EFFICACY AND SAFETY OF CALCIPOTRIENE/BETAMETHASONE DIPROPIONATE CREAM FOR THE TREATMENT OF PLAQUE PSORIASIS EVALUATED FROM POOLED PHASE 3 DATA

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INTRODUCTION

- The fixed dose combination of calcipotriene (CAL 0.005% w/w, 50 µg/g) and betamethasone dipropionate (BDP 0.064% w/w, 0.5 mg/g - as betamethasone) is a well-established treatment option for psoriasis based on strong scientific rationale for the single agents having complementary efficacy and safety.
- CAL/BDP PAD-cream is an easily spreadable cream based on PAD Technology™, an innovative formulation and drug delivery system[1].

METHODS

- CAL/BDP PAD-cream was evaluated in two Phase 3, multicentre, randomized, investigator-blinded, parallel-group trials (NCT03802344 and NCT03308799) comparing the efficacy of CAL/BDP PAD-cream with CAL/BDP gel/topical suspension (TS) and PAD-cream vehicle. Adult patients with mild-moderate psoriasis according to the Physician Global Assessment (PGA) were enrolled and applied trial medication once daily for up to 8 weeks.
- The primary endpoint in the US trial (NCT03308799) was the proportion of subjects who achieved minimum 2-points improvement in PGA to clear or almost clear disease from Baseline to Week 8. The primary endpoint of the EU trial (NCT03802344) was the percentage change in modified Psoriasis Area and Severity Index (mPASI) from Baseline to Week 8.
- The two phase 3 trials each evaluated superiority of CAL/BDP PAD-cream versus PAD-cream vehicle, and non-inferiority versus CAL/BDP gel/TS.
- The statistical analysis of pooled phase 3 data presented herein was performed as an exploratory, post-hoc analysis to evaluate statistical differences between CAL/BDP PAD-cream and CAL/BDP gel/TS based on a modified intention-to-treat population (n=1271) having at least one assessment of PGA after Baseline. Multiple imputation for missing data was applied for endpoints, except for Psoriasis Treatment Convenience Scale (PTCS) for which missing data was imputed using a Last Observation Carried Forward approach.

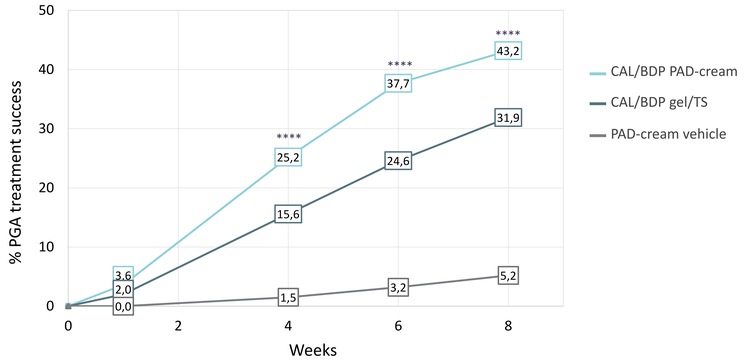
RESULTS

- Overall, 1271 patients were included in this analysis, 551 patients were in the CAL/BDP PAD-cream group, 542 patients were in the CAL/BDP gel/TS group, and 178 patients were in the PAD-cream vehicle group. Overall, demographic and baseline characteristics were comparable between the three treatment groups **(Table 1)**.
- The proportion of patients achieving PGA treatment success (at least 2-step improvement to clear or almost clear) at Week 8 was statistically significantly higher in the CAL/BDP PAD-cream group (43.2%) compared to the CAL/BDP gel/TS group (31.9%) (p<0.0001). Moreover, a statistically significant difference in PGA between CAL/BDP PAD-cream and CAL/BDP gel/TS was observed as early as Week 4 (p=0.0001) **(Figure 1).**

Table 1. Baseline demographics and characteristics

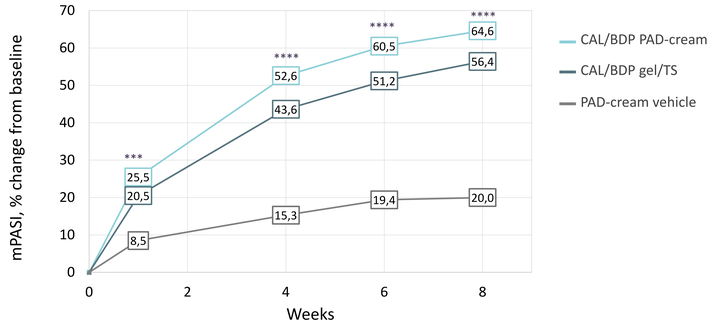
	CAL/BDP PAD-cream (n=551)	CAL/BDP gel/TS (n=542)	PAD-cream vehicle (n=178)
Mean age, years (SD)	50.9 (14.1)	52.2 (14.2)	50.6 (13.8)
Male, n (%)	337 (61.2)	333 (61.4)	113 (63.5)
Mean PGA (SD)	2.8 (0.4)	2.8 (0.4)	2.8 (0.4)
Mean mPASI (SD)	7.5 (3.9)	7.8 (4.0)	7.6 (4.0)
Mean DLQI (SD)	9.6 (6.0)	9.9 (6.7)	9.3 (6.2)

Figure 1. PGA Treatment Success



- The mean percentage reduction in mPASI from Baseline to Week 8 was significantly greater for CAL/BDP PAD-cream (64.6%) than CAL/BDP gel/TS (56.4%) (p<0.0001). The difference in mPASI treatment effect between CAL/BDP PAD-cream and CAL/BDP gel/TS was statistically significant as early as Week 1 (p=0.0009) **(Figure 2)**.

Figure 2. mPASI, percentage change from baseline



*: p<0.05; **: p<0.01; ***: p<0.001; ****: p<0.0001; CAL/BDP PAD-cream vs. CAL/BDP gel/TS

- The mean Dermatology Life Quality Index (DLQI) improvement from Baseline to Week 8 was significantly greater for CAL/BDP PAD-cream (6.5 points) compared to CAL/BDP gel/TS (5.6 points) (p<0.0001) **(Figure 3)**. A DLQI between 0 and 1 (no or little impact of disease on the patient's life) at Week 8 was obtained by 43.8% in the CAL/BDP PAD-cream group and 34.2% in the CAL/BDP gel/TS group (p=0.0005).
- CAL/BDP PAD-cream treatment convenience, as measured by the PTCS **(Table 2)** was higher than for CAL/BDP gel/TS at all studied time points, and significantly higher for all individual questions at week 8 compared to CAL/BDP gel/TS **(Fig. 4)**.
- CAL/BDP PAD-cream was well tolerated with no adverse drug reactions with a frequency above 1%.

Figure 3. Mean DLQI improvement

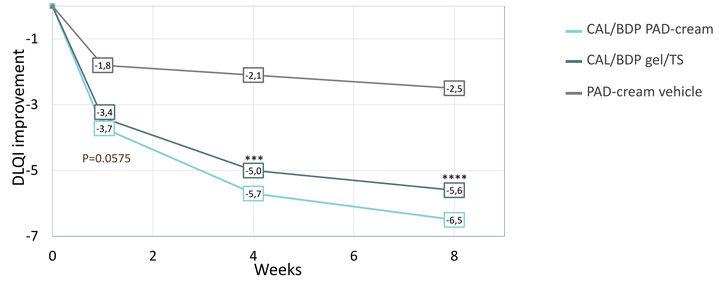
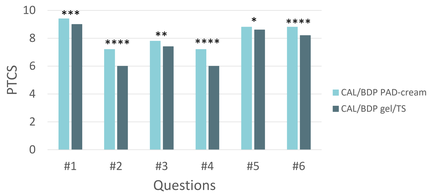


Table 2. PTCS Questions

#	PTCS questions
1	How easy was the treatment to apply to the skin?
2	How greasy was the treatment when applying it to the skin?
3	How moisturized did your skin feel after applying the treatment?
4	How greasy did your skin feel after applying the treatment?
5	How much did treating your skin disrupt your daily routine?
6	Overall, how satisfied were you with the medical treatment?

Figure 4. PTCS at week 8



CONCLUSIONS

- In an exploratory post-hoc statistical analysis of the pooled phase 3 data, CAL/BDP PAD-cream showed significantly greater efficacy than CAL/BDP gel/TS. Patient-reported outcomes demonstrate that CAL/BDP PAD-cream generally offers greater patient satisfaction when compared to CAL/BDP gel/TS.

REFERENCES

[1]Praestegaard M, Steele F, Crutchley N. Polyaphron dispersion technology, a novel topical formulation and delivery system combining drug penetration, local tolerability and convenience of application. Dermatol Ther (Heidelb). 2022 Oct;12(10):2217-2231.

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- PGA, Physician Global Assessment. mPASI, modified Psoriasis Area and Severity Index. DLQI, Dermatology Life Quality Index. BDP, betamethasone dipropionate. CAL, calcipotriene. PTCS, Psoriasis Treatment Convenience Scale. SD, standard deviation. TS, Topical suspension.