

# **A Novel Aerosol Foam Formulation of Calcipotriol and Betamethasone Has No Impact on HPA Axis and Calcium Homeostasis in Patients With Extensive Psoriasis Vulgaris**

## **Supplementary file**

### **Methods**

#### ***Study design***

A safety follow-up visit was scheduled 2 weeks after week 4 in the event of an ongoing adverse event (AE) with a possible, probable or not assessable relationship to study medication, or in the event of elevated albumin-corrected serum calcium levels or clinically significant abnormal values of another laboratory parameter at week 4. A safety follow-up visit was scheduled 4 weeks after study day 28 in the event of abnormal results on the adrenocorticotrophic hormone (ACTH) challenge test (serum cortisol  $\leq 497$  nmol/L 30 minutes after ACTH challenge test), wherein another ACTH challenge test would be performed at the follow-up visit.

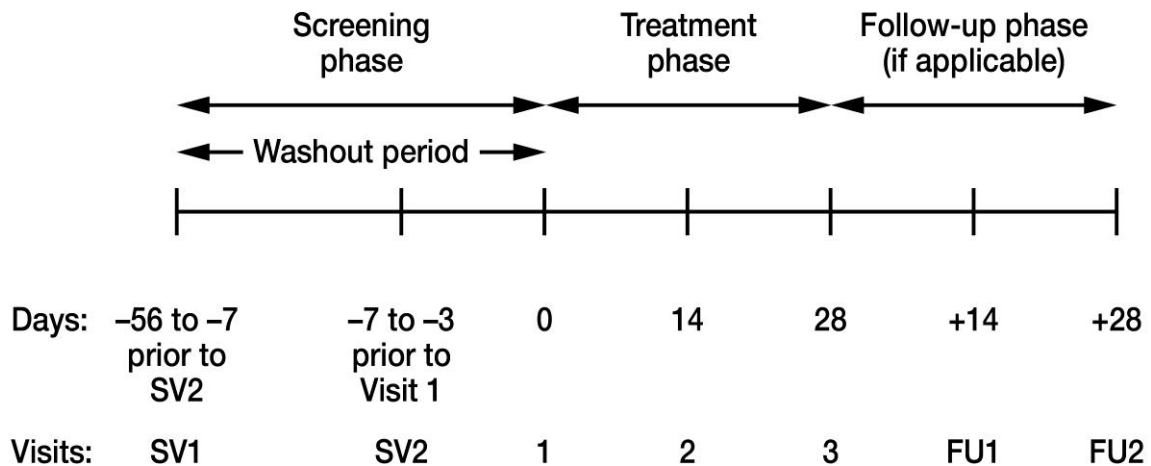
#### ***Exclusions and washouts***

Patients were excluded from the trial if they had a history of allergic asthma, serious allergy, serious allergic skin rash or known/suspected hypersensitivity to any of the agents applied during the study.

A washout period of up to 8 weeks was required for treatments known to affect cortisol levels or hypothalamic–pituitary–adrenal (HPA) axis integrity (corticosteroids, cytochrome P [CYP] 3A4 inducers, CYP 3A4 inhibitors, antidepressive medications, oestrogen), calcium metabolism (vitamin D supplements  $>400$  IU/day and calcium supplements), or which could affect psoriasis (systemic/topical/ultraviolet [UV] antipsoriatic therapy, although emollients were allowed). Systemic treatment for psoriasis within the following time windows was forbidden: corticosteroids within 12 weeks prior to screening visit 2; etanercept within 4 weeks of baseline; adalimumab, alefacept, infliximab within 8 weeks of baseline; ustekinumab within 16 weeks of baseline; other systemic products within 4 weeks or five half-lives, whichever is longer, of baseline. Combination psoralen plus UVA treatment was disallowed within 4 weeks of baseline. UVB therapy and topical treatment of psoriasis on the trunk, limbs and scalp

were disallowed within 2 weeks of baseline, and topical treatment with corticosteroids or vitamin D analogues on any location was forbidden within 2 weeks of screening visit 2.

**Figure. Study design**



Day 0 is treatment baseline; SV2 is considered the same as baseline for laboratory tests. FU, follow-up; SV, screening visit.

### ***Cortisol assay***

The cortisol assay used was the Siemens ADVIA Centaur<sup>®</sup> XP, which had an assay precision of 5.5% coefficient of variation. The analytic range was 5.5–2070 nmol/L and the sensitivity was 5.5 nmol/L.

### ***Statistical analysis***

It was calculated that with this sample size, the upper limit of an exact 95% confidence interval would be 12% of the risk of a patient experiencing serum cortisol levels  $\leq 497$  nmol/L 30 minutes after the ACTH challenge test, assuming that the event was not observed for any of the 30 patients.

**Table. PGA definitions**

<b>Score</b>	<b>Category description</b>
Clear	Plaque thickening = no elevation or thickening over normal skin Scaling = no evidence of scaling Erythema = none (no residual red colouration, but post-inflammatory hyperpigmentation may be present)
Almost clear	Plaque thickening = none or possible thickening, but difficult to ascertain whether there is a slight elevation above normal skin level Scaling = none or residual surface dryness and scaling Erythema = light pink colouration
Mild	Plaque thickening = slight but definite elevation Scaling = fine scales partially or mostly covering lesions Erythema = light red colouration
Moderate	Plaque thickening = moderate elevation with rounded or sloped edges Scaling = most lesions at least partially covered Erythema = definite red colouration
Severe	Plaque thickening = marked or very marked elevation typically with hard or sharp edges Scaling = non-tenacious or thick tenacious scale, covering most or all of the lesions Erythema = very bright red colouration, extreme red colouration, or deep red colouration