Safety of long-term proactive management with fixed-dose combination calcipotriene 0.005% and betamethasone dipropionate 0.064% foam in patients with psoriasis vulgaris: results of a Phase III, multicentre, randomized, 52-week, vehicle-controlled trial

Poster #12797

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Introduction

- Topical therapies are considered first-line treatment for psoriasis,[1] however maintaining long-term disease control is a challenge, with many patients untreated or undertreated.[2] Current topical psoriasis treatment relies on a reactive approach to disease flares, as opposed to a more long-term proactive approach.[3]
- Data supporting the efficacy and safety of calcipotriene 0.005% and betamethasone dipropionate 0.064% (Cal/BD) foam approved as a reactive treatment are available from trials of 4- and 12-weeks duration in patients with psoriasis vulgaris (plaque psoriasis).[4,5,6,7]
- Here, we report the safety of Cal/BD foam for the long-term proactive management of psoriasis over 52 weeks (NCT02899962). Data from the open-label lead-in phase of this trial are presented in poster #16830.

Materials and Methods

- This Phase III, multicenter trial included a 4-week open-label lead-in phase in adult patients with:
  - Trunk and/or limb psoriasis, involving 2–30% of body surface area (BSA); physician's global assessment (PGA) of disease severity ≥'mild'; modified psoriasis area and severity index (m-PASI) ≥2.
- Following the open-label lead-in phase, patients with treatment success (PGA score of 'clear' or 'almost clear' [PGA<2] with at least a 2-grade improvement from baseline) were randomized to the 52-week double-blind, vehicle-controlled maintenance phase.
- The trial included a subgroup of patients at assigned sites who underwent hypothalamic pituitary adrenal (HPA) testing. The HPA-axis group was required to have more severe disease:
  - At least 'moderate' psoriasis, affecting 10–30% BSA and normal adrenal function at baseline.

Double-blind treatment

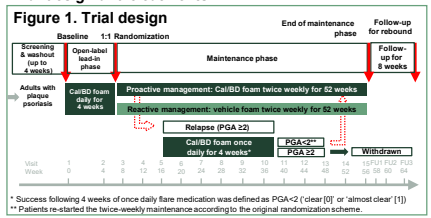
- 'Proactive' management was treatment with Cal/BD foam twice-weekly for 52 weeks when in remission.
- 'Reactive' management was treatment with vehicle foam twice-weekly for 52 weeks when in remission.
- Relapse: PGA≥2 [either previously treated and/or new skin area]). Flare medication (as separate flare bottles) was Cal/BD foam once-daily for 4 weeks for both the proactive and reactive management groups (Figure 1).

Primary objective

- Efficacy objectives, endpoints and data are presented in poster #18223.

Trial design and treatments

Figure 1. Trial design



* Success following 4 weeks of once daily flare medication was defined as PGA<2 ('clear [0]' or 'almost clear' [1])
** Patients re-started the twice-weekly maintenance according to the original randomization scheme.

Safety objectives and endpoints

- To evaluate the long-term safety of proactive management with Cal/BD foam (up to 52 weeks) in patients with psoriasis. Safety endpoints included:
  - Adverse events (AEs) associated with long-term corticosteroid use.
  - Incidence of rebound (see table 3 for definition).
  - Effect on calcium metabolism based on serum/urinary calcium.
  - Effect on HPA-axis based on serum cortisol.

Results

Patient population

- 545 patients were randomized (safety analysis set [SAS]; proactive n=272; reactive n=273). 251 (46.1%) patients completed the trial. Mean age was 52.2 years; 91% patients were white and 68% were male.

AEs during maintenance phase

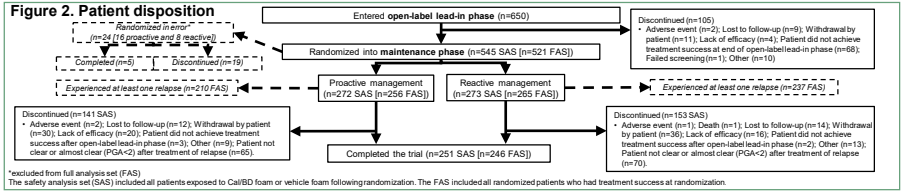
Table 1. Overview of AEs

AE category	Proactive (N=272)		Reactive (N=273)	
	Number of AEs	Number (%) of patients	Number of AEs	Number (%) of patients
All AEs	303	133 (48.9)	279	130 (47.6)
Serious AEs	15	14 (5.1)	14	11 (4.0)
Treatment-related AEs[1]	5	5 (1.8)	8	7 (2.6)
AEs leading to withdrawal	2	2 (0.7)	1	1 (0.4)
Severe AEs	8	8 (2.9)	15	14 (5.1)

[1]Considered possibly or probably related to trial product by the investigator

- One patient in each group had an AE of pigmentation disorder considered possibly related to trial product by the investigator. No AEs of skin atrophy were reported.

Figure 2. Patient disposition



*excluded from full analysis set (FAS)
The safety analysis set (SAS) included all patients exposed to Cal/BD foam or vehicle foam following randomization. The FAS included all randomized patients who had treatment success at randomization.

Table 2. Rate of AEs per 100 patient-years

	Proactive (N=272)	Reactive (N=273)
AEs per 100 patient-years	168.6	158.4
Serious AEs per 100 patient-years	8.3	7.9
Treatment-related AEs per 100 patient-years	2.8	4.5

Most frequently reported AEs

- AEs reported in >5% of patients: nasopharyngitis (8.1% proactive vs 7.0% reactive) and upper respiratory tract infection (5.9% vs 5.5%); all were considered not related to trial product by the investigator.

AEs adjudicated as associated with long-term corticosteroid use in maintenance phase

- Chorioretinopathy in one patient: severe intensity, onset on Day 310, considered possibly related to treatment by investigator, led to withdrawal of treatment [proactive].
- Pain of skin in one patient: moderate intensity, onset on Day 73, not considered related to treatment by investigator, no action taken with treatment [proactive].
- Application site pain in one patient: 3 events of mild intensity, onset on Days 1, 12 and 20, considered probably related to treatment by investigator, no action taken with treatment [reactive].

Rebound

Table 3. Summary of rebounds*

Number of rebounds within 2 months	Proactive (N=272)	Reactive (N=273)
After discontinuation of open-label treatment	6	7
After discontinuation of relapse treatment	4	17
After discontinuation of proactive management	0	1

*Rebound defined as i) m-PASI ≥12 AND increase from baseline in m-PASI ≥125% or ii) development of more inflammatory disease within 2 months after discontinuation of open-label, maintenance or flare medication.

Other safety results

- No consistent changes or differences in serum or urinary calcium between the two treatment groups.
  - No difference in the number of patients moving from low or normal to high calcium or from normal or high to low calcium in either serum or urine. Most patients had levels that remained stable over time.
  - No clinically significant abnormalities in calcium metabolism were observed.
- In the HPA-axis group, no patient had serum cortisol ≤18 µg/dL at both 30 and 60 min after ACTH challenge.

Conclusions

- Proactive management with Cal/BD foam was well tolerated, with a favorable safety profile over the extended treatment period that was similar to the vehicle-controlled reactive treatment group.
- Proactive management with Cal/BD foam had no clinically significant effects on the HPA-axis or calcium metabolism.

References
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Acknowledgements
The authors thank the investigators and patients who participated in this trial. The authors would like to thank Lauren Whyte, PhD, a freelance Medical Writer contracted by Ashfield Healthcare Communications, part of UDG Healthcare plc, for medical writing support, funded by LEO Pharma in accordance with Good Publications Practice (GPP3) guidelines (http://www.ismpp.org/gpp3).

Disclosures
All authors met the ICMJE authorship criteria and had full access to the relevant data. Neither honoraria nor payments were made for authorship. ML, J-PL, DT, RBW, CL have consulted for, conducted studies funded by, or received honoraria for services provided to LEO Pharma; ML, MHM are employees of LEO Pharma. Fixed-dose combination calcipotriene (Cal) 0.005%/betamethasone dipropionate (BD) 0.064% aerosol foam is approved for the treatment of psoriasis vulgaris (plaque psoriasis) for up to 4 weeks in adults (under the trade name Enstilar® in the US and Enstilar® or Enstilum® in the EU). Cal/BD foam is also approved in the US for adolescents 12–18 years.

Funding
This study was funded by LEO Pharma.