
Race, n (%)				
White	63 (81.8)	68 (84.0)	131 (82.9)	105 (80.8)
Black or African American	14 (18.2)	10 (12.3)	24 (15.2)	22 (16.9)
Asian	0 (0.0)	2 (2.5)	2 (1.3)	2 (1.5)
Hawaiian/Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	1 (1.2)	1 (0.6)	1 (0.8)
Ethnicity, n (%)				
Non-Hispanic or Latino	70 (90.9)	76 (93.8)	146 (92.4)	123 (94.6)
Hispanic or Latino	7 (9.1)	5 (6.2)	12 (7.6)	7 (5.4)

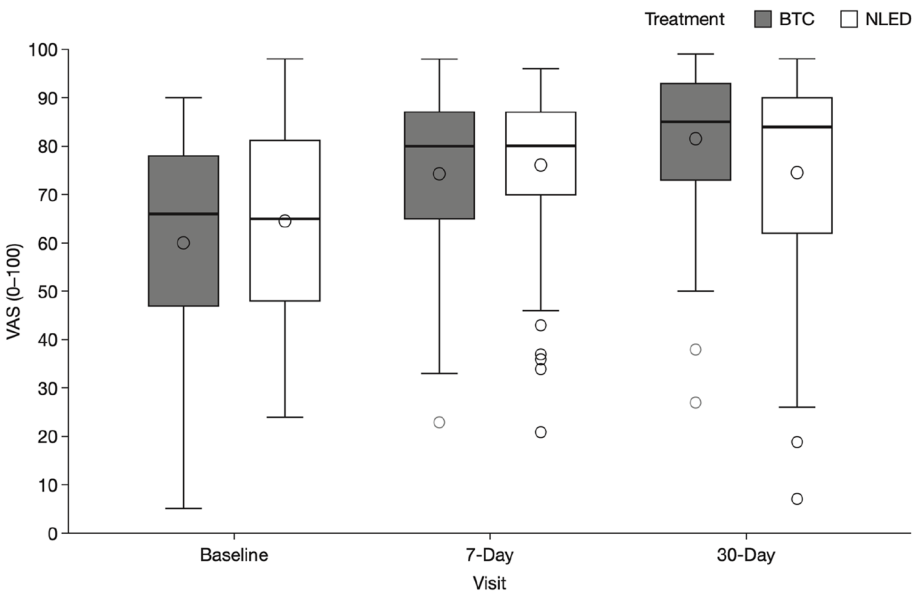

Fig. 2 Boxplot for subjective overall comfort (PP population)

Using these data, the OR (95% CI) for test over control in the safety population was 1.601 (0.178, 19.616), p = 0.6757; therefore, there was no statistically significant difference between the BTC and NLED groups for the secondary outcome of proportion of subjects with at least one corneal staining Grade 2 or higher throughout the study, regardless of the time points.

The change in overall vision quality was statistically significantly greater in the BTC group versus the NLED group at both day 7 [LS mean difference (95% CI) 8.0 (0.7, 15.4)] and day 30 [9.3 (1.7, 17.0)] (Table 2); however, overall vision scores for the BTC and NLED groups at days 7 and 30 were similar (Fig. 3). Data were similar, with statistically significant differences, in the ITT

Table 2 Change in overall vision scores from baseline (LSM, PP population)

Timepoint	Treatment	LS mean(95% CI)	Noninferioity margin	Noninferiority met?	Statistically different?
Day 7	BTC	13.3 (7.9, 18.6)			
	NLED	5.2 (0.1, 10.3)			
	Difference	8.0 (0.7, 15.4)	-20	Yes	Yes
Day 30	BTC	14.2 (8.7, 19.7)			
	NLED	4.9 (-0.4, 10.2)			
	Difference	9.3 (1.7, 17.0)	-20	Yes	Yes

Non-inferiority was concluded if lower 95% CI was greater than -20
No statistical difference between Test and Control was concluded if the 95% CI contained 0

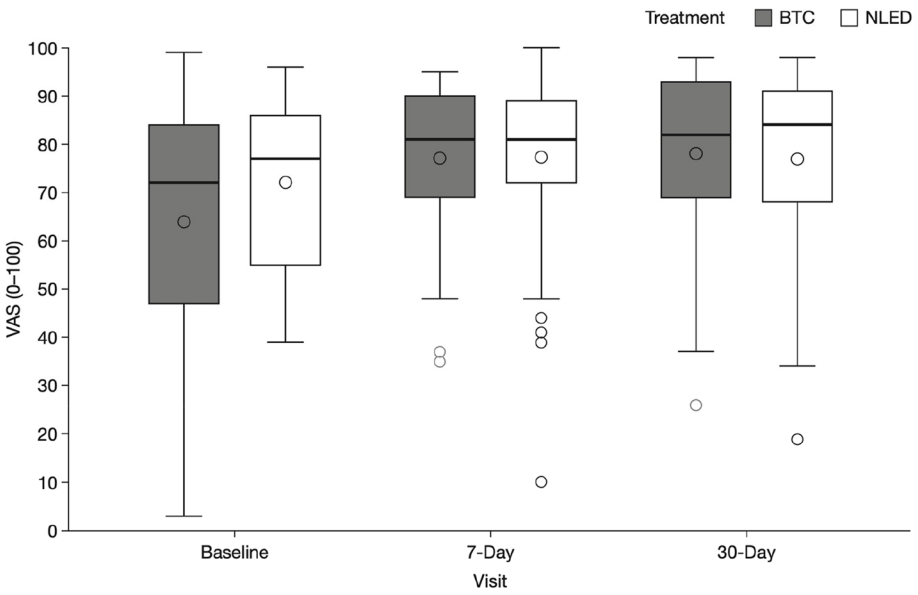

Fig. 3 Boxplot for subjective overall vision (PP population)

population [LS mean difference (95% CI): day 7, 6.7 (0.3, 13.0); day 30, 8.6 (1.9, 15.4)].

There was no significant difference in the proportion of eyes with reported ocular symptoms between the BTC and NLED groups in the safety population. At day 7, the OR (95% CI) was 0.967 (0.528, 1.770) and at day 30 the OR (95% CI) was 1.160 (0.610, 2.203). BTC was noninferior to NLED for change in ocular comfort from baseline to day 7, with an LS mean (95% CI) difference of 2.6 (-5.3, 10.4).

There was one ocular serious AE, of corneal edema due to trauma, during the study. This was not considered by the investigator to be related to the study treatment or procedures. The event was reported as resolved but the participant discontinued from the study. One participant reported mild, non-significant ocular redness in both eyes (two ocular AEs) when using study drops at home and discontinued use. Due to a lack of signs of redness per slit lamp examination during in-office administration and lack of signs during an unscheduled follow-up visit, these AEs were considered by the investigator unlikely to be caused by the study product and not related to the study procedure. The participant discontinued from the study.

There were no Grade 3 or higher corneal edema, corneal neovascularization, corneal staining, conjunctival injection, tarsal abnormalities or any other biomicroscopy findings, and no corneal infiltrates observed at baseline or during the study.

There was one non-ocular serious AE (pancreatitis) and 5 non-ocular AEs (bronchitis, headaches after the use of study drops, torn cartilage in right knee, fractured right foot, and bruised chest from seat belt caused by car accident) reported in this study, of which headaches was considered by the investigator to be possibly related to study product.

The mean (SD) NIBUT between the BTC and NLED groups were comparable in the safety population: 8.8 (± 6.08) and 9.2 (± 6.47), respectively, at baseline; 9.5 (± 7.07) and 9.7 (± 6.24), respectively, at day 7; and 10.1 (± 8.21) and 9.4 (± 5.89), respectively, at day 30.

End-of-day ocular comfort (as measured by a VAS from 0, least comfortable, to 100, most comfortable) increased numerically from baseline to follow-up in both groups in the PP population. Mean (± SD) for the BTC and NLED groups were: 40.4 (± 22.12) and 45.3 (± 20.87) points, respectively, at baseline; 69.1 (± 21.84) and 70.1 (± 20.08) points, respectively, at day 7; and 75.0 (± 20.55) and 69.8 (± 24.53) points, respectively, at day 30 (Fig. 4). Results for the ITT population were similar [baseline mean (SD) for BTC and NLED, respectively: baseline, 43.4 (± 21.34) and 40.8 (± 21.42); day 7, 70.2 (± 19.21) and 68.9 (± 20.90); and day 30, 71.0 (± 23.18) and 74.3 (± 20.67)].

Self-reported severe eye dryness was lower at the end of the study compared with baseline. At baseline, 8 eyes in each group were reported to experience severe eye dryness versus 2 eyes in each group at the 7-and 30-day follow-up.

Visual acuity was similar at baseline and follow-up in both groups, with the majority of eyes demonstrating binocular vision of 20/15 and 20/20 at baseline and at the 7- and 30-day follow-up assessments.

Discussion

Dry eye disease is one of the most common ocular disorders. Ocular discomfort can represent early symptoms of dry eye with the potential to progress to DED and should be seen as a call-to-action to intervene and break the vicious circle of dry eye. There is often a considerable delay from a patient first experiencing discomfort relating to the symptoms of dry eye to seeking medical attention and receiving a formal diagnosis [22], representing a missed opportunity to alleviate the burden and begin effective treatment to reduce the likelihood of progression to and of DED and, ultimately, potential vision loss. Many patients report not seeking any professional medical help with symptoms of dry eye [23], relying on self-medication with over-the-counter treatment options. For all patients with symptoms of dry eye, lipid-based artificial tears provide the opportunity to improve the efficacy of treatment compared with conventional eye drops by addressing both EDE and ADDE components driving individual symptoms. This study demonstrates the noninferiority of BTC, a novel, lipid-based therapy, in comparison with an active comparator control of a commercially available non-lipid artificial tear. BTC was comparable with the control for patient-reported and objective measures of comfort, safety and tolerability, and vision improvements.

BTC successfully demonstrated noninferiority to the NLED control for all parameters assessed and there was a statistically significant difference in the overall vision quality findings, in favour of BTC. Whether this is clinically relevant is unclear. Both the BTC and NLED groups

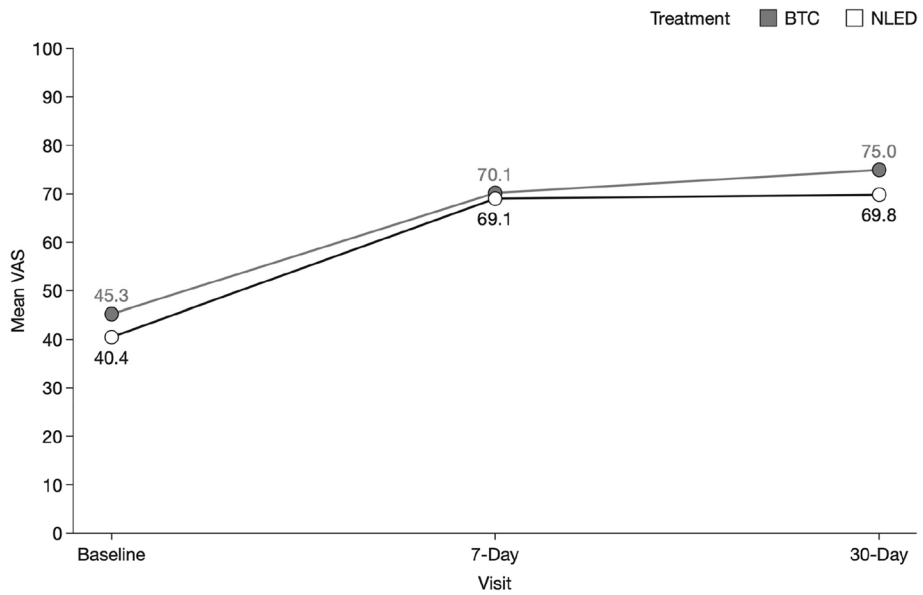

Fig. 4 Descriptive Mean Subjective End of the Day Comfort (PP population)

had numerically similar VAS scores for overall vision at the day 7 and day 30 assessments; therefore, the difference between the groups is likely to be the result of the lower baseline VAS scores in the BTC group (LS mean 64.2) versus the NLED group (LS mean 70.8). For all parameters, the data suggest improvements with treatment during the study period of 30 days. Crucially, overall comfort scores with the lipid eye drops were positive, highlighting the potential benefit for patients for alleviating symptoms of ocular discomfort in diagnosed DED or self-reported dry eye symptoms.

Non-prescription eye drops are cost effective, easily accessible, and have been reported to be the mainstay of daily treatment for nearly three-quarters of patients with DED [24]. Surveys indicate that 19% of patients use topical drops at least 5 times per week [25]. Over-the-counter medications are often the first therapeutic option accessed by those with symptoms of dry eye – before seeking the opinion of a healthcare professional and a confirmed diagnosis of DED – with only ~ 40% of patients seeking professional help for dry eye disease [24, 25]. Although 64% of individuals using non-prescription medications reported satisfaction with their treatment, only 37.3% were satisfied with the symptom relief provided by these treatments [24]; therefore, the availability of a novel effective and comfortable artificial tear provides the opportunity for meaningful symptom relief.

The inclusion of lipids in artificial tear formulations is designed to better mimic crucial lipid components of natural tear [26] with the aim of increasing the break-up time of the tear film [27]. The ingredients of the control and test products in the current study are identical, with the exception of the lipid components of the test formulation. Therefore, it is likely that any differences in the study outcomes are due to the lipid component of the test product. Furthermore, because the control product, Blink® Tears, is a commercially available, over-the-counter treatment for dry eye disease with documented efficacy [28], it is an appropriate control for a study assessing relief in subjects with symptoms of dry eye.

The results reported here may have specific implications for particular dry eye subtypes, such as meibomian gland dysfunction and EDE, which have components of excessive evaporation [29]. In subjects with these underlying pathologies, a lipid component is likely to confer a therapeutic advantage [17, 18]. However, as the two dry-eye subtypes can overlap and progress, such as the development of lacrimal gland failure in patients with EDE-type disease [4], BTC offers the opportunity to act early on a broad range of pathogenic drivers and limit disease progression by breaking the inflammatory vicious circle.

Concerns have been raised about lipid-based therapies with respect to causing blurred vision [11], although many reports relate to the use of ointments [30]. Novel therapeutic options must demonstrate minimal or appropriate and manageable adverse events [31], in addition to the convenience of an artificial tear formulation. The data presented here indicate that the test drops were similar in tolerability to a well-established – non-lipid-containing – active control product, without any reports of blurred vision. The absence of grade 3 or higher adverse events relating to corneal, conjunctival or tarsal symptoms (including corneal staining) indicate a well-tolerated therapeutic option. Crucially, the ocular-related adverse events leading to discontinuation in the study were not considered related to the study product.

The strengths of this study include its double masked and randomized design, as well as the inclusion of an active control group and patient-reported outcomes as a key outcome measure. However, there are some limitations. For example, there was the potential for variation between the test and control groups because ocular symptoms at baseline were self reported and therefore subjective. Because products were not prescribed based on clinical findings, but a combination of objective investigation and subjective reports at baseline, variability of disease severity among patients at study entry cannot be ruled out and participants were not differentiated by disease severity at baseline. Although randomization should minimize this, there remains the potential for inequality among baseline measurements to cause statistical but not clinical differences in results. This may have been observed in this study with the differences overall vision quality at baseline. Furthermore, participants who were not previously using (or inconsistently using) artificial tears might achieve a greater improvement on study; however, a large difference would not be expected. Finally, participants were not stratified by underlying pathophysiology. Participants with lipid deficiency or meibomian gland disorder may be hypothesized to achieve a greater improvement in subjective comfort scores following treatment compared with participants with dry eye caused by other pathologies.

Conclusions

BTC was noninferior to the commercially available non-lipid drops in all parameters measured, with no differences in Grade 2 or greater clinically assessed ocular signs and symptoms despite reported concerns over blurred vision from lipid-containing artificial tears. Therefore, BTC has the potential to provide an effective alternative therapy for individuals with dry eye who would benefit from a lipid-based artificial tear.

Abbreviations

ADDE	Aqueous-deficient dry eye
AE	Adverse event
BTC	Investigational lipid-containing artificial tear
CI	Confidence interval
DED	Dry eye disease
EDE	Evaporative dry eye
FDA	Food and Drug Administration
GCP	Good clinical practice
LS	Least squares
IRB	Institutional review board
ITT	Intent to treat
OR	Odds ratio
PP	Per protocol
PRO	Patient-reported outcome
NIBUT	Non-invasive tear break up time
NLED	Non-lipid-containing eye drop
SAE	Serious adverse event
SROS	Subject-reported ocular symptoms
VAS	Visual analog scale

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Authors' contributions
NRJ contributed to the design of the study. NRJ, KB and RR analyzed and interpreted the data. All authors were involved in reviewing and editing this manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from Robert Ryan (Robert.Ryan@bausch.com) on reasonable request.

Declarations

Ethics approval and consent to participate
This study was performed in accordance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice (GCP). The study was approved by Sterling IRB (Atlanta, GA, USA). Participants must have read, understood and signed the informed consent statement.

Consent for publication
No individual patient data included: not applicable.

Competing interests
Krista Barbour and Robert Ryan are employees of Bausch + Lomb, Inc. Nabin R Joshi is an employee of Johnson & Johnson, Inc. The remaining authors declare that they have no competing interests.

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