

PHASE 3 TRIAL DEMONSTRATING HIGH EFFICACY, FAVOURABLE SAFETY, AND CONVENIENCE OF A NOVEL CALCIPOTRIENE AND BETAMETHASONE DIPROPIONATE CREAM

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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 system¹.

METHODS

- CAL/BDP PAD-cream was evaluated in a Phase 3, multicentre, randomized, investigator-blind, active, and vehicle-controlled trial (NCT03802344) enrolling 490 adult patients with mild to moderate psoriasis according to the Physician Global Assessment (PGA) scale.
- The aim of the trial was to evaluate the efficacy and safety of CAL/BDP PAD-cream as well as treatment acceptability compared to cream vehicle and to CAL/BDP Topical Suspension (TS)/gel (sourced in the EU as Dovobet®/Daivobet® gel).
- Patients applied trial medication once daily for up to 8 weeks.
- The trial was conducted at 32 clinical sites across three European countries.
- Primary endpoint was percentage change in modified Psoriasis Area and Severity Index (mPASI) from baseline to week 8.
- Except for Psoriasis Treatment Convenience Scale (PTCS), the endpoints were analysed using the treatment-policy estimand for the full analysis set. As per protocol, the percentage change in mPASI from baseline to week 8 for CAL/BDP PAD-cream and the active comparator were first compared with cream vehicle for a superiority evaluation. Also per protocol, CAL/BDP PAD-cream was next compared to active comparator for a non-inferiority evaluation. Secondary endpoints were tested in a predefined testing hierarchy. Multiple imputation for missing data was applied for endpoints, except for PTCS for which missing data was imputed using a Last Observation Carried Forward approach.

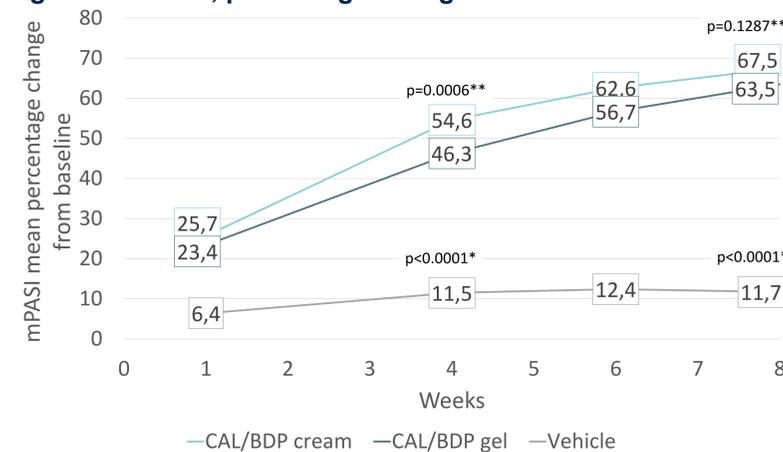
RESULTS

- Overall, 490 patients were randomised, 213 patients were in the CAL/BDP PAD-cream group, 209 patients were in the CAL/BDP TS/gel group, and 68 patients were in the cream vehicle group. Overall, all demographic characteristics were comparable between the three treatment groups (Table 1).
- The percentage mean change from baseline to week 8 in mPASI for CAL/BDP PAD-cream (67.5%) was superior compared to vehicle (11.7%; $p<0.0001$) and non-inferior to CAL/BDP TS/gel (63.5%) (Figure 1).

Table 1. Baseline demographics and characteristics

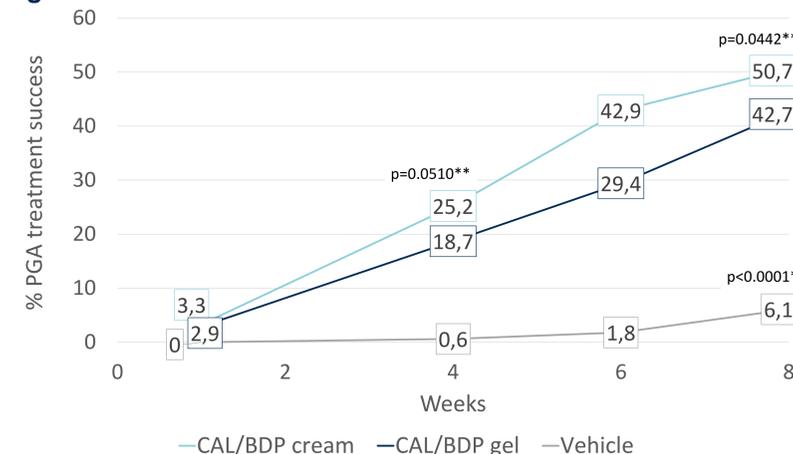
	CAL/BDP Cream (n=213)	CAL/BDP TS/gel (n=209)	Cream Vehicle (n=68)
Mean age, years (SD)	48.6 (13.7)	51.5 (14.8)	50.8 (13.3)
Male, n (%)	136 (63.8%)	113 (54.1)	46 (67.6)
Mean PGA (SD)	2.8 (0.4)	2.8 (0.4)	2.8 (0.5)
Mean mPASI (SD)	7.9 (4.0)	8.0 (3.8)	8.3 (3.8)
Mean DLQI	9.8	9.5	10.0

Figure 1. mPASI, percentage change from baseline



- At week 4, CAL/BDP PAD-cream demonstrated statistically significantly greater mean percentage change from baseline in mPASI compared to vehicle ($p<0.0001$) and to CAL/BDP TS/gel ($p=0.0006$) (Figure 1).
- The proportion of patients achieving PGA treatment success (2-step improvement to clear or almost clear) after 8 weeks was significantly greater for CAL/BDP PAD-cream (50.7%) compared to vehicle (6.1%, $p<0.0001$) and CAL/BDP TS/gel (42.7%, $p=0.0442$) (Figure 2).

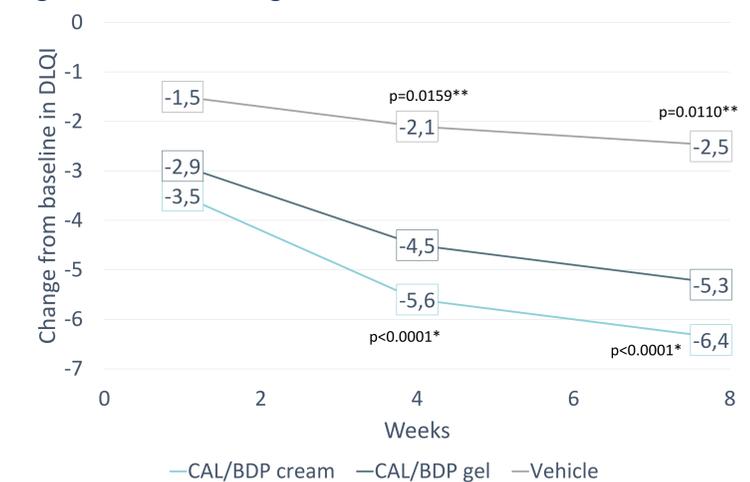
Figure 2. PGA Treatment Success



No subjects with PGA success were observed at Week 4 in the vehicle group. For this reason, statistical analysis of the difference between CAL/BDP PAD-cream and vehicle was inconclusive due to wide 95% Confidence Intervals, although substantial differentiation is demonstrated by the separation.

- Also at week 4, the proportion of patients achieving PGA treatment success was higher in the CAL/BDP PAD-cream group (25.2%) compared to the vehicle group (0.6%) and numerically higher than the CAL/BDP TS/gel group (18.7%; $p=0.0510$) (Figure 2).
- The patient reported PTCS score for CAL/BDP PAD-cream was rated superior to CAL/BDP TS/gel at week 8 ($p<0.0001$) and was also significantly higher at week 4 ($p<0.0001$), demonstrating that CAL/BDP PAD-cream has superior treatment convenience compared to CAL/BDP TS/gel.
- The mean change in Dermatology Life Quality Index (DLQI) score from baseline to week 8 improved statistically significantly more in the CAL/BDP PAD-cream group compared to both vehicle ($p<0.0001$) and CAL/BDP TS/gel ($p=0.0110$) (Figure 3). A statistically significant difference was also observed at week 4 for CAL/BDP PAD-cream compared to vehicle ($p<0.0001$) and CAL/BDP TS/gel ($p=0.0159$) (Figure 3).
- Safety assessments during the trial demonstrated that CAL/BDP PAD-cream was well-tolerated with all adverse reactions reported at a frequency below 1%.

Figure 3. Mean change in DLQI



A negative change from Baseline indicates a decrease in DLQI, i.e., an improvement in the patient's quality of life.

CONCLUSIONS

- CAL/BDP PAD-cream, an innovative topical treatment for plaque psoriasis based on PAD Technology, offers high efficacy combined with a favourable safety profile and a superior patient reported treatment convenience compared to CAL/BDP TS/gel.

REFERENCES

¹Praestegaard 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.

ACKNOWLEDGEMENTS & ABBREVIATIONS

- Writing support was provided by Anja Snel-Prentø, MedLink.
- The trial was funded by MC2 Therapeutics.
- 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. *comparison of CAL/BDP PAD-cream to vehicle. **comparison of CAL/BDP PAD-cream to CAL/BDP TS/gel.