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Calcipotriene and Betamethasone Dipropionate PAD-Cream Demonstrates Greater Treatment Efficacy in Patients with Moderate-to-Severe Psoriasis Compared to Topical Suspension/Gel: A Subgroup Analysis of Two Phase 3 Studies

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ORIGINAL RESEARCH

Calcipotriene and Betamethasone Dipropionate PAD-Cream Demonstrates Greater Treatment Efficacy in Patients with Moderate-to-Severe Psoriasis Compared to Topical Suspension/Gel: A Subgroup Analysis of Two Phase 3 Studies

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ABSTRACT

Introduction: Psoriasis ranges from mild to severe with the majority of patients having mild disease. Mild to moderate disease is often treated with topical therapies while photo-, oral, and biologic therapies are generally reserved for moderate-to-severe disease. There is a strong scientific rationale for the combination of calcipotriene (CAL) and betamethasone dipropionate (BDP) with respect to mode of action, efficacy, and safety and CAL/BDP has shown an inhibitory effect on key pathogenic cytokines in psoriasis including tumor necrosis factor-α, interleukin (IL)-17, and IL-23.

Methods: The objective of this pooled post hoc analysis is to investigate the efficacy of CAL/BDP polyaphron dispersion (PAD)-cream in subgroups of patients with moderate-to-severe psoriasis from two completed phase 3 studies conducted in the USA and Europe.
Results: The proportion of patients achieving Physician Global Assessment (PGA) treatment success as well as a modified Psoriasis Area and Severity Index (mPASI)75 response was higher in the subgroup with a body surface area > 10% and mPASI > 10 and Dermatology Life Quality Index > 10 at baseline compared to the overall patient population. Furthermore, the numerical difference in treatment efficacy between CAL/BDP PAD-cream and CAL/BDP topical suspension/gel increased in patient subgroups with higher baseline severity. Similar patterns were shown for the patient-reported outcomes.

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Conclusion: In this subgroup analysis, patients who had higher disease severity at baseline achieved greater efficacy than the total patient population when treated with 8 weeks of CAL/ BDP PAD-cream as compared to a currently marketed active comparator. Additionally, as indicated by this analysis, CAL/BDP PAD-cream treatment may also be more convenient and less greasy, which may reduce the burden of daily treatment and improve adherence to therapy.
Trial Registration: NCT03308799 and NCT03802344.

Key Summary Points

There is a need for topical psoriasis treatments that in addition to being highly efficacious also are convenient and easy to use, as this could reduce the burden of daily treatment and improve adherence to therapy and real-life outcome.

The objective of this pooled post hoc analysis is to investigate the efficacy of calcipotriene (CAL)/betamethasone dipropionate (BDP) polyaphron dispersion (PAD)-cream in patients with moderate-to-severe psoriasis from two completed phase 3 studies conducted in the USA and Europe.

The proportion of patients achieving Physician Global Assessment treatment success as well as a modified Psoriasis Area and Severity Index (mPASI)75 response was higher in the subgroup with a body surface area > 10% and mPASI > 10 and Dermatology Life Quality Index > 10 at baseline compared to the overall patient population.

As indicated by this subgroup analysis, patients who had higher disease severity at baseline achieved greater efficacy than the total patient population when treated with 8 weeks of CAL/BDP PAD-cream as compared to a currently marketed active comparator.

CAL/BDP PAD-cream is a non-greasy, easy spreadable cream that is scored high in convenience even by patients with moderate-to-severe disease, which makes it an option for some patients with moderate-to-severe psoriasis either as monotherapy or as adjunctive therapy to systemic/biologic agents.

INTRODUCTION

Psoriasis is a common, chronic, immune-mediated, inflammatory skin disease. The prevalence of diagnosed psoriasis in the USA and Europe is approximately 3% [1–3]. Chronic stable plaque psoriasis (psoriasis vulgaris) is the most common form of the disease, accounting for 85–90% of cases [4] and manifests as raised, red patches or plaques with silvery scales. Psoriasis ranges from mild to severe with the majority of patients having mild disease (> 80%) [5]. The severity of chronic plaque psoriasis is generally assessed according to the Psoriasis Area and Severity Index (PASI), the body surface area (BSA), and the Physician Global Assessment (PGA). A patient's quality of life (QoL) is commonly assessed by questionnaires including the Dermatology Life Quality Index (DLQI) [6]. Psoriasis severity can be categorized by BSA as mild (< 3%), moderate (3–10%), or severe (> 10%) [7]. Further, a PASI of > 10 is indicative of severe psoriasis [8] and with a DLQI of > 10 a skin disease is having a very severe impact on the patient's QoL [9]. Based on this, the rule of tens (BSA > 10% or PASI > 10 or DLQI > 10) has been proposed as a criterion to identify patients with severe psoriasis [8].

Immunological and genetic studies have identified interleukin (IL)-17 and IL-23 as key drivers of psoriasis pathogenesis [10, 11] and multiple biologic therapies targeting these cytokines and tumor necrosis factor (TNF)-α are available. However, there is no cure for psoriasis. The goal of treatment is to reduce or eliminate its signs, symptoms, and impact on QoL. Mild to moderate disease is often treated with topical therapies while photo-, oral, and biologic therapies are generally reserved for moderate-to-severe disease [12]. Further, topical medications are frequently used as adjunctive therapies for patients on phototherapy or systemic therapy [13]. Of notice, some patients with severe psoriasis (BSA > 10%) are even treated with topicals alone [14]. Among topical therapies, the fixed combination treatment of a vitamin D analogue and a corticosteroid is commonly used [15, 16]. There is strong scientific rationale for the combination of vitamin D and corticosteroids with respect to mode of action, efficacy, and safety [17–19], and the combination of calcipotriene (CAL) and betamethasone dipropionate (BDP) is superior to each of the single agents [20–22]. Furthermore, CAL/BDP has an inhibitory effect on key pathogenic cytokines in psoriasis including TNFα, IL-17, and IL-23, and CAL normalizes keratinocyte differentiation and proliferation [17, 23]. The combination treatment with a vitamin D analogue and a topical corticosteroid is recommended in both American and European guidelines [24–28].

Application of topical therapies can be cumbersome, messy, and time-consuming. Thus, there is a need for topical psoriasis treatments that in addition to being highly efficacious also are convenient and easy to use, as this could reduce the burden of daily treatment and improve adherence to therapy and real-life outcome [29]. A CAL/BDP polyaphron dispersion (PAD)-cream has been developed, which contains a fixed dose combination of 0.005 w/w% CAL and 0.064 w/w% BDP using the proprietary PAD Technology[TM] that protects the drug substances from degradation during storage [30]. PAD Technology is a novel formulation and delivery system with enhanced drug penetration and high local tolerability [30].

Further, CAL/BDP PAD-cream is a non-greasy, easily spreadable white cream with a high patient satisfaction and treatment convenience [31–33]. CAL/BDP PAD-cream has been approved as Wynzora® both by the US Food and Drug Administration and several European Regulatory Agencies.

The objective of this pooled post hoc analysis is to investigate the efficacy of CAL/BDP PAD-cream in patients with moderate-to-severe psoriasis from two completed phase 3 studies conducted in the USA (NCT03308799) and Europe (NCT03802344).

METHODS

Study Design

Study MC2-01-C2 (registered at ClinicalTrials.gov, NCT03308799) and study MC2-01-C7 (NCT03802344) were both phase III, randomized, investigator-blinded, multicenter, vehicle and comparator controlled, parallel-group, three-arm studies.

The studies comprised three periods (screening, treatment, and follow-up) as illustrated in Supplementary Fig. S1. Participants were randomly assigned into three treatment groups with a ratio of 3:1:3 for treatment with CAL/BDP PAD-cream (calcipotriene/betamethasone dipropionate, 0.005%/0.064 cream), matching vehicle and active comparator, respectively. Active comparators were marketed products in the USA and Europe: Taclonex® Topical Suspension (TS) and Dovobet®/Daivobet® Gel, respectively, with the exact same composition, that were approved for 8 weeks of treatment. The studies were investigator blinded as a result of differences in formulation, storage conditions, and packaging.

Subjects were to apply the investigational products (IPs) topically once daily preferable in the evening for 8 weeks to affected areas on the trunk (including the neck), the limbs, i.e., arms (including the back of the hands), the legs (including the buttocks and the top of the feet) and, in MC2-01-C7 only, and out of scope of this analysis, on the scalp.

Study Participants

Eligible subjects were generally healthy adults ages 18 years or above with mild-to-moderate chronic plaque psoriasis (according to PGA) of at least 6 months duration, involving the trunk and/or limbs, involving 2–30% of BSA, and a modified PASI (mPASI) $\geq$ 2 in MC2-01-C2 and an mPASI $\geq$ 3 in MC2-01-C7.

The studies were performed in accordance with the Helsinki Declaration of 1964 and its later amendments. The study protocols were approved by institutional review boards at each site, and all participants provided written informed consent prior to any study-related procedures. Both studies were designed to show therapeutic non-inferiority of CAL/BDP PAD-cream to the active comparator.

Study Assessments

The full analysis of the two phase III studies are presented elsewhere [34, 35]. This post hoc analysis focused on the following efficacy parameters in patients with moderate-to-severe psoriasis:

- PGA success at week 8—defined as a PGA score of 0 (clear) or 1 (almost clear) and with a minimum 2-point improvement from baseline.
- mPASI75 at week 8—proportion of subjects achieving $\geq$ 75% reduction from baseline in mPASI.
- DLQI satisfaction (0/1) at week 8—indicating the disease burden has no impact on QoL.
- Psoriasis Treatment Convenience Scale (PTCS) total score (the sum of question 1–5) at weeks 1 and 8—the scale evaluates treatment convenience and satisfaction and consists of 6 disease-specific, self-reported questions with a recall period of 1 week and rated on a numerical scale from 1 to 10.
- The score of the 6 disease-specific PTCS questions at week 8.

Baseline characteristics that were used for the subgroup analysis of patients with moderate-to-severe psoriasis included the following:

- BSA—The total psoriatic involvement on the trunk and limbs (excluding genital and intertriginous areas) was recorded as a percentage of the total BSA, estimating that the surface of the subject's full, flat palm (including the five digits) correlating to approximately 1% of the total BSA.
- The DLQI total score, which is the sum of the 10 equal-weighted questions relating to the degree to which the participants' skin condition affects their daily activities. The scores from DLQI range between 0 and 30 with lower scores indicating better QoL. The DLQI is a validated patient-reported outcome where a score of 0 or 1 indicates that the disease burden has no impact on QoL (defined as DLQI satisfaction).
- mPASI—the extent and severity of the subjects' psoriasis on the body (trunk and/or limbs) excluding the scalp using an mPASI scoring system.

Analysis Methods

Patients in the "all patients" population (n = 1271) were from the pooled modified intention-to-treat (MITT) dataset and included subjects who were:(1) randomly assigned to any IP; (2) treated with the IP; and (3) had at least one assessment of PGA after starting treatment. For the subgroup analysis, subjects were grouped according to baseline severity; one group with subjects who had a BSA of > 10% at baseline (n = 321), one group with a mPASI of > 10 at baseline (n = 289), and one group with subjects who had a DLQI of > 10 at baseline (n = 505). Moderate-to-severe MITT patients were based on the rule of tens and included subjects who had BSA > 10% or mPASI > 10 or DLQI > 10 at baseline (n = 705) [8]. The "high severity" subgroup of patients (n = 104) was defined as patients who had all three of the severe baseline characteristics at baseline (BSA > 10% and mPASI > 10 and DLQI > 10) (Fig. 1). Post-baseline missing or invalid data were multiply imputed within treatment groups.

RESULTS

Study Participants

A total of 796 participants were enrolled at 55 clinical sites in the US study, and 490 participants were enrolled at 32 clinical sites in the European study.

Demographic data (age, sex, and race) for the pooled MITT population was comparable between treatment arms. Baseline BSA, mPASI, PGA, Subject's Global Assessment (SGA), and DLQI were also comparable between treatment arms [35]. Patient demographics were similar between the all patients (pooled MITT) population (n = 1271) and the subgroups, except that the baseline disease characteristics for the subgroups as expected showed increasing severity in all parameters compared to the all patients population (Table 1). The baseline disease characteristics of the BSA, mPASI, and DLQI for the high severity subgroup consisting of patients with baseline BSA > 10, mPASI > 10, and DLQI > 10 was approximately twice the level found in the all patients group.

Fig. 1 Illustration of the analyzed subgroups according to baseline severity and the overlap of patients between the various groups

PGA Treatment Success

As shown in Fig. 2, the CAL/BDP PAD-cream treatment group had a statistically higher proportion of patients achieving PGA treatment success as compared to CAL/BDP TS/gel treatment in the all patients population at week 8 (43.2% vs. 31.9%, respectively) [35]. Significantly higher efficacy in favor of CAL/BDP PAD-cream compared to CAL/BDP TS/gel was also observed for all subgroups analyzed (Fig. 2). Further, the proportion of patients achieving PGA treatment success with CAL/BDP PAD-cream was higher in the high severity subgroup compared to the all patients population. In contrast, fewer patients in the high severity subgroup achieved PGA treatment success in the CAL/BDP TS/gel group compared to the all patients population. The numerical difference in treatment efficacy between CAL/BDP PAD-cream and CAL/BDP TS/gel was most pronounced in the high severity subgroup (difference of 28.6%, i.e., 48.1% (95% CI 34.5, 61.7) − 19.5% (95% CI 6.2, 32.8)).

Proportion of Subjects Achieving mPASI 75

In the all patients population, the CAL/BDP PAD-cream treatment group had a statistically higher proportion of subjects who achieved a mPASI75 response at week 8 as compared to active CAL/BDP TS/gel treatment (44.3% vs. 34.5%, respectively; Fig. 3) [35]. Significantly higher efficacy in favor of CAL/BDP PAD-cream compared to CAL/BDP TS/gel was also observed for all subgroups analyzed in this study (Fig. 3). Further, the proportion of patients achieving mPASI75 at week 8 was higher in the high severity subgroup compared to the all patients population. The numerical difference in treatment efficacy between CAL/BDP PAD-cream and CAL/BDP TS/gel increased in patient subgroups with a higher baseline severity. The largest numerical difference in efficacy was observed in the high severity subgroup (difference of 36.0%) with the CAL/BDP PAD-cream treatment group having a mPASI75 of 54.6 (95% CI 40.9, 68.2) at week 8 versus a mPASI75
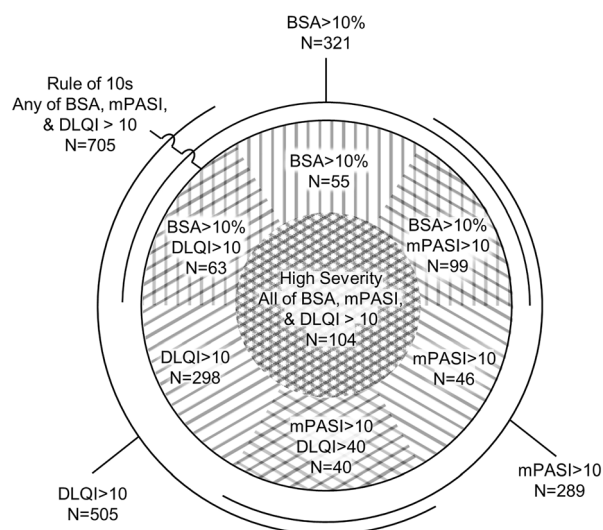
Table 1 Baseline demographics and disease characteristics by subgroups (modified intention to treat (MITT) pooled data)

	All patients $n = 1271$	BSA > 10% subgroup $n = 321$	mPASI > 10 subgroup $n = 289$	DLQI > 10 subgroup $n = 505$	Rule of tens subgroup[a] $n = 705$	High severity subgroup[b] $n = 104$
Age, mean (SD) years	51.4 (14.1)	50.7 (14.2)	51.3 (14.5)	49.6 (14.1)	50.3 (14.1)	50.1 (14.8)
Gender (%)						
Female	38.4	31.2	27.0	44.0	37.9	37.5
Male	61.6	68.8	73.0	56.0	62.1	62.5
Race, %						
White	91.3	91.0	89.6	87.5	89.2	89.4
Black/African American	5.2	6.2	7.6	7.7	6.8	6.7
Asian	0.5	1.6	1.7	2.6	2.1	2.9
American Indian/ Alaska Native	0.5	–	–	0.6	0.4	–
Native Hawaiian/ Pacific Islander	0.2	–	–	0.4	0.3	–
Other	0.9	1.2	1.0	1.2	1.1	1.0
Psoriasis duration years, mean (SD)	17.4 (13.5)	18.7 (13.3)	18.2 (13.7)	16.4 (13.3)	17.1 (13.4)	16.7 (13.4)
% BSA, mean (SD)	8.4 (6.6)	17.5 (6.3)	15.7 (7.3)	9.5 (6.8)	11.3 (7.6)	18.7 (5.9)
mPASI, mean (SD)	7.7 (4.0)	11.6 (4.1)	13.5 (3.1)	8.5 (4.0)	9.4 (4.3)	14.0 (3.3)
PGA, mean (SD)	2.8 (0.4)	3.0 (0.2)	3.0 (0.2)	2.9 (0.3)	2.9 (0.3)	3.0 (0.1)
SGA, mean (SD)	2.8 (0.8)	3.1 (0.7)	3.0 (0.8)	3.3 (0.6)	3.1 (0.7)	3.4 (0.6)
DLQI, mean (SD)	9.7 (6.3)	11.9 (6.2)	11.1 (6.6)	16.1 (4.4)	13.2 (6.1)	16.4 (4.7)

BSA body surface area, *mPASI* modified Psoriasis Area and Severity Index, *DLQI* Dermatology Life Quality Index, *SD* standard deviation, *PGA* Physician Global Assessment, *SGA* Subject's Global Assessment
[a]Rule of tens subgroup = BSA or mPASI or DLQI > 10
[b]High severity subgroup = BSA and mPASI, and DLQI > 10

of 18.6% (95% CI 5.4, 31.8) in the CAL/BDP TS/ gel group.

Patient-Reported Outcomes

Patient-reported outcomes in the combined phase 3 studies included DLQI and PTCS. PTCS was used to evaluate treatment convenience and overall patient satisfaction with treatment.

As shown in Fig. 4, CAL/BDP PAD-cream treatment had a significantly higher proportion of patients achieving a DLQI satisfaction (score of 0/1) at week 8 ($p = 0.0005$) as compared to the CAL/BDP TS/gel group. As would be expected, a trend towards a lower proportion of patients achieving DLQI satisfaction was
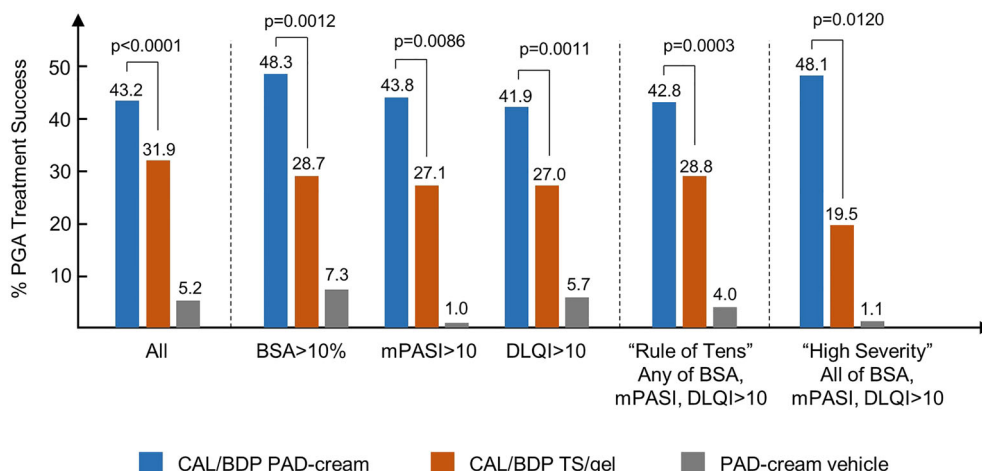
Fig. 2 Physician Global Assessment (PGA) treatment success at week 8. Proportion of patients (%) achieving PGA treatment success after 8 weeks of treatment with calcipotriene (CAL)/betamethasone dipropionate (BDP) present polyaphron dispersion (PAD)-cream, CAL/BDP topical suspension (TS)/gel, or vehicle in the all patient population and higher severity subgroups

present among the higher baseline severity subgroups. The numerical differences between the CAL/BDP PAD-cream and CAL/BDP TS/gel treatments were greater in the rule of tens subgroup and the high severity subgroup than in the all patients population with the highest numerical difference in the high severity subgroup (difference of 17.4%, i.e., 27.7% (95% CI 15.4, 40.1) − 10.3% (95% CI − 0.3, 20.9)). Interestingly, a significantly higher proportion of patients in the CAL/BDP PAD-cream arm achieved a DLQI of 0 or 1 compared to CAL/BDP TS/gel when looking at patients with a DLQI > 10 at baseline.
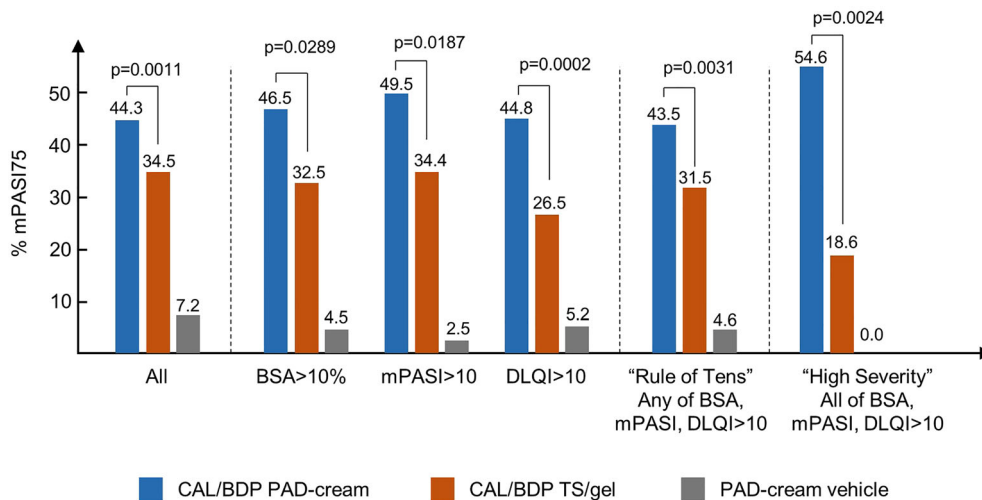

Fig. 3 Modified Psoriasis Area and Severity Index (mPASI)75 at week 8. Proportion of subjects achieving mPASI75 after 8 weeks of treatment with CAL/BDP PAD-cream, CAL/BDP TS/gel, or vehicle in the all patients population and higher severity subgroups. *CAL* calcipotriene, *BDP* betamethasone dipropionate, *TS* topical suspension, *PAD* polyaphron dispersion

Patients assessed the impact and convenience of the psoriasis treatment using the PTCS during the phase 3 studies. The scale consisted of six disease-specific, self-reported questions with a recall period of 1 week and rated on a numerical scale from 1 to 10. The PTCS total score was the sum of questions 1–5 and question 6 related to satisfaction with the treatment [36].

As shown in Table 2, the mean PTCS total score at week 1 of the CAL/BDP PAD-cream treatment group was significantly greater compared to the CAL/BDP TS/gel group both in the all patients population and in all individual subgroups. The significant differences in PTCS total scores between the treatment groups were maintained at week 8. Additionally, numerical differences between the CAL/BDP PAD-cream and CAL/BDP TS/gel treatments were greater in all higher baseline severity subgroups than the all patients population. The highest preference for CAL/BDP PAD-cream versus CAL/BDP TS/gel at week 8 was driven mainly by the individual PTCS questions concerning greasiness (questions 2 and 4) both for the all patients population and the rule of tens subgroup (Table 3).

DISCUSSION

As shown in this post hoc subgroup analysis, the proportion of patients achieving PGA treatment success as well as an mPASI75 response was higher in the high severity subgroup compared to the all patients population. Furthermore, the numerical difference in treatment efficacy between CAL/BDP PAD-cream and CAL/BDP TS/gel increased in patient subgroups with higher baseline severity with the high severity subgroup having the highest numerical difference. Similar patterns were shown for the patient-reported outcomes.

Indicated by the investigator-evaluated efficacy data, patients who had greater disease severity at baseline achieved greater efficacy than the total pooled patient population when treated with 8 weeks of CAL/BDP PAD-cream treatment and the difference in treatment efficacy compared to CAL/BDP TS/gel generally increased as well.

Topical therapies can be used as a treatment option for moderate-to-severe psoriasis as indicated by previous studies [37, 38]. In a post hoc subgroup analysis of a phase 3 study, patients with baseline severity according to the rule of
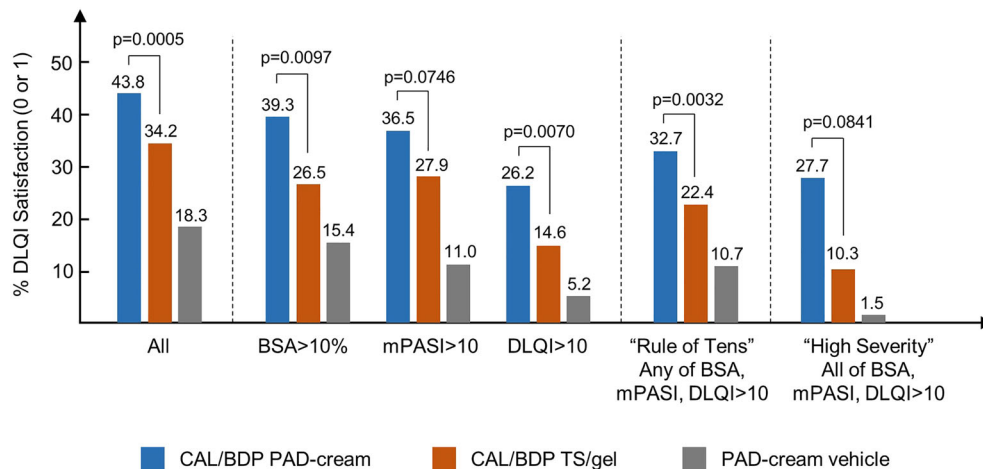

Fig. 4 Dermatology Life Quality Index (DLQI) satisfaction at week 8. Proportion of subjects achieving DLQI of 0 or 1 (DLQI satisfaction) after 8 weeks of treatment with CAL/BDP PAD-cream, CAL/BDP TS/gel, or vehicle in the all patients population and higher severity subgroups. *CAL* calcipotriene, *BDP* betamethasone dipropionate, *TS* topical suspension, *PAD* polyaphron dispersion

Table 2 Differences in mean Psoriasis Treatment Convenience Scale total scores at week 1 and week 8

	Week 1				Week 8			
	PAD-cream	TS/gel	Difference	P value	PAD-cream	TS/gel	Difference	P value
All patients, n = 1271	39.1	36.4	2.7	< 0.0001	40.4	37	3.4	< 0.0001
BSA > 10% subgroup, n = 319	39.7	36.0	3.7	< 0.0001	41.3	37.7	3.6	< 0.0001
mPASI > 10 subgroup, n = 288	40.7	37.0	3.7	< 0.0001	40.5	36	4.5	< 0.0001
DLQI > 10 subgroup, n = 505	38.7	34,7	4.0	< 0.0001	39.3	35.3	4.0	< 0.0001
Rule of tens subgroup,[a] n = 705	39.0	35.1	3.8	< 0.0001	39.7	35.9	3.8	< 0.0001
High severity subgroup,[b] n = 104	38.9	35.4	3.5	0.0196	41.7	36.3	5.5	0.0001

MITT using last observation carried forward, while-on-treatment strategy. Differences and p values are for CAL/BDP PAD-cream vs. CAL/BDP TS/gel

TS topical suspension, *MITT* modified intention to treat, *BSA* body surface area, *mPASI* modified Psoriasis Area and Severity Index, *DLQI* Dermatology Life Quality Index, *CAL* calcipotriene, *BDP* betamethasone dipropionate, *PAD* polyaphron dispersion

[a]Rule of tens subgroup = BSA or mPASI or DLQI > 10
[b]High severity subgroup = BSA and mPASI and DLQI > 10

tens achieved numerically or statistically significant improvements with CAL/BDP foam compared to CAL/BDP TS/gel in PGA treatment success, mPASI75, and DLQI [39]; however, this was mainly at similar treatment success rates (32.0% for CAL/BDP foam) relative to the total mild-to-severe population (38.3%) [39, 40] in contrast to what we have shown here.

PASI75 is a measure of relative improvement with respect to baseline and therefore better treatment responses seen in the high severity subgroup compared to the all patients population may at least in part be explained as a function of the sensitivity of the measure. It is easier for an effective treatment to achieve a mPASI75 response in patients with a high PASI at baseline compared to patients with a lower PASI at baseline. However, the sensitivity of the measure cannot explain the observed differences between the PAD-cream and the gel formulation of CAL/BDP.

The high satisfaction and convenience of CAL/BDP PAD-cream demonstrated in this analysis may lead to better adherence to therapy and thereby potentially contribute to the better efficacy outcomes for this patient population. This may also translate into the real world, as seen in a non-interventional study with a topical agent where efficacy was higher in severe patients (Investigator's Global Assessment = 4) compared to the total population of mild-to-severe patients [41]. In a survey, the most cited reason from the patient's perspective for using topical therapy alone was fewer adverse effects than other treatments [14]. The safety profile of CAL/BDP PAD-cream is favorable and on par with other CAL/BDP products with no adverse drug reactions reported at a frequency > 1%. Another common reason for discontinuation is lack of effectiveness [14]. The efficacy outcomes we have shown here may contribute to the

Table 3 Differences in mean of individual PTCS questions at week 8

	All patients (*n* = 1271)		Rule of tens subgroup[a] (*n* = 705)	
	Difference, PAD-cream vs. TS/gel	*P* values, PAD-cream vs. TS/gel	Difference, PAD-cream vs. TS/gel	*P* values, PAD-cream vs. TS/gel
Q1. How easy was the treatment to apply to the skin?	0.2	0.0001	0.3	0.0084
Q2. How greasy was the treatment when applying it to the skin?	1.3	< 0.0001	1.4	< 0.0001
Q3. How moisturized did your skin feel after applying the treatment?	0.4	0.0018	0.6	0.0020
Q4. How greasy did your skin feel after applying the treatment?	1.2	< 0.0001	1.3	< 0.0001
Q5. How much did treating your skin disrupt your daily routine?	0.3	0.0136	0.3	0.0269
Q6. Overall, how satisfied were you with the medical treatment?	0.7	< 0.0001	0.6	0.0009

PTCS Psoriasis Treatment Convenience Scale, *TS* topical suspension, *PAD* polyaphron dispersion, *BSA* body surface area, *mPASI* modified Psoriasis Area and Severity Index, *DLQI* Dermatology Life Quality Index
[a]Rule of tens subgroup = BSA or mPASI or DLQI > 10

increased satisfaction with the treatment observed in this population.

Applying topical agents to a large BSA can be challenging. However, CAL/BDP PAD-cream is a non-greasy, easy spreadable cream that is scored high in convenience even by patients with moderate-to-severe disease, which makes it an option for some patients with moderate-to-severe psoriasis either as monotherapy or as adjunctive therapy to systemic/biologic agents. The high convenience of CAL/BDP PAD-cream is important. A survey conducted in 1281 European patients with psoriasis confirmed that cosmetic acceptability together with efficacy and safety is a very important aspect of a successful psoriasis treatment [42].

Limitations of this study include that it was a subgroup post hoc analysis of two pooled studies, which were not specifically designed for this analysis. Furthermore, the subgroups in this analysis are based on the rule of tens, although there is little consensus on the categorization and severity criteria of psoriasis.

CONCLUSIONS

In this subgroup analysis, patients who had higher disease severity at baseline achieved greater efficacy than the total patient population when treated with 8 weeks of CAL/BDP PAD-cream as compared to a currently marketed active comparator. Additionally, as indicated by this analysis, CAL/BDP PAD-cream treatment may also be more convenient and less greasy, which may reduce the burden of daily treatment and improve adherence to therapy.

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Compliance with Ethics Guidelines. The studies were performed in accordance with the Helsinki Declaration of 1964 and its later amendments. The study protocols were approved by institutional review boards at each site, and all participants provided written informed consent prior to any study-related procedures. A list of study sites is available as Supplementary Table 1.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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