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An App Supporting Psoriasis Patients Improves Adherence to Topical Treatment: A randomised controlled trial

Running head testing an adherence-improving app for psoriasis patients

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LEO Pharma provided the medication (calciptoriol/betamethasone dipropionate (Cal/BD) cutaneous foam), app, and electronic monitor used in the trial.

Conflicts of interests:

Part of M.T.S.' salary during the trial was paid by funding from Leo Pharma. A.P. has received funding from LEO Pharma. B.A. is an employee at LEO Pharma, which has the copyright for the calcipotriol/betamethasone dipropionate foam used as the study medication and is the owner of the electronic monitor and app used in this trial. S.R.F. is a speaker for Janssen and Taro; a consultant and speaker for Galderma, Stiefel/GlaxoSmithKline, Abbott Labs, Leo Pharma Inc.; has received

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Statements

What's already known about this topic?

- Psoriasis affects 2-4% of the Western adult population, has detrimental socio-economic effects and negatively affects quality of life.
- Topical corticosteroid/calcipotriol combinations are recommended first-line treatments for mild-to-moderate psoriasis, but poor adherence to topical treatments result in low efficacy.
- Several smartphone applications (apps) are available to psoriasis patients, but the adherence-improving potential of this technology has not been evaluated in a randomized controlled setting.

What does this study add?

- This randomized controlled trial investigates the effects of a supporting app on adherence to a once-daily topical calciptoriol/betamethasone dipropionate cutaneous foam preparation over a 28-day period.
- The app provided daily reminders and informed patients whether they had applied their treatment. Information on adherence was obtained with a chip attached to the dispenser that synchronized to the app.
- The app significantly improved adherence rates and reduced psoriasis severity in the short-term.

Summary

Background Adherence to topical psoriasis treatments is low which leads to unsatisfactory treatment results. Smartphone applications (apps) for patient support exist, but their potential to improve adherence has not been systematically evaluated.

Objective To evaluate whether a study-specific app improves adherence and reduces psoriasis symptoms compared to standard treatment.

Methods We conducted a randomized controlled trial. Patients received once-daily medication (calcipotriol/betamethasone dipropionate (Cal/BD) cutaneous foam) and were randomized to no app (n = 66) or app intervention (n=68) groups. 122 patients (91%) completed the 22-week follow-

up. Primary outcome: Adherence was defined as medication applied ≥ 80% of days during the treatment period and assessed by a chip integrated into the medication dispenser. Secondary outcomes: Psoriasis severity was measured by the Lattice System Physician's Global Assessment (LS-PGA), and quality of life was measured by Dermatology Life Quality Index (DLQI) scales at all visits.

Results Intention to treat analyses using regression was performed. Primary outcome: more patients in the intervention group were adherent to Cal/BD cutaneous foam compared to patients in the non-intervention group at week four (65% vs. 38%, P = 0.004). Secondary outcomes: the intervention group showed a greater LS-PGA reduction compared to the non-intervention group at week 4 (mean 1.86 vs. 1.46, P = 0.047). A similar effect was seen at weeks 8 and 26, though it did not reach statistical significance.

Conclusion This RCT demonstrates that the app improved short term adherence to Cal/BD cutaneous foam treatment and psoriasis severity.

(clinicaltrials.gov registration NCT02858713)

Key words

Adherence, app, electronic monitor, psoriasis, topical corticosteroid

Introduction

Psoriasis is a chronic inflammatory disease affecting 2–4% of the Western population.[1] Psoriasis severely impacts quality of life[2,3] and creates a large socio-economic burden.[4,5] Mild-to-moderate psoriasis can be treated with topical corticosteroid preparations,[6-8] but adherence rates to these treatments are generally low and present a barrier for treatment success.[9]

Previous studies including psoriasis patients treated with topical corticosteroids in Western dermatology outpatient clinics have reported non-adherence rates from 8-88%.[10] Patients tend to

self-report higher adherence rates than those obtained by objective measurements,[11,12] therefore it is recommended to objectively measure adherence by using either an electronic monitor (gold standard) or medication weight.[13,14] Two studies have reported interventions improving adherence to topical corticosteroid treatment. One study tested the effects of weekly self-reporting of psoriasis status to a webpage for one year.[15] That intervention improved adherence to topical fluocinonide ointment in the intervention group relative to the control group. The other study did not use a control group and reported that 2 months of an individualized multifactorial patient-supporting intervention provided at dermatology clinics led to improved adherence rates relative to baseline.[16] There is a new and growing field of eHealth interventions for adherence improvement,[17] however there is a little evidence for their effectiveness.[18]

The aim of this study is to test whether the use of a study-specific app (Table 1) for 4 weeks improves short-term adherence to a recommended standard topical treatment regimen with Cal/BD cutaneous foam. As secondary outcomes, we also evaluated i) short (week 4) and long-term (week 8 and 26) psoriasis severity (Lattice System Physician's Global Assessment (LS-PGA)[19,20]) and ii) quality of life (Dermatology Life Quality Index (DLQI)[21]).

Methods

A six-month investigator-initiated single-site, parallel-group, phase-4 superiority block randomized controlled trial (RCT) with an allocation ratio of 1:1 was conducted according to the principles expressed in the Declaration of Helsinki as revised in 1983, the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) Guideline E6 (R2), and Danish national laws (clinicaltrials.gov registration NCT02858713). The protocol was approved by the Regional Ethics Committees on Health Research Ethics for Southern Denmark and the Danish Medicines Agency (EudraCT 2016-002143-42).[22]The study was conducted between 9 January 2017 and 29 August 2017 at an outpatient clinic for dermatology at Odense University Hospital. Written informed consent was obtained from all patients at inclusion and prior to randomization.

Potential study patients were recruited at the dermatology outpatient clinic and by advertisement. We included legally competent patients between 18-75 years of age who owned a smartphone or had skills for the use of a smartphone provided by the investigator (if the study-specific app was not supported by the patient's smartphone's operating system), who were diagnosed with mild-to-moderate psoriasis, and who were candidates for topical treatment with Cal/BD cutaneous foam. Individuals were excluded if they: (i) had a known sensitivity to topical Cal/BD, (ii) were unable to complete all study-related visits, (iii) had inadequate internet access or skills for use of a smartphone with an English-language app, (iv) had extensive disease not amenable to topical treatment, (v) were reluctant to be treated with a foam product, (vi) were breastfeeding or pregnant women, or (vii) were fertile women who did not use reliable contraception.

Patients were block-randomized in eight blocks based on sex and age and the investigator was blinded to allocation sequence using a computer-generated sequence in a 1:1 ratio. Patients were not paid for participating in the study. They received study medication free of charge (estimated market value 33 GBP after reimbursement from the National Health Service). The medication was prescribed for once daily application in a 28-day treatment period, excluding body sites for which treatment with topical Cal/BD cutaneous foam is contraindicated (face, axillae, and genitals). Cal/BD cutaneous foam was delivered in canisters with foam dispensers containing an electronic monitor with a chip registering the day and time the patient used the dispenser. Patients were given Cal/BD cutaneous foam in the canister with attached dispenser at the initial study visit, the canister could be replaced whenever empty. Patients were told to bring their medication canisters and dispensers for destruction at the week 4 return visit, but were not told in advance about the use of the data obtained by the electronic monitor or that each medication canister was weighed before and after use (on a precision balance Mettler Toledo PR802 weight with 0.01 g accuracy) until the final study visit (week 26). The appropriate quantity for each application on diseased skin was calculated by determining the involved area expressed as Body Surface Area (BSA) and multiplying by 0.5 g foam per 1% BSA. This dosage was then multiplied by 28 for once daily

application during the 28-day treatment period. The intervention group additionally received a supporting app, which provided once-daily compulsory treatment reminders and information on number of treatment applications and amount of prescribed Cal/BD cutaneous foam applied. The information was obtained by the electronic monitor chip synchronized to the app via Bluetooth® (Table 1). A laboratory assistant provided guidance on how to install and synchronize the app to the electronic monitor. The patients were also entitled to telephone support provided by the laboratory assistant, who answered any questions regarding use of the supporting app and electronic monitor. The app design was informed by previous research published by members of this research team,[10,18,22,23,24] and the tested prototypes were MyPso SmarTop™ Version 1.0 (the app) (for detailed description of the app, see Supplementary Material 1) and SmarTop™ number 053776 (the electronic monitor) (Fig. 1). After 28 days use of the app was terminated and no further adherence data were obtained. From week 4-26 all patients were provided with Cal/BD cutaneous foam to be used once daily when needed.

To make the visits similar to a normal visit, the investigator and laboratory assistant were not blinded to the intervention and data. Data were reviewed by a non-blinded GCP-experienced person. All socio-demographic and clinical data[10] were obtained by the investigator through interviews and medical chart reviews at baseline visits prior to randomization (Table 2).

Return visits were scheduled for weeks 4, 8 and 26. The primary outcome variables for adherence rates over 28-days were collected at week 4 by the chip in the electronic monitor measuring number of treatment applications, an electronic balance at the clinic, and by patient self-reporting on a study-specific scale (4-point ordinal scale). The secondary variables were collected using the validated measurements for psoriasis severity (Lattice System Physician's Global Assessment (LS-PGA), 8-point ordinal scale [25]). LS-PGA was chosen as a measurement of psoriasis severity, since it takes less time than e.g. Psoriasis Area and Severity Index (PASI) score and, unlike PASI, is consistent with the European Medicines Agency's (EMA) recommendations for psoriasis scoring in clinical trials.[19]

LS-PGA and Quality of life (Dermatology Life Quality Index (DLQI), 30-point ordinal scale[21]) were obtained at baseline and weeks 4, 8, and 26. Secondary long-term variables were obtained long-term after termination of the intervention, as recommended by the Cochrane Group.[26]

Sample size calculation

The study was powered assuming that use of the app would increase treatment applications by at least 8% in the intervention group compared to the non-intervention group. Based on findings from *Alinia et al.*, [15] the mean number of treatment sessions in the non-intervention group was assumed to be 63 % of the recommended number of applications / 28 days, the mean number of applications in the intervention group was assumed to be 71% of the recommended number of applications / 28 days and the standard deviation (SD) in the non-intervention and intervention groups was assumed to be 15% of the recommended number of applications / 28 days. We required a power of 80%, a two-sided significance of 95%, 1:1 treatment allocation, and expected drop-out of 12.5%. We applied a sample size calculation for an unpaired t-test as we modelled the mean adherence of each patient (numerically on a %-scale, expected to be normally distributed due to the Central Limit Theorem). This calculation resulted in a planned sample size of 128 participants (Stata-script provided in Supplementary Material 2).

Statistical analyses

Normality assumptions were checked by quantile plots. No adjustments for baseline covariates were considered relevant in the main analyses.[27,28] P-values <0.05 were considered statistically significant,[29] and we conducted all analyses using Stata 15.

Baseline characteristics for the two treatment groups are presented as counts and percentages.

Analyses of primary outcomes (adherence)

For chip data, all registered applications within one hour were regarded as a single treatment session. We set chip adherence as binary, defined as treated or non-treated each day, to avoid

errors related to multiple treatments in one day. Data were analysed using an intention to treat (ITT) approach.

Main analysis of primary outcomes (adherence): We dichotomized adherence rates obtained by chip and medication weight with a selected cut-off of 80%, with adherence rates above 80% considered adherent (a cut-off typically used when studying adherence in other chronic diseases[29]). We compared the dichotomized adherences by using logistic regression.

Sensitivity analysis of primary outcomes (adherence): Adherence measures or their natural logarithm (if necessary to ensure normality of model residuals) were compared between treatment groups using linear regression. The analyses were carried out excluding missing data and after 100 multiple imputations by multivariate normal regression on the logarithms of the three adherence measures, without included covariates as well as with an imputation including treatment, age, sex and smoking as covariates.[10]

Analysis of secondary outcomes (LS-PGA and DLQI)

Changes between LS-PGA and DLQI measurements from baseline to week 4 and from baseline to weeks 8 and 26 were compared between the two treatments by linear regression. LS-PGA and DLQI measurements including means are presented in box-plots.

Results

134 patients with mild-to-moderate psoriasis and a mean age 48 years (21-75 years) were enrolled (Table 2). The study participants were mostly males under 50 years of age, who were married, non-smokers, and employed full-time in a vocational or academic profession. The majority of patients had been diagnosed with psoriasis for more than 20 years and only a few had a history of using systemic anti-psoriatic treatments (Table 2).

The included patients were randomized into non-intervention (n = 66) and intervention (n = 68) groups at the baseline visit. The two groups were comparable based on measured baseline

covariates (Table 2). 21/68 [31%] of patients in the intervention group borrowed a smartphone from the investigator for the intervention period. 122/134 (91%) of all patients returned for the week 26 visit (Fig. 2), and the numbers of patients lost to follow-up were equally divided between non-intervention and intervention groups. Missing data on primary outcome measurements obtained at week 4 were comparable for non-intervention and intervention groups, whether they were chip-registered applications (6/66 [9%] vs. 8/68 [12%]), canister weight (1/66 [2%] vs. 4/68 [6%]), or patient-reported non-adherence rates (1/66 [2%] vs. 3/68 [4%]) (Fig. 2).Comparisons between missing data for the 3 adherence measurements in non-intervention and intervention groups are provided in Supplementary Material 3 and considered missing at random. No serious adverse reactions were observed.

In the main analysis of chip adherence data (data were coded for adherent patient rates, defined as medication applied ≥80% of days in the treatment period), more patients in the intervention group were adherent compared to patients in the non-intervention group (65% vs. 38%, P = 0.004) (Table 3). The sensitivity analysis of chip adherence data revealed that patients in the intervention group were more adherent to number of treatment sessions compared to patients in the non-intervention group (82% vs. 69%, P = 0.001) (Table 3), similar results were obtained when allowing for multiple treatments sessions on the same day (data not shown), and imputing for missing data did not change the results (Table 3).

Adherence to amount of cutaneous foam in the main analysis showed that more patients in the intervention group were adherent compared to patients in the non-intervention group, although not reaching statistical significance (14% vs. 8%) (Table 3). Also, in the sensitivity analysis, adherence to amount of cutaneous foam used revealed that patients in the intervention group were more adherent compared to patients in the non-intervention group (43% vs. 33%, P = 0.026) (Table 3); data imputed for missing values revealed similar results (Table 3).

Adherence rates reported by patients were higher than those objectively obtained by weight, but there was no significant difference between the non-intervention and intervention groups (59% vs. 67%), neither when imputed for missing values (Table 3).

Impact of the intervention on severity of psoriasis and quality of life

Improved adherence was associated with a greater change in LS-PGA from baseline to week 4 between the intervention and non-intervention groups (mean 1.86 vs. 1.46, P = 0.047) (Table 4). A similar trend was seen at weeks 8 and 26, although it did not reach statistical significance (Fig. 3). DLQI initially changed from baseline to week 4 in the non-intervention vs. intervention group (4.54 vs. 4.12) (Table 4), which is considered a reduction above minimal clinically important difference (MCID).[31] DLQI was further reduced at week 8, followed by a minor relapse at week 26 (Fig. 4) (Table 4).

Discussion

This RCT demonstrates that an app designed to support daily topical treatment by psoriasis patients improved treatment adherence (as measured by electronic monitors or medication canister weight) and reduced psoriasis severity (as measured by LS-PGA).

The app improved adherence rates to topical treatment during a 28-day intervention period, in agreement with one study reporting improved adherence rates when patients reported their psoriasis status weekly.[15] Another study reported improved adherence rates for use of systemic treatment in psoriasis patients when they received daily text messages.[32] The app used in this study also improved severity of psoriasis, in agreement with reports of adherence-improving interventions for psoriasis[32] and other chronic diseases.[33,34] Inspired by previous adherence studies, we dichotomized adherence rates obtained by chip and canister weight with a cut-off of 80%, and classified adherence rates above 80% as adherent.[29] The optimal cut-off should be based on the adherence level necessary for the drug to work.[30] In this case we do not know how forgiving the drug is to missed doses, which represents a weakness of the study.

Adherence was measured by the number of treatment sessions, and patients in the non-intervention group had a 69% adherence rate, meaning that they used medication on 69% of days. This result is in agreement with *Alinia et al.,*[15] who measured adherence to topical fluocinonide ointment by number of treatment days among psoriasis patients over one year and reported that adherence among patients receiving standard-treatment of care was 63% during the first month.

Adherence was also measured by canister weight, and we found that patients in the non-intervention group used 33% of the prescribed amount of medication. This is in agreement with a report by *Storm et al*.,[35] who found that patients seen at a dermatology clinic used 35% of the expected doses of topical treatments over a two-week treatment period.[35]

The low rate of patients adherent to amount of medication in both non-intervention and intervention group (8% vs. 12%) suggest that the estimated amount of cutaneous foam used during the 4-weeks was too high. Measuring adherence by weight is challenging and requires that the prescriber first estimate the amount of topical treatment to be used during a treatment period. One limitation of the study is that we do not know the amount of medication that should be applied to get the full benefits of treatment. The majority of the patients in this study had been diagnosed with psoriasis for over 20 years and may be less inclined to follow a dosing instruction that would pose a risk of side-effects[36] (mainly pain, erythema and pruritus).[37,38] The generally low rates of adherence as measured by weight might also indicate a need for clinicians to provide patients with specific advice and motivation for the appropriate quantity of medication to be used.

A strength of the study is the collection and comparison of adherence measurements by number of treatment sessions, applied medication weight, and patient self-report.[39] It is important that adherence studies reflect what is considered to be clinically relevant; i.e. we consider it more important for patients to apply the topical product regularly than in large amounts.

LS-PGA and DLQI improved considerably over the study period as an effect of the topical treatment (Fig. 3 and 4), in agreement with the international literature.[7,38,40] PASI as a tool for measuring severity of psoriasis was not applied in this study, because EMA recommended the use of LS-PGA in clinical trials. The reduction in DLQI for both groups was caused by the Cal/BD foam treatment.[8] The DLQI measurement should be interpreted with caution: the DLQI is unidimensional and underrepresents the emotional aspects of the dermatological patients' lives.[41] In order to capture the full range of the Quality of Life (QoL) aspect, we could have combined the DLQI measurement with one of the available psoriasis-specific QoL instruments.[42] It is a limitation of the study that we did not obtain outcomes on patient-perceived severity and patient-physician relationship as reported in other adherence-improving interventions,[32] since improved patient-physician relationship may motivate patients and improve treatment adherence and outcome.[43] We did not report patients' use of the optional diary functions or patients' satisfaction with the app, which is a limitation for interpreting the results for app designers and medical device engineers.

The patients received study drugs, which may provide better results than those obtained in real-life settings, such as that reported by *Storm et al.* in which 1/3 of prescriptions were never redeemed.[44] Our study patients were partly recruited by advertisement, which poses a risk of including patients who are more motivated to adhere to prescribed topical treatment than the background psoriasis population.[35,45]

The local ethics committee would not approve blinding patients to the fact they were in a trial until the end of the study, a method used in other adherence studies.[46] The assessors were not blinded, which introduced a risk of attrition and observer bias.[47] This study was performed simultaneously with the introduction of the new Cal/BD cutaneous foam on the Danish market. The patient information session at the initial study visit was focused on the new drug reformulation[48] and to a lesser degree on the adherence measurement, which partially concealed that the primary outcome of the study was adherence.

In conclusion, this RCT demonstrated that a study-specific patient-supporting app improved adherence rates and psoriasis severity in a statistically and clinically significant manner. There is potential for implementing patient-supporting apps in the dermatology clinic.

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Table 1. Available functions in the 28-day adherence-supporting app

Function	Compulsory	Optional
Daily treatment reminder	X	
Daily information on amount of treatment and number of treatment applications[a]	X	
Symptom rating[b] **on an interval scale, i.e. itching, pain, inflammation, dryness, scaling, stress, and social discomfort**		X

[a]Foam dispensers had an electronic monitor with a chip registering each time the patient used the dispenser. Information from the electronic monitor synchronized via Bluetooth® to the app.
[b]Optional daily or weekly symptom rating reminder.

Table 2. Baseline characteristics

Data for non-intervention vs. intervention group

	Non-intervention		Intervention	
Variables	**N**	**(%)**	**N**	**(%)**
Total number of participants	66	(49)	68	(51)
Sex				
Male	**41**	**(62)**	**41**	**(60)**
Female	25	(38)	27	(40)
Age (years)				
18 – 40	**21**	**(32)**	**20**	**(29)**
41 - 50	**13**	**(20)**	**14**	**(21)**
51 - 60	16	(24)	18	(26)
61 - 75	16	(24)	16	(24)
Marital status				
Married	**39**	**(59)**	**44**	**(65)**
Cohabit	11	(17)	12	(18)
Divorced	4	(6)	3	(4)
Unmarried	11	(17)	7	(10)
Widowed	1	(2)	2	(3)
Highest obtained level of education				
Primary and lower secondary education	2	(3)	7	(10)
Upper secondary education	2	(3)	1	(1)
Vocational education and training	**29**	**(44)**	**32**	**(47)**
Academy profession degree	**17**	**(26)**	**17**	**(25)**
Bachelor's degree	12	(18)	7	(10)
Master's degree	4	(6)	4	(6)
Employment status				
Full-time	**43**	**(65)**	**42**	**(62)**
Part-time	4	(6)	1	(1)
Retired	12	(18)	17	(25)
Unemployed	4	(6)	5	(7)
Studying	3	(5)	3	(4)
Smoking status				
Non-smoker	**52**	**(79)**	**53**	**(78)**
Smoker	14	(21)	15	(22)
Duration of psoriasis (years)				
0 – 5	5	(8)	4	(6)
6 – 10	8	(12)	10	(15)
11 – 15	5	(8)	6	(9)

16 – 20	8	(12)	9	(13)
> 20 years	**40**	**(61)**	**39**	**(57)**
Prior antipsoriatic therapies				
Methotrexate	10	(15)	16	(24)
Acitretin	5	(8)	2	(3)
Cyclosporine	0	(0)	1	(1)
Biologics	5	(8)	5	(7)
NB UVB[a]	**25**	**(38)**	**25**	**(37)**
Coal tar therapy	4	(6)	5	(7)
Climate therapy	1	(2)	4	(6)
None of the above therapies	**29**	**(44)**	**32**	**(47)**
Current antipsoriatic therapies				
Methotrexate	5	(8)	10	(15)
Acitretin	1	(2)	0	(0)
Cyclosporine	0	(0)	0	(0)
Biologics	1	(2)	0	(0)
NB UVB	0	(0)	2	(3)
None of the above therapies	**59**	**(89)**	**56**	**(82)**

Abbreviation: NB-UVB, Narrow band ultraviolet B phototherapy. Baseline data describing the majority of study patients is highlighted in bold.

Table 3. Primary outcomes: Adherence rates and rate of adherent patients in a 28-day treatment period

Non-intervention and intervention groups measurements were compared by regression analyses.

Main analysis						
Rate of adherent patients, based on dichotomized adherence rates (without imputation)						
	Non-intervention (patients, N)	Intervention (patients, N	Non-intervention N (%) (95% CI)	Intervention N (%)	OR (95% CI)	P-value
Adherent to treatment sessions[a]	61	59	**23 (38%) (26%, 51%)**	**39 (65%) (53%, 77%)**	**2.99 (1.42, 6.28)**	**0.004***
Adherent to amount of foam[b]	65	64	5 (8%) (1%, 14%)	9 (14%) (5%, 23%)	1.96 (0.620, 6.22	0.251
Sensitivity analysis						
Adherence rates for patients, numerical outcomes (without imputation)						
	Non-intervention (patients, N)	Intervention (patients, N)	Non-intervention (mean) (95% CI)	Intervention (mean) (95% CI)	Coefficient (95% CI)	P-value
Adherence rates obtained by chip[c]	61	59	**0.686 (0.629, 0.742)**	**0.822 (0.764, 0.879)**	**0.136 (0.056, 0.216)**	**0.001***
Adherence rates obtained by weight[d] (log)[e]	65	64	**0.325 (0.265, 0.385)**	**0.427 (0.353, 0.501)**	**0.328 (0.041, 0.615)**	**0.026***
Adherence rates reported by patients[f]	65	65	0.591 (0.530, 0.652)	0.665 (0.613, 0.716)	0.074 (-0.006, 0.153)	0.069
Adherence rates for patients, numerical outcomes (with multiple imputations on adherence outcomes)						
	Non-intervention (patients, N)	Intervention (patients, N)	Non-intervention (mean) (95% CI)	Intervention (mean) (95% CI)	Coefficient (95% CI)	P-value
Adherence rates obtained by chip[c]	66	68	**0.691 (0.625, 0.757)**	**0.824 (0.749, 0.898)**	**0.133 (0.036, 0.230)**	**0.008***
Adherence rates obtained by weight[d] (log)[e]	66	68	**0.327 (0.264, 0.391)**	**0.429 (0.350, 0.508)**	**0.321 (0.034, 0.609)**	**0.029***
Adherence rates	66	68	0.592	0.666	0.074	0.083

reported by patients[f]			(0.530, 0.655)	(0.608, 0.723)	(-0.010, 0.157)	
Adherence rates for patients, numerical outcomes (with extended multiple imputations)[g]						
	Non-intervention (patients, N)	Intervention (patients, N)	Non-intervention (mean) (95% CI)	Intervention (mean) (95% CI)	Coefficient (95% CI)	P-value
Adherence rates obtained by chip[c]	66	68	**0.684 (0.620, 0.749)**	**0.833 (0.753, 0.913)**	**0.149 (0.048, 0.249)**	**0.004***
Adherence rates obtained by weight[d] (log)[e]	66	68	**0.324 (0.264, 0.385)**	**0.426 (0.348, 0.505)**	**0.321 (0.033, 0.609)**	**0.029***
Adherence rates reported by patients[f]	66	68	0.590 (0.528, 0.652)	0.667 (0.609, 0.725)	0.077 (-0.006, 0.160)	0.070

[a]Patients adherent to number of treatment sessions, defined as having applied foam treatment >= 80% of days in the treatment period. [b]Patients adherent to prescribed amount of foam, defined as having used >= 80% weight of estimated amount of foam for the treatment period. [c]Adherence rates obtained by chip, number of days with at least one treatment session were divided by number of days in the treatment period. [d]Adherence rates obtained by weight, weight of returned canisters were divided by weight of estimated amount of use for the treatment period. [e]Mean of the original (non-logaritmized) observations presented in the table. [f]Adherence rates were reported by patients on a study-specific ordinal scale from 0-4, from 0 (did not use treatment) to 4 (used all prescribed medication). [g]multiple imputations by multivariate normal regression on the logarithms of the three adherence measures with an imputation including treatment, age, sex and smoking as covariates.

*Statistically significant results. Significant results are in addition highlighted in bold. Abbreviation: CI, Confidence Interval; OR, Odds Ratio.

Table 4. Secondary outcomes: Quality of life and psoriasis severity during the 26-week treatment period

Non-intervention and intervention group measurements were compared by regression analyses.

LS-PGA						
	Non-intervention (patients, N)	Intervention (patients, N)	Non-intervention (mean) (95% CI)	Intervention (mean) (95% CI)	Coefficient (95% CI)	P-value
Change 0 to 4 weeks	65	65	**1.46 (1.17, 1.75)**	**1.86 (1.59, 2.13)**	**0.400 (0.005, 0.795)**	**0.047***
Change 0 to 8 weeks	63	64	2.16 (1.86, 2.46)	2.25 (1.96, 2.54)	0.091 (-0.321, 0.504)	0.662
Change 0 to 26 weeks	61	61	1.80 (1.49, 2.11)	1.98 (1.66, 2.31)	0.180 (-0.264, 0.625)	0.424
DLQI						
	Non-intervention (patients, N)	Intervention (patients, N)	Non-intervention (mean) (95% CI)	Intervention (mean) (95% CI)	Coefficient (95% CI)	P-value
Change 0 to 4 weeks	65	65	4.54 (3.47, 5.61)	4.12 (3.27, 4.98)	-0.415 (-1.770, 0.939)	0.545
Change 0 to 8 weeks	63	64	5.17 (3.92, 6.43)	4.59 (3.71, 5.48)	-0.581 (-2.099, 0.938)	0.450
Change 0 to 26 weeks	61	61	5.00 (3.69, 6.31)	4.23 (3.25, 5.21)	-0.770 (-2.389, 0.848)	0.348

*Statistically significant results, significants result are additionally highlighted in bold.

Abbreviations: CI, Confidence Interval; DLQI, Dermatology Life Quality Index; LS-PGA, Lattice System Physician's Global Assessment.