Vasoconstrictor potency of fixed combination calcipotriol plus betamethasone dipropionate foam versus other corticosteroid psoriasis treatments

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Introduction

- Many topical corticosteroids (CS) of differing potencies and formulations are available for treating psoriasis vulgaris
- Topical CS potency can be assessed by the vasoconstriction assay (McKenzie-Stoughton), which is based on the blanching response of skin induced by topical CS application on healthy skin[1]
  - This assay is recommended for topical CS potency ranking based on a correlation with clinical efficacy in psoriasis
- A foam formulation of fixed-dose combination calcipotriol 50 µg/g (Cal) and betamethasone 0.5 mg/g (as dipropionate; BD) has been developed as a treatment option for patients with psoriasis
  - Clinical studies have demonstrated greater efficacy with Cal/BD foam versus the gel and ointment formulations[2-6]
- The objective of this study was to compare the CS potency of BD in Cal/BD foam with existing CS-containing topical products

Methods

PATIENTS

- The study enrolled healthy, non-smoking volunteers aged 18–50 years
  - All subjects were required to demonstrate adequate vasoconstriction prior to the study, defined as a visual skin blanching score of at least one unit following non-occlusive BD 0.05% ointment application for 4–6 hours
- Subjects were excluded if they received systemic treatments or any medications that could interfere with the blanching reaction within 2 weeks, or had used topical CS on the test sites within 4 weeks prior to enrolment

STUDY DESIGN

- This was a Phase I, single-centre, investigator-blinded, vehicle-controlled, intra-individual comparison study (NCT02973776)
- Each volunteer received a single application, under non-occlusive conditions of: Cal/BD foam, clobetasol propionate 0.05% cream (CP; very potent), BD 0.05% ointment (potent), mometasone furoate 0.1% cream (MF; potent), hydrocortisone-17-butyrate 0.1% ointment (HB; moderately potent) and foam vehicle to six circular test sites (each 2.2 cm in diameter) on the anterior forearms
- After 16 hours of exposure, any remaining product was removed

STUDY OBJECTIVES AND ASSESSMENTS

- The primary objective was to compare the vasoconstriction potential of Cal/BD foam with the other treatments using the human skin blanching test (McKenzie-Stoughton vasoconstriction assay)[1]
- Skin blanching for each treatment was assessed 2 hours after the 16-hour application period by two independent, trained observers
  - Visual assessment of skin blanching was scored on a 9-point scale from 0–4 (0 = no change, 4 = maximal blanching; half-point scores were used for intermediate changes)
- Local tolerability was assessed at the same time as skin blanching and at follow-up; safety was assessed throughout the study by evaluation of adverse events (AEs)

STATISTICAL ANALYSIS

- The mean of the two individual skin blanching visual scores were calculated for each treatment, and non-parametric tests were performed. Kruskal-Wallis test for the overall effect, and Wilcoxon Signed Rank test for the pairwise comparisons (Cal/BD foam vs other treatments)

Results

PATIENTS

- A total of 36 healthy volunteers were randomized and analysed (Table 1)

Table 2. Baseline demographic and characteristics of randomized subjects

	Subjects (n=36)
Median age (range), years	34.5 (19–50)
Males:Females, n (%)	14:22 (38.9:61.1)
Race, n (%)	
White	36 (100.0)
Fitzpatrick skin type, n (%)	
II	5 (13.9)
III	30 (83.3)
IV	1 (2.8)
Median BMI (range), kg/m^2	22.9 (16.2–34.5)

BMI, body mass index

ASSESSMENT OF SKIN BLANCHING

- All active treatments resulted in greater skin blanching compared with foam vehicle (Figure 1; Table 2)

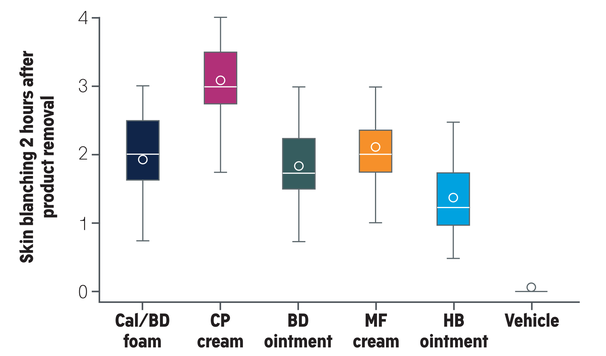

Figure 1. Box plot showing visual assessment of skin blanching 2 hours after 16 hours of treatment application

The horizontal line represents the median, and the circle represents the mean; the box represents the interquartile range (IQR), and the whiskers represent the range within 1.5 x IQR

Table 2. Skin blanching scores by treatment, assessed 2 hours after 16 hours of treatment application

Treatment	Mean (SD)	Median (range)	*P* value (v Cal/BD foam)
Cal/BD foam	1.93 (0.56)	2.00 (0.75–3.00)	–
CP cream	3.09 (0.55)	3.00 (1.75–4.00)	<0.001
BD ointment	1.85 (0.59)	1.75 (0.75–3.00)	0.30
MF cream	2.11 (0.59)	2.00 (1.00–3.75)	0.22
HB ointment	1.40 (0.66)	1.25 (0.50–3.00)	<0.001
Foam vehicle	0.06 (0.13)	0 (0–0.50)	<0.001

SD, standard deviation

- Skin blanching with Cal/BD foam was significantly lower than with CP cream (P<0.001), similar to BD ointment and MF cream, and significantly higher than HB ointment and foam vehicle (P<0.001 for both) [Figure 1; Table 2]
- No AEs were reported, and all subjects had a local tolerability score of 0 (ie, no reaction)

Conclusions

- **Understanding topical CS potency is important to ensure the appropriate use of treatments for psoriasis:**
  - **The degree of skin blanching is used as a measure of the inherent potency of a CS, and its ability to diffuse into the skin**
- **This study showed that, consistent with CS potency classifications, the steroid potency of Cal/BD foam was similar to BD ointment and MF cream, significantly stronger than that of HB ointment, but weaker than that of very potent CP cream**
- **These findings expand on those from a previously reported Phase I study, which showed that Cal/BD foam was a more potent formulation than Cal/BD ointment[7]**

Acknowledgements

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References

1. McKenzie AW & Stoughton RB. *Arch Dermatol* 1962;86:608–10
2. Leonardi C *et al. J Drugs Dermatol* 2015;14:1468–77
3. Koo J *et al. J Dermatolog Treat* 2016;27:120–7
4. Paul C *et al. J Eur Acad Dermatol Venereol* 2017;31:119–26
5. Queille-Roussel C *et al. Clin Drug Investig* 2015;35:239–45
6. Stein GL *et al. J Drugs Dermatol* 2016;15:951–7
7. Queille-Roussel C *et al. J Eur Acad Dermatol Venereol* 2016;30:1951–6

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