Long-term proactive management of psoriasis vulgaris with fixed-dose combination of calcipotriene 0.005% and betamethasone dipropionate 0.064% foam: results of a Phase III randomized controlled trial

Poster #18223

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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 efficacy of Cal/BD foam in 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

- Eligible patients for this Phase III, multicentre trial received once-daily Cal/BD foam during the 4-week open-label lead-in phase (Figure 1).
  - 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.
- Patients achieving success at the end of the open-label lead-in phase (PGA score 'clear'/'almost clear' [PGA <2] with ≥2-grade improvement from baseline of the open-label lead-in phase) were randomized 1:1 to twice-weekly Cal/BD foam or vehicle foam for 52 weeks (Figure 1).

Double-blind treatment during the maintenance phase

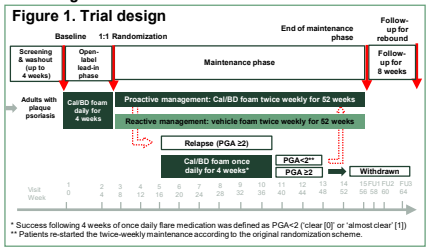
- 'Proactive' management was treatment with Cal/BD foam twice-weekly for 52 weeks when in remission.
- 'Reactive' management was treatment with vehicle foam twice-weekly for 52 weeks when in remission.
- Relapse: PGA≥2 [either previously treated and/or new skin area]). Flare medication (as separate flare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

Primary objective and endpoints

- To evaluate the efficacy of a twice-weekly proactive maintenance regimen with Cal/BD foam compared with reactive management with vehicle foam in the prevention of relapse in patients with psoriasis.
  - Time to first relapse (defined as a PGA score of at least 'mild' [PGA≥2]).

Trial design and treatments

Figure 1. Trial design



Secondary objective and endpoints

- To evaluate the long-term efficacy (up to 52 weeks) of proactive management twice weekly as maintenance therapy compared with reactive management in patients with psoriasis.
  - Number of relapses.
  - Proportion of days in remission (PGA<2).

Safety objective

- Safety objectives, endpoints and data are presented in poster #12797.

Results

Patient population

- 545 patients were randomized (safety analysis set [SAS]); 521 achieved treatment success in the open-label lead-in phase (proactive n=256; reactive n=265 [full analysis set (FAS)]). 251 (46.1%) patients completed the trial.
- Disease characteristics at randomization were similar between groups. Mean age of randomized patients was 52.2 years; 91% of patients were white and 68% male.
- 82% of randomized patients in each treatment group had a PGA score of 'moderate' at baseline of the open-label lead-in phase.

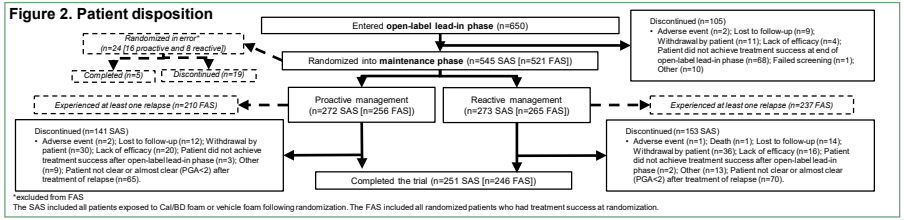
Time to first relapse

Table 1. Time to first relapse

	Proactive (N=256)	Reactive (N=265)
Median time to first relapse*	56 days	30 days

*Number of days from randomization until 50% of patients had experienced their first relapse.

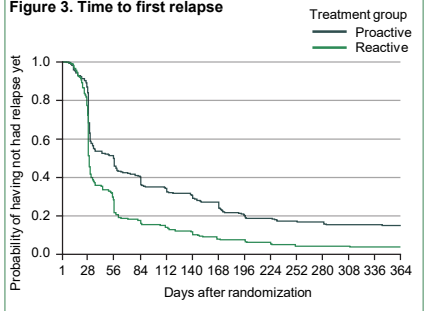
Figure 2. Patient disposition



*excluded from FAS

The 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.

Figure 3. Time to first relapse



Number of patients with no relapse yet

Proactive	256	219	128	100	83	75	65	47	41	36	34	31	31	24
Reactive	265	198	73	40	32	25	17	15	11	8	8	7	6	5

Patients who did not achieve PGA<2 after 4 weeks of once-daily flare medication following relapse were withdrawn from the trial.

- **43% reduction in risk of experiencing a first relapse** for patients in the proactive group compared to reactive group (hazard ratio, 0.57; 95% confidence interval [CI], 0.47–0.69; p<0.001).

Rate of relapse

- **Rate of relapse over 1 year was reduced by 46%** in the proactive group compared to the reactive group (95% CI, 37–54%; p<0.001).
- Predicted number of relapses in 1 year was 4.0 in the proactive group and 7.5 in the reactive group.

Remission

- Patients in the proactive group had **41 extra days in remission** compared to patients in the reactive group (p<0.001), **over 1 year** (95% CI, 29–53 days).

Safety results

- Proactive management was **well tolerated** over the 52-week trial period (data presented in poster #12797).

Conclusions

- Proactive management with Cal/BD foam was superior in prolonging time to first relapse, reducing number of relapses and increasing days in remission versus vehicle-controlled reactive management.
- The results of this trial are promising. They are the first to demonstrate that proactive management with fixed-dose Cal/BD foam could offer improved long-term control of psoriasis over conventional reactive treatment.

References

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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 Ènstilum® in the EU). Cal/BD foam is also approved in the US for adolescents 12–18 years.

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