

# A 12-Week Study to Evaluate the Safety and Efficacy of a New Topically Applied LCD (Coal Tar) Solution versus Calcipotriol Cream for the Treatment of Moderate Plaque Psoriasis

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## Introduction

Topical application of coal tar has been used to control the symptoms of plaque psoriasis for centuries.<sup>1</sup> Generally recognized as a safe, effective, and inexpensive treatment,<sup>2</sup> coal tar appears to suppress the hyperproliferation of keratinocytes,<sup>3</sup> leukocytes, and pro-inflammatory cytokines<sup>4</sup> during psoriatic flares and to restore the appearance of normal, healthy skin.<sup>5</sup> However, its historically unappealing aesthetic profile and the availability of topical corticosteroids, Vitamin D analogues (calcipotriol), and synthetic retinoids (tazarotene) have reduced the use of coal tar formulations by patients and dermatologists. A new leave-on topical coal tar solution – containing 15% liquor carbonis distillate (LCD, equivalent to 2.3% coal tar) in a novel vehicle that reduces messiness, odor, and staining – has been developed to increase patient satisfaction and compliance with psoriasis therapy.

## Objective

The objective of this study was to compare the safety, efficacy, and patient satisfaction with use of LCD solution to calcipotriol cream over 12 weeks in 60 adults with moderate plaque psoriasis. Interim results for 48 patients are presented herein.

## Study Methodology

<b>Design</b>	Randomized, investigator-blind, monadic, active-controlled
<b>Population/Inclusion</b>	60 patients including males and females in general good health, 18 years or older, with moderate chronic plaque psoriasis involving 3-15% body surface area (BSA), excluding scalp, face, palms, soles, and groin
<b>Exclusion Criteria</b>	Topical psoriasis treatment within previous 2 weeks; phototherapy or oral therapy within previous 4 weeks; systemic immunomodulatory therapy within previous 12 weeks; impaired renal or liver function; pregnancy/lactation
<b>Duration</b>	12 weeks
<b>Treatments</b>	Group 1 (n=30): LCD solution 15% (Psorent <sup>®</sup> ), twice daily Group 2 (n=30): Calcipotriol cream 0.005% (Dovonex <sup>®</sup> ), twice daily Groups 1 & 2: Commercially available topical moisturizing lotion used as needed.
<b>Evaluation Visits</b>	Baseline, Week 2, Week 4, Week 8, and Week 12
<b>Evaluation Tools</b>	<ul style="list-style-type: none"> <li><b>Investigator</b> <ul style="list-style-type: none"> <li>PASI (Psoriasis Area Severity Index): scalp was excluded from PASI calculations and scores were adjusted in a proportional manner</li> <li>PGA (Physician's Global Assessment)</li> </ul> </li> <li><b>Patient</b> <ul style="list-style-type: none"> <li>Pruritus scale</li> <li>DLQI (Dermatology Life Quality Index)</li> <li>Self-Assessment Questionnaire: effectiveness, tolerability, and overall satisfaction with treatment</li> </ul> </li> <li><b>Photography</b> <ul style="list-style-type: none"> <li>Digital images via a Canfield camera system</li> </ul> </li> <li><b>Drug Safety</b> <ul style="list-style-type: none"> <li>Observed and reported adverse events</li> </ul> </li> </ul>

## Statistics

Data were analyzed using a modified intent-to-treat (ITT) population. Patients were included in data analysis if one follow-up visit was completed after baseline, using the last observation carried forward (LOCF) method for patients not completing the study according to protocol. Data were analyzed using the following statistical methods:

- > Categorical PASI Improvement (PASI 75 or PASI 50): Fisher's Exact test
- > Mean change in PASI Scores: 2-sided T-test
- > PGA, Pruritus, DLQI: Cochran-Mantel-Haenszel (CMH) test
- > Self-Assessment: Wilcoxon Rank Sum test

## Results

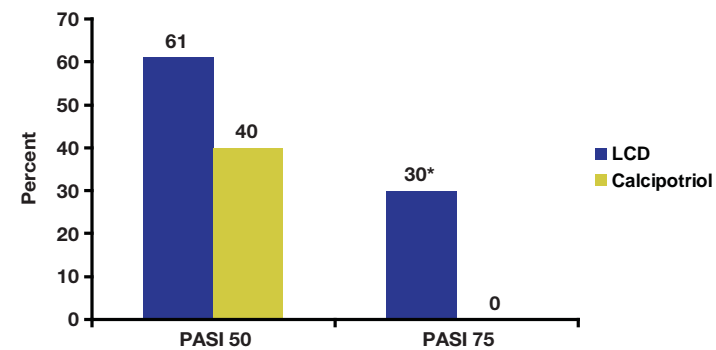
> 60 patients have been enrolled into the study: 48 patients have completed treatment and represent the modified ITT population for this interim analysis (n=23 LCD, n=25 calcipotriol); 5 patients failed to return after baseline; 7 patients are currently receiving treatment.

> Enrolled patients include 26 females and 34 males with an average age of 48.4 years; 52 Caucasians, 2 Hispanics, 3 African-Americans, 2 Asian, and 1 Other.

## PASI: Primary Efficacy Endpoint

- > **PASI 50** (50% or greater PASI improvement): More patients achieved PASI 50 in the LCD solution group (14/23, 61%) than in the calcipotriol cream group (10/25, 40%),  $p > 0.10$ .
- > **PASI 75** (75% or greater PASI improvement): Significantly more patients achieved PASI 75 in the LCD solution group (7/23, 30%) than in the calcipotriol cream group (0/25, 0%),  $p < 0.05$ .
- > **Mean Percentage Change in PASI** versus Baseline: Mean PASI scores were improved 55% with LCD solution versus 39% with calcipotriol cream,  $p < 0.10$ .

## Proportion of Patients Achieving PASI 50 and PASI 75



## PGA, Pruritus, DLQI: Secondary Efficacy Endpoints

- > **PGA scores** versus baseline improved for both treatment groups over the 12-week study,  $p < 0.05$ . At week 12, the LCD treatment group improved 45% relative to baseline versus the calcipotriol treatment group, 29%,  $p = 0.054$ .
- > Treatment with LCD solution and calcipotriol cream significantly reduced pruritus and improved mean DLQI scores versus baseline; there were no statistically significant differences between treatments,  $p < 0.05$ .

## Drug Safety

- Treatment-related adverse events were comparable for LCD and calcipotriol. Both treatments were safe and well tolerated.
- > LCD: moderate worsening of psoriasis (n=2); mild folliculitis (n=1), mild phototoxic reaction after unprotected sun exposure (n=1).
  - > Calcipotriol: moderate worsening of psoriasis (n=2); mild irritant contact dermatitis (n=1), mild burning pain after application (n=1).

## Clinical Photography



## Self-Assessment

- > **Drug product aesthetics** were evaluated using a 9-point ordinal scale: 1=poor, 3=fair, 5=good, 7=very good, 9=excellent. LCD solution was comparable to calcipotriol cream, and both treatments were rated better than "good" (score of 5) at all time points.

## Mean Aesthetic Scores at Week 12

	LCD (n=21)	Calcipotriol (n=19)
<b>Ease of use</b>	7.7* (very good)	7.1 (very good)
<b>Speed of absorption</b>	6.9 (very good)	6.2 (very good)
<b>Dries quickly</b>	6.6* (very good)	6.2 (very good)
<b>Feels comfortable on skin</b>	7.0 (very good)	6.6 (very good)

\*LCD solution dab-on applicator was rated between "very easy" and "extremely easy" to use at all time points.  
\*LCD solution patients reported waiting an average of 5 minutes before dressing.

- > **Staining and scent** were evaluated to understand potential barriers to using LCD solution relative to calcipotriol, an aesthetically acceptable prescription cream formulation. Patients were asked to compare the study drug to psoriasis medications they had used previously using a 9-point ordinal scale: -2=worse, 0=same, 2=slightly better, 4=somewhat better, 6=much better. LCD patients also evaluated other scent parameters (like/dislike, lingering) using a 7-point descriptive scale. Staining and scent were found to be acceptable for LCD solution and calcipotriol cream.

## Compared with other psoriasis medications, how would you rate:

	Staining		Scent	
	LCD (n=21)	Calcipotriol (n=19)	LCD (n=21)	Calcipotriol (n=19)
<b>Week 4</b>	2.0 (slightly better)	n/a	0.7 (same)	3.0 (slightly - somewhat better)
<b>Week 12</b>	2.0 (slightly better)	4.1 (somewhat better)	1.3 (slightly better)	4.2 (somewhat better)

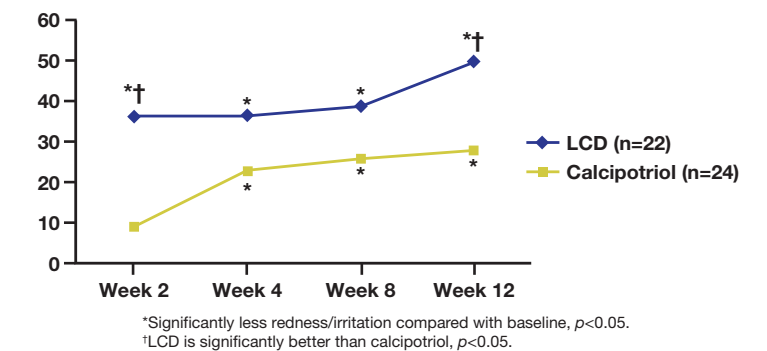
## Evaluation of LCD Scent\*

	Mean Score	Description
<b>Do you like the scent?</b>	-0.4	0 = neutral, -1 = "dislike a little"
<b>Does the scent linger?</b>	0.4	0 = neutral, 1 = "short time/no bother"

\* (7-point scale: -3 to +3, n=21).

- > **Severity of psoriasis symptoms** was self-assessed using a 7-point ordinal scale: 0=none, 2=mild, 4=moderate, 6=severe. LCD reduced self-assessed redness/irritation, itch and burning significantly faster than calcipotriol, week 2,  $p < 0.05$ . Both treatments significantly reduced all self-assessed parameters relative to baseline at weeks 4, 8 and 12: redness/irritation, burning, flaking/scaling, itching, roughness, and overall discomfort,  $p < 0.05$ ; LCD was statistically better than calcipotriol in reducing redness/irritation at week 12,  $p < 0.05$ .

## Self-Assessment Erythema/Irritation



- > **Drug product tolerability** was self-assessed using a 9-point ordinal scale: 1=poor, 3=fair, 5=good, 7=very good, 9=excellent. LCD and calcipotriol were comparable and rated better than "good" (score of 5) at all time points.

## Mean Tolerability Scores

	LCD (n=21)	Calcipotriol (n=19)
<b>Does not sting or burn</b>	6.8 (very good)	7.3 (very good)
<b>Not irritating</b>	7.0 (very good)	7.3 (very good)

## Summary

At this time point, this ongoing study demonstrates that, in patients with moderate plaque psoriasis, the topical LCD solution with a favorable aesthetic profile was clinically effective compared with calcipotriol, a widely used topical therapy for psoriasis. In addition, patient satisfaction with the aesthetics and ease of use of LCD solution was high, suggesting that this novel formulation of coal tar is an important addition to the therapeutic armamentarium for psoriasis. LCD solution provides a needed alternative in topical drug therapy for psoriasis. Specifically, this interim analysis shows that:

- > **Efficacy:** PASI and PGA scores significantly improved versus baseline for both treatment groups at the end of therapy. LCD solution outperformed calcipotriol cream in terms of the proportion of subjects achieving PASI 75.
- > **Safety/Tolerability:** LCD solution and calcipotriol cream were safe and well tolerated, as well as nonirritating and nonstinging.
- > **Patient Satisfaction:** LCD solution and calcipotriol cream significantly reduced the self-assessed severity of psoriasis symptoms and were rated very easy to use. LCD solution reduced redness/irritation, itch and burning significantly faster than calcipotriol. LCD solution dabs onto skin easily and dries quickly.
- > **Aesthetics:** Calcipotriol cream was rated favorably; LCD solution was also rated well and equivalent to calcipotriol cream in most cases. LCD solution's staining and scent were rated near neutral and were found to be acceptable to patients; no residual staining is apparent in the clinical photographs.

## References

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