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ARTICLE

Effectiveness and safety of a thermomechanical action device vs thermal pulsation device in the treatment of meibomian gland dysfunction

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Purpose: To evaluate the safety and effectiveness of thermomechanical action (Tixel C) compared with thermal pulsation (LipiFlow) in meibomian gland dysfunction (MGD).

Setting: Private clinics and University clinic.

Design: Prospective, randomized (1:1), evaluator-masked, multicenter study.

Methods: Participants with Ocular Surface Disease Index (OSDI) between 23 and 79, fluorescein tear break-up time (TBUT) <10 seconds, and meibomian gland score (MGS) ≤12 in each eye received bilateral thermomechanical action (TMA) or thermal pulsation (TP). The treatment consisted of 3 sessions, 2 weeks apart, for TMA and 1 session for TP. TBUT, OSDI, MGS, and corneal and conjunctival staining (CCS) were assessed at baseline and at weeks 4 and 12 after last treatment session. The primary effectiveness endpoint was change in TBUT at week 4.

Results: Among the 106 treated participants (N = 53 per group), TBUT improved significantly ($P < .001$) by 3.0 ± 3.2 and 3.1 ± 4.3 seconds after TMA and 2.7 ± 2.7 and 3.3 ± 3.6 seconds after TP, at week 4 and week 12, respectively. The change in TBUT for TMA was noninferior to TP (linear mixed-effects model, $P < .001$). OSDI, MGS, and CCS significantly improved from baseline ($P < .001$), with no significant between-group differences ($P > .05$). OSDI improved by 26.4 ± 21.1 and 28.6 ± 22.4 after TMA and 18.8 ± 21.0 and 21.9 ± 18.5 after TP, at week 4 and week 12, respectively. No device-related adverse event occurred in either group.

Conclusions: TMA safely and effectively improved clinical signs and symptoms of evaporative dry eye disease associated with MGD over a 12-week period, comparable with TP.

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The meibomian glands in the eyelid tarsal plate secrete meibum which contributes to the superficial lipid layer of the tear film. Meibomian gland dysfunction (MGD) can lead to increased tear evaporation, tear film instability, eye irritation, inflammation, and ocular surface diseases.[1] The reported prevalence of MGD based on clinical signs ranges from 38% to 68% over the age of 40 years.[2]

The mainstay of MGD treatment is lid hygiene, eyelid warming, and meibum expression to liquefy the meibum and facilitate its outflow, improving lipid profile and allowing a more uniform tear dispersion.[3–5] Other treatments depending on indications can include artificial tears and medical management such as systemic doxycycline.[3,4]

Adherence is a restrictive factor in the first-line therapy of in-home warm compress, with only 55% of the participants reporting compliance based on a survey.[6] In-office devices, including those that apply localized heat and pressure, have been used to provide effective treatment.[7–10] Recently, a thermomechanical action (TMA) device (Tixel C, Novoxel) to treat skin indications such as periorbital wrinkles, ageing skin, actinic keratosis, acne vulgaris, rosacea, and hypertrophic scars showed encouraging results for effectiveness and safety in symptomatic dry eye disease

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(DED).[11–17] The pilot studies were prompted by observation of improved DED symptoms in older patients after fractional skin treatment with Tixel for periorbital wrinkles.[18,19]

The objective of this study was to characterize the safety and effectiveness of Tixel in the treatment of adults with MGD in comparison with a commercially available thermal pulsation device (LipiFlow Thermal Pulsation System, Johnson & Johnson Vision), in a randomized controlled trial.[7,8] The study objective included assessment of key clinical signs and symptoms, namely, tear break-up time (TBUT), Ocular Surface Disease Index (OSDI), meibomian gland score (MGS), and rate of adverse events (AEs).

METHODS

Study Design

This randomized, assessor-masked, controlled trial was conducted at 5 U.S. centers between September 2022 and June 2023. This 12-week study was prospectively registered at ClinicalTrials.gov (NCT05162261).

Randomization After confirming that the participant met all selection criteria, eligible participants were randomized to either the Tixel or LipiFlow group in a 1:1 ratio (Supplemental Figure 1, available at http://links.lww.com/JRS/B269). After randomization, the participant either underwent the Tixel or LipiFlow procedure immediately or were scheduled to have the procedure within 5 days of the baseline visit and 7 days of the screening visit. The day the study procedure was first performed was considered day 0.

Masking Study endpoint evaluations for effectiveness at baseline and at follow-up visits of week 4 and week 12 were performed by a masked assessor who was not aware of the treatment arm to which the participant was randomized. The masked assessors were optometrists (ODs) or ophthalmologists (MDs).

Key Outcome Measures

The primary effectiveness endpoint was the change in TBUT from baseline at the 4-week follow-up visit. The secondary effectiveness endpoints were the change from baseline in OSDI at week 4 and week 12, change from baseline in MGS at week 4 and week 12, and change from baseline in TBUT at week 12. The primary safety endpoint was the incidence of ocular AEs. Secondary safety endpoints included evaluation of pain and discomfort, ocular surface staining, intraocular pressure (IOP), and corrected distance visual acuity (CDVA) at distance.

Ethics

This study adhered to the tenets of the Declaration of Helsinki and was approved by Advarra, a central Institutional Review Board. Informed consent was obtained from all participants, and HIPAA regulations were followed.

Participants

Participants were 22 years or older with dry eye symptoms for the previous 3 or more months, reported use of lubricants for the previous 1 or more months, and had an OSDI score between 23 and 79. The key clinical criteria were TBUT <10 seconds in both eyes, MGS ≤12 in each eye, and at least 15 glands in each lower eyelid that were expressible during slitlamp examination. Key exclusion criteria included the use of dry eye treatments (other than lubricants) and contact lens wear within a prespecified period before the study. In addition, eligibility required no history of major dermatologic, systemic or ocular conditions, no tattoos, permanent make-up, or irritated skin in the treatment area.

Procedures: Intervention/Treatment

The Tixel device used in the study consisted of a small tip with an array of 24 (6 × 4) pyramids, spaced evenly within a 0.30 cm^2 area. The pyramids were 1.25 mm tall with a blunt apex of approximately 0.01 mm^2 (Figure 1). The parameters used in this study for a single pulse had a duration of 6 milliseconds and tip protrusion distance of 400 μm.

The Tixel procedure involved 3 bilateral sessions at 2-week intervals. After both lids were cleaned and anesthetized, the clinician delivered a row of 5 pulses near each lid margin in the nasal, medial, and temporal regions. A second row of 5 pulses was delivered to each eyelid, adjacent to the first row and distal from the lid margin for a total of 20 pulses applied to both the upper and lower eyelids (Figure 2). This was repeated for the contralateral eyelids. The first treatment session was day 0.

Participants randomized to the LipiFlow arm underwent 1 treatment session in both eyes per the manufacturer's instructions for use.[7]

Assessments

TBUT assessment using fluorescein was performed as previously described.[20] Three consecutive measurements were recorded and averaged.

MGS assessment using the Meibomian Gland Evaluator (Johnson & Johnson Vision) was performed on the lower eyelids to evaluate the quality of meibomian gland secretions.[21] Each gland was graded on a scale of 0 to 3 (0 = nothing, 1 = toothpaste, 2 = cloudy, and 3 = clear).[7] Total possible MGS score could range from 0 to 45.

The OSDI is a validated 12-item questionnaire that was used to grade the participant's dry eye symptoms on a scale of 0 to 100.[22] Severity was categorized as normal (0 to 12), mild (13 to 22), moderate (23 to 32), or severe (33 or higher). Participants were instructed to record their daily use of lubricants or artificial tears for symptomatic relief.

Corneal and conjunctival staining scores were graded using National Eye Institute scale.[23] Corneal staining with fluorescein was graded in 5 corneal regions on a scale of 0 to 3. Conjunctival staining using lissamine green strips was graded in 6 regions on a scale of 0 to 3.

Pain and discomfort level immediately after the procedure were assessed using a visual analog scale, ranging from 0 (no pain/discomfort) to 10 (maximal pain/discomfort), and measured (in centimeters) between the left end of the scale and the participant's response. Slitlamp examination of the anterior segment included eyelid margin assessment for entropion/ectropion, floppy eyelids, loss of lash integrity, and a number of lid margin abnormalities (irregular lid margin, vascular engorgement, plugged gland

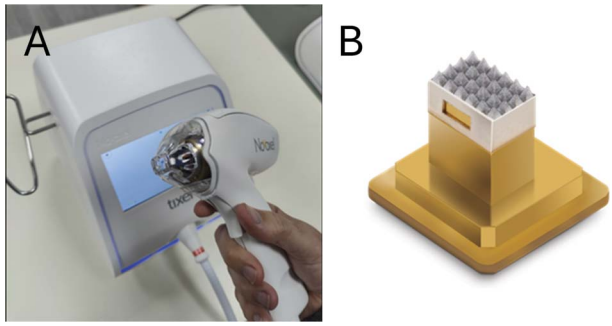

Figure 1. The Tixel system used for treatment in the periorbital area is comprised of a console, connected through a cord to a small handpiece (panel *A*). The small handpiece has a small tip, which consists of an array of 24 (6 × 4) evenly spaced square-based pyramids, that are 1.25 mm in height with a blunt apex of approximately 0.01 mm^2 (panel *B*).

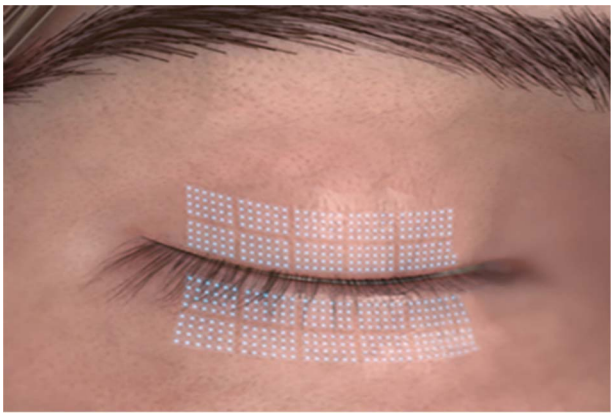

Figure 2. Tixel pulse pattern for evaporative DED treatment. Ten pulses were delivered to each eyelid in 2 rows. DED = dry eye disease

orifices, and anterior/posterior displacement of mucocutaneous junction) scored from 0 to 4.

Statistical Analysis

The per protocol population who underwent the assigned study treatment and had data at week 4 with no major protocol deviations was used for effectiveness analyses. The primary analysis was repeated with the intent-to-treat (ITT) population that included all randomized participants, as a sensitivity analysis. All treated participants comprised the safety population.

For outcomes measured in each eye (ie, TBUT, MGS, staining, and IOP measures), the difference between groups in changes from baseline was analyzed using the linear mixed-effects model, with a random effect for participants and fixed effect for treatment and baseline score as covariates. The random effect adjusts the within-participant correlation between eyes. The two-sample *t* test was used for between-group differences by participant. A paired *t* test was used for within-group differences.

The primary hypothesis was noninferiority of change in TBUT from baseline to week 4 in the Tixel group compared with the LipiFlow group. For a noninferiority margin of 2.5 seconds and an expected standard deviation of 4.5 seconds, a sample size of 44 per group yielded 80% power with a 1-sided 0.05 significance level.[9] The target sample size was 55 participants per group, accounting for a 20% drop-out rate. The justification of noninferiority margin was based on the difference between dry and normal tear stability of 5 seconds, with a moderate change of 50% as clinically relevant, similar to studies of iLUX and TearCare.[9,10] Data were analyzed using SAS v. 9.4 (SAS Institute, Inc.).

RESULTS

A total of 109 participants were randomized (54 Tixel, 55 LipiFlow) of which 106 participants, ranging from 29 to 88 years of age, received either of the study treatments. The mean age was 62.3 ± 12 years in the Tixel group and 61.6 ± 13 years in the LipiFlow group. Participant demographics and baseline characteristics are presented by the treatment group in Table 1. There were no significant differences between groups (all $P > .05$).

Nine ITT participants were excluded from the effectiveness analysis per protocol population (6 in Tixel and 3 in LipiFlow). Details are provided in Supplemental Tables 1–3 (available at http://links.lww.com/JRS/B268).

Effectiveness

For the effectiveness outcomes, Table 2 presents the mean and range of observed scores at baseline, week 4 and week 12, along with mean change from baseline and 95% CI of the change.

TBUT The within-group observed changes from baseline to week 4 and week 12 were significant for Tixel and LipiFlow groups (Table 2). The difference in least-squares mean change in TBUT from baseline to week 4 between LipiFlow and Tixel was −0.17 second (standard error [SE], 0.55) with the upper bound of 1-sided 95% CI of 0.73 within the noninferiority margin ($P < .001$); therefore, Tixel was determined to be noninferior to LipiFlow, meeting the success criterion for primary effectiveness in the study (Figure 3). Sensitivity analysis in the ITT population confirmed these results, with an estimated mean difference of −0.12 second (SE, 0.53; 95% CI, −1.31 to 1.06), $P < .001$.

In addition, the study also met the noninferiority criterion at week 12. The difference in least-squares mean change in TBUT from baseline to week 12 between LipiFlow and Tixel was 0.39 second (SE, 0.79) with the upper bound of 1-sided 95% CI of 1.70 within the 2.5 seconds noninferiority margin ($P = .004$) (Figure 3, A).

OSDI OSDI significantly improved from baseline to week 4 and week 12 follow-up in the Tixel and LipiFlow groups (Table 2). Figure 3, B shows the OSDI scores for each group, although they were not statistically different (2-sample *t* test; $P = .079$ at week 4, $P = .074$ at week 12). The mean change in each treatment group, stratified by OSDI grading of severity at baseline, is presented in Table 3.

MGS There were statistically significant increases in MGS from baseline to week 4 and week 12 in the Tixel and LipiFlow groups, with no significant between-group differences; least-squares mean difference was −1.48 (SE, 1.80; 95% CI, −5.06 to 2.10) at week 4 ($P = .414$) and −0.66 (SE, 2.34; 95% CI, −5.31 to 3.99) at week 12 ($P = .779$) (Table 2, Figure 3, C).

Use of Lubricating Drops

The use of lubricating drops per day preprocedure was 2.3 ± 1.5 drops in the Tixel group (range, 1 to 8) and 2.9 ± 1.7 drops (range, 0.5 to 8) in the LipiFlow group. Participants had a mean decrease in usage by −1.3 ± 1.9 and −0.8 ± 1.2 drops at week 4 and by −1.1 ± 1.6 and −1.0 ± 1.7 drops at week 12 in the Tixel and LipiFlow groups, respectively. These data demonstrate that the effectiveness outcomes were not confounded by an increase in drop use from baseline in either group.

Safety

Adverse Events No device-related or procedure-related AEs occurred in either group. The percentage of ocular AEs was similar between the groups; 4 ocular AEs in 3 of 53 participants (5.7%) in the Tixel group and 3 ocular AEs in 2 of 53 participants (3.8%) in the LipiFlow group. The 4 ocular AEs in the Tixel group were viral conjunctivitis (10 days after first session), corneal abrasion (46 days after last session), and retinal detachment and retinal tear (27 days after last session). The AEs of retinal detachment and retinal tear occurred in the left and right eyes, respectively, of a participant and were reported as serious adverse events (SAEs), although not attributed to the Tixel procedure

Table 1. Participant demographics and baseline characteristics

Characteristic	Tixel (N = 53 participants, 106 eyes)		LipiFlow (N = 53 participants, 106 eyes)		*P* value[b]
	[a]Mean ± SD n (%)	Range	[a]Mean ± SD n (%)	Range	
Age (y)	62.3 ± 12.0	29, 81	61.6 ± 13.0	31, 88	0.76
Female sex	37 (68.5)		35 (63.6)		0.54
Ethnicity					1.00
Hispanic or Latino	5 (9.3)		5 (9.1)		
Not Hispanic or Latino	49 (90.7)		50 (90.9)		
Race					0.56
White	50 (92.6)		51 (92.7)		
Asian	1 (1.9)		3 (5.5)		
Black or African American	1 (1.9)		1 (1.8)		
Native Hawaiian or other Pacific Islander	1 (1.9)		0 (0.0)		
Other	1 (1.9)		0 (0.0)		
Fitzpatrick skin type					0.85
Type I	1 (1.9)		1 (1.8)		
Type II	18 (33.3)		17 (30.9)		
Type III	15 (27.8)		21 (38.2)		
Type IV	16 (29.6)		13 (23.6)		
Type V	3 (5.6)		2 (3.6)		
Type VI	1 (1.9)		1 (1.8)		
OSDI	49.8 ± 17.7	25.0, 77.3	49.6 ± 15.4	25.0, 77.5	0.94
TBUT (s)[c]	4.3 ± 1.4	1.5, 7.6	4.6 ± 1.8	0.9, 9.7	0.15
MGS[c]	7.2 ± 2.4	0.0, 12.0	7.4 ± 2.5	0.0, 12.0	0.47
Corneal staining[c]	3.1 ± 2.4	0.0, 14.0	2.9 ± 2.2	0.0, 10.0	0.56
Conjunctival staining[c]	2.4 ± 2.8	0.0, 12.0	2.4 ± 2.5	0.0, 12.0	0.92

MGS = meibomian gland score; OSDI = Ocular Surface Disease Index; TBUT = tear break-up time
[a]Data presented as mean ± SD or number of participants (% participants), as applicable
[b]Significance by the chi-square test, except for age by the *t* test
[c]Data presented for 106 eyes of 53 participants in each group

because of preexisting risk factors including peripheral retinal pathology. The viral conjunctivitis was deemed unrelated because of the timing of presentation 10 days postprocedure and the corneal abrasion was deemed unrelated because it occurred because of a tree branch injury. The ocular AEs in the LipiFlow group were allergic conjunctivitis in both eyes of a participant (days 34 and 57) and one occurrence of conjunctival cyst (day 9). All ocular AEs were resolved by treatment with medication except ocular SAEs which were resolved by surgical and laser treatment.

The nonocular SAEs in the Tixel group included sepsis in a participant that resolved in 10 days and spondylodiscitis in a participant that resolved in 3 months. The nonocular SAE in the LipiFlow group presented as facial melanoma in situ in a participant with a family history of malignant melanoma and resolved in 2 months.

Pain/Discomfort Both Tixel and LipiFlow participants experienced mild discomfort and pain during the procedure, as indicated by mean scores on the visual analog scale between 0 (indicating no discomfort/pain) and 10 (indicating worst possible discomfort/pain) (Supplemental Table 4, available at http://links.lww.com/JRS/B268). Mean scores for discomfort and pain were numerically greater in the Tixel group than LipiFlow (Supplemental Table 4, available at http://links.lww.com/JRS/B268). The mean discomfort score was 2.8 ± 1.9 and 2.6 ± 1.8 in the right and left eyes, respectively, for Tixel; 1.5 ± 1.6 and 1.7 ± 2.1 in the right and left eyes, respectively, for LipiFlow. The mean pain score was 2.5 ± 1.9 in right and left eyes for Tixel; 0.8 ± 1.2 and 0.9 ± 1.5 in the right and left eyes, respectively, for LipiFlow.

Corneal and Conjunctival Staining There was significant improvement from baseline in corneal staining in Tixel and LipiFlow groups with no significant between-group differences ($P > .05$) at week 4 and week 12 (Table 2, Figure 3, D). The mean change from baseline in corneal staining was −1.9 ± 2.3 and −1.7 ± 2.3 with Tixel and −1.4 ± 2.2 and −1.6 ± 2.1 with LipiFlow at weeks 4 and 12, respectively. Similar results were observed for conjunctival staining. The mean change from baseline in conjunctival staining was −0.9 ± 2.3 and −1.3 ± 2.7 with Tixel and −1.2 ± 2.7 and −1.2 ± 3.0 with LipiFlow at weeks 4 and 12, respectively.

CDVA CDVA was stable in both groups. CDVA was 20/40 or better in 106 eyes (100%), 96 eyes (100%), and 90 eyes (100%) in the Tixel group, and in 105 eyes (99%), 103 eyes (99%), and 105 eyes (99%) in the LipiFlow group at baseline, week 4 and week 12, respectively.

IOP There was no significant change from baseline IOP at week 4 and week 12 in the Tixel group and in the LipiFlow group (all $P > .05$; paired *t* test).

Table 2. Observed data of TBUT, OSDI, MGS, and staining at BL, week 4, and week 12

Assessment[a]	Visit	Group	N	Scores at visit		Change from BL[b]	
				Mean ± SD	Range	Mean ± SD	95% CI
			Eyes				
TBUT	BL	Tixel	n = 96	4.3 ± 1.5	1.5, 7.6		
		LipiFlow	n = 104	4.6 ± 1.8	0.9, 9.7		
	Week 4	Tixel	n = 96	7.3 ± 3.2	2.4, 20.3	3.0 ± 3.2*	2.4, 3.7
		LipiFlow	n = 104	7.3 ± 3.0	1.6, 18.2	2.7 ± 2.7*	2.2, 3.2
	Week 12	Tixel	n = 90	7.5 ± 4.3	1.2, 25.0	3.1 ± 4.3*	2.2, 4.0
		LipiFlow	n = 104	8.0 ± 3.9	2.2, 20.5	3.3 ± 3.6*	2.6, 4.1
			Participants				
OSDI	BL	Tixel	n = 48	50.2 ± 18.3	25.0, 77.3		
		LipiFlow	n = 52	49.4 ± 15.5	25.0, 77.5		
	Week 4	Tixel	n = 48	23.9 ± 17.5	0.0, 64.6	−26.4 ± 21.1*	−32.5, −20.2
		LipiFlow	n = 52	30.6 ± 20.5	0.0, 87.5	−18.8 ± 21.0*	−24.6, −12.9
	Week 12	Tixel	n = 45	20.6 ± 18.8	0.0, 75.0	−28.6 ± 22.4*	−35.3, −21.9
		LipiFlow	n = 52	27.5 ± 18.6	0.0, 75.0	−21.9 ± 18.5*	−27.1, −16.7
			Eyes				
MGS	BL	Tixel	n = 96	7.2 ± 2.5	0, 12		
		LipiFlow	n = 104	7.4 ± 2.6	0, 12		
	Week 4	Tixel	n = 96	16.2 ± 9.8	1, 44	9.0 ± 10.4*	6.9, 11.1
		LipiFlow	n = 104	14.7 ± 8.7	0, 41	7.3 ± 8.8*	5.6, 9.0
	Week 12	Tixel	n = 90	18.5 ± 11.1	3, 42	11.3 ± 11.4*	8.9, 13.7
		LipiFlow	n = 104	17.9 ± 12.1	0, 44	10.5 ± 12.2*	8.1, 12.9
			Eyes				
Corneal staining	Week 4	Tixel	n = 96	1.2 ± 1.9	0, 15	−1.9 ± 2.3*	−2.4, −1.5
		LipiFlow	n = 104	1.5 ± 1.6	0, 7	−1.4 ± 2.2*	−1.9, −1.0
	Week 12	Tixel	n = 90	1.3 ± 2.2	0, 11	−1.7 ± 2.3*	−2.2, −1.2
		LipiFlow	n = 106	1.3 ± 1.8	0, 9	−1.6 ± 2.1*	−2.0, −1.1
			Eyes				
Conjunctival staining	Week 4	Tixel	n = 96	1.5 ± 2.2	1, 12	−0.9 ± 2.3*	−1.4, −0.4
		LipiFlow	n = 104	1.2 ± 1.8	0, 9	−1.2 ± 2.7*	−1.8, −0.7
	Week 12	Tixel	n = 90	1.2 ± 1.9	0, 9	−1.3 ± 2.7*	−1.9, −0.8
		LipiFlow	n = 106	1.2 ± 2.2	0, 12	−1.2 ± 3.0*	−1.8, −0.7

BL = baseline; MGS = meibomian gland score; OSDI = Ocular Surface Disease Index; SD = standard deviation; TBUT = tear break-up time
*Statistically significant
[a]Data based on per protocol population for TBUT, OSDI, and MGS, and safety set for staining scores
[b]Change from baseline calculated as week 4 − baseline and week 12 − baseline

Slitlamp Examination (Lid Margin) No remarkable changes were noted from baseline in lid margin abnormality score or eyelid margin assessment.

DISCUSSION

In this randomized controlled study of Tixel device compared with LipiFlow (control) device in the treatment of MGD, both treatments provided significant improvements from baseline in clinical signs of TBUT and MGS as well as symptom scores of OSDI at 4 weeks, which were sustained at 12 weeks. The results support the hypothesis of noninferiority of change in TBUT from baseline of the Tixel group to that of the LipiFlow group at week 4 and week 12. The least-squares mean change in TBUT at week 4 was 3.0 seconds in the Tixel group and 2.8 seconds in the LipiFlow group; the difference between LipiFlow and Tixel was −0.17 seconds (SE, 0.55) with the upper bound of 1-sided 95% CI of 0.73 within the noninferiority margin. There were no significant between-group differences in MGS over the 12-week period, with improvement in mean MGS showing an 11-point change in both treatment groups. The observed values of OSDI score were improved more in the Tixel group (29 ± 22) than in the LipiFlow group (22 ± 19), $P = .07$. The safety profile of the Tixel device was comparable with that of LipiFlow. Corneal and conjunctival staining improved with no significant between-group differences.

The design of this study is similar to those used by other studies evaluating commercially available devices, such as iLUX MGD Treatment System (Alcon Laboratories, Inc.) and TearCare (Sight Sciences), in the use of LipiFlow as a comparator, in the choice of key effectiveness and safety assessments (TBUT, MGS, OSDI, staining, and recording AEs), and timepoint of primary endpoint evaluation at 4 weeks.[9,10] A key difference in this study was a longer study duration with follow-up out to 12 weeks to assess the longevity of the treatment effect.

In 2 initial single-arm open-label studies using Tixel in patients with DED, significant improvement in TBUT and symptomatic improvement by OSDI were noted, which prompted further investigation in this randomized controlled pivotal trial.[18,19] Results of this controlled study are consistent with the promising clinical results in the 2 earlier

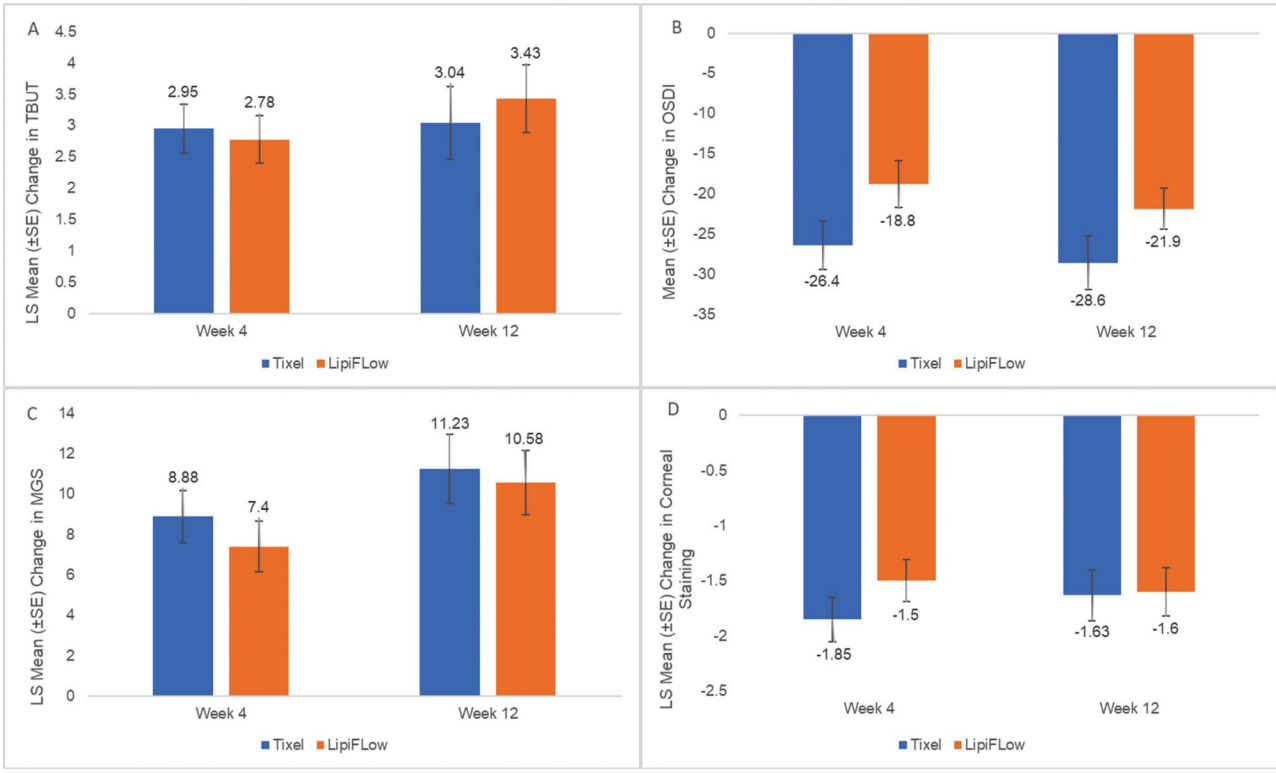

Figure 3. Change from baseline at week 4 and week 12 in (*A*) LSmean TBUT, (*B*) mean OSDI, (*C*) LSmean MGS, and (*D*) LSmean corneal staining. LS means changes from baseline are presented by the treatment arm in TBUT, MGS, and corneal staining at week 4 and week 12. These were estimated from a linear mixed-effects model, with a random effect for participants, fixed effect for treatment and baseline score as covariate. Observed means and SE are presented by the treatment arm for change from baseline in OSDI. LS = least-squares; MGS = meibomian gland score; OSDI = Ocular Surface Disease Index; SE = standard error; TBUT = tear break-up time

reports. In 1 pilot study, fluorescein-TBUT improved from 2.7 ± 0.8 seconds at baseline to 6.5 ± 2.2 at 4 weeks.[18] Similarly, fluorescein-TBUT in this study improved from 4.3 ± 1.5 seconds at baseline to 7.3 ± 3.2 at 4 weeks. The difference in baseline measures may reflect a cohort with more severe disease in the earlier Tixel study, where the TBUT inclusion criterion was less than 5 seconds, compared with less than 10 seconds required in this study.[18] In another pilot study report, OSDI improved by 18 ± 7 and 33 ± 9, for participants with moderate and severe symptoms at baseline, respectively, at 18-week posttreatment, consistent with an improvement of 16 ± 10 and 35 ± 24 for moderate and severe symptoms at baseline, respectively, after 12 weeks in this study.[19]

OSDI is known to correlate with the use of artificial tear lubricants.[22] In this study, the OSDI showed improvement in both groups from baseline, as artificial tear usage decreased by approximately 1 drop in each eye from baseline, consistent with previously reported results.[18] This result indicated that the observed improvement in TBUT, MGS, and ocular symptoms was not confounded by permitting use of lubricants during the study.

No device-related AEs occurred during treatment. During the follow-up period, 2 retinal SAEs were reported for a participant in the Tixel group, with a history of peripheral retinal pathology. AEs were resolved by surgical and/or laser intervention and were determined to be unrelated to the study treatment by the investigator. The incidence of other ocular AEs was similar in both groups; these were resolved by medication and deemed unrelated to the study treatment.

Table 3. Mean change in OSDI from baseline by OSDI severity grading at baseline

Treatment group	OSDI severity[a]	n	Baseline OSDI	Change from baseline – week 4		Change from baseline – week 12	
			Mean ± SD	n	Mean ± SD	n	Mean ± SD
Tixel	Moderate	15	27.8 ± 2.5	15	−11.0 ± 14.9	15	−15.8 ± 10.0
	Severe	33	60.4 ± 12.2	33	−33.4 ± 19.9	30	−35.0 ± 24.1
LipiFlow	Moderate	8	28.8 ± 1.9	8	−14.0 ± 12.4	8	−20.9 ± 4.9
	Severe	44	53.1 ± 13.8	44	−19.6 ± 22.2	44	−22.1 ± 20.1

OSDI = Ocular Surface Disease Index
[a]Severity grading based on a baseline OSDI score of 23 to 32 for moderate and 33 to 100 for severe disease

In-office procedures are commonly used in clinical practice to offer patients the option to treat MGD with devices which promote efficient heat transfer to the eyelid area, may be more effective than daily treatment with warm compresses, and may address patient compliance issues with warm compress use.[24] Differences exist in the use of available treatments, including whether 1 or both eyelids are treated concurrently, total duration of treatment procedure, use of an in-eye applicator, or other eyelid device to aid the procedure. The Tixel device offers another tool in the armamentarium of eyecare practitioners for MGD treatment. The phased treatment was administered to both upper and lower eyelids, with a brief pulse duration of 6 milliseconds for rapid heat transfer. The device does not require contact with the ocular surface and is not limited by the size of palpebral fornices. The procedure takes 2 minutes, does not require gel, and does not use radiation. The Tixel i device has been 510(k)-cleared by the FDA for the treatment of evaporative dry eye due to MGD. This is similar to the study device Tixel C, with the only major difference being fixed parameters of 6 milliseconds pulse and 400 μm protrusion.

Assessment of the treatment effect over a longer duration is warranted in future randomized controlled trials. Further studies with Tixel in combination with meibomian gland expression or compared with other devices could additionally evaluate its impact on daily activities and treatment satisfaction.

In conclusion, the Tixel device, a TMA system intended for the application of localized heat and pressure therapy in adult patients with evaporative DED due to MGD was found to be noninferior to LipiFlow in the improvement of TBUT over a 12-week trial period. The device safely and effectively improves clinical signs of TBUT, quality of MG secretions (MGS), and ocular symptoms and provides a viable alternative to the currently available treatments for this population.

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WHAT WAS KNOWN

- The mainstay of treatment in meibomian gland dysfunction (MGD) is warm compress to facilitate liquefaction of meibum.
- Compliance is a restrictive factor in the first-line therapy of in-home warm compress.
- In-office devices that apply localized heat and pressure have been used in an effort to provide effective and efficient management of dry eye disease in MGD.

WHAT THIS PAPER ADDS

- Thermomechanical treatment using a new device is evaluated for the treatment of MGD in an assessor-masked randomized controlled trial.
- The device safely and effectively improves ocular surface signs and symptoms, comparable with the currently marketed eyelid thermal pulsation device.
- The treatment is applied to both eyelids, without contact to the ocular surface and without using radiation or gel, in about 2 minutes per session.

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