Phase IV Open Label Evaluation of the Adrenal Suppression Potential and Pharmacokinetic Properties of Twice Daily Halobetasol Propionate Foam, 0.05% in Adolescent Subjects with Plaque Psoriasis

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Introduction

While psoriasis is most commonly thought to be an adult disease, studies show that approximately 30% of cases begin in childhood, with a current incidence approximately 205/100,000 in the adolescent population.[1,2] While there is consensus among clinicians that early treatment may help to prevent long-term psychosocial impact in adolescent patients, there is a general lack of clinical trial data and few approved medications in this age group, limiting treatment options.[2,3] Topical therapies such as corticosteroids are commonly used, but there is concern regarding long term side effects, especially the risk of adrenal suppression with the more potent corticosteroids.[3] A novel foam formulation of halobetasol propionate (HBP), 0.05%, was approved by the FDA in 2019 for the treatment of plaque psoriasis in adult patients, having been proven efficacious and well tolerated at doses of 3.5 grams per application with minimal systemic exposure and a favorable safety profile in patients 18 years and older.[4] The data shown here are the results of an adrenal safety and pharmacokinetic (PK) study of the HBP foam in adolescent patients with plaque psoriasis

Objectives

- Primary objective was to determine adrenal axis suppression potential and PK of HBP foam, 0.05% applied BID up to 2 weeks in patients age 12-17 years with stable plaque psoriasis.

Methods

- 24 subjects* aged 12 to <18 years with stable plaque psoriasis on at least 10% BSA (excluding face, scalp, groin, axillae, and other intertriginous areas), and an IGA of at least 3 (moderate) were instructed to apply HBP foam twice daily (approximately 12 hours apart) to all psoriatic plaques identified at baseline for up to 2 weeks, or until the investigator verified subjects' psoriasis had cleared.
- At screening, Day 15, and 4 weeks post end of study (EOS) HPA axis response to cosyntropin stimulation test (CST) was assessed.
- Plasma concentrations of HBP were measured at screening, Day 8, and Day 15.
- Changes in Investigator's Global Assessment (IGA) were at Screening, Baseline Visit/Day 1, Day 8, and Day 15.
- % body surface area (BSA) was estimated at Baseline Visit/Day 1, Day 8, and Day 15/EOS.
- Patient compliance with the prescribed treatment regimen also assessed at each follow-up visit.
- Adverse events, local skin reactions associated with topical application of corticosteroids (telangiectasia, skin atrophy, burning/stinging, and folliculitis), laboratory tests (chemistry, hematology, and urinalysis), and urine pregnancy tests were also assessed throughout the study.

Table 1: Baseline Demographics

GENDER	n(%)	IGA	n(%)
Female	11 (45.8)	3-moderate	22 (91.7)
Male	13 (54.2)	4-Severe	2 (9.3)
ETHNICITY	**n(%)**	**% BSA**	**Mean (Range)**
Hispanic or Latino	6 (25)	Affected	15.1 (11-23)
Not Hispanic or Latino	18 (75)	To be treated	14.5 (10-20)
RACE	**n(%)**	**AGE**	**Mean (Range)**
White	24 (100)	Years	14.7 (12.1-17.7)

***one subject was excluded from the evaluable and PK populations due to use of a prohibited medication**

Results

Laboratory evidence of HPA axis suppression, as evidenced by post-CST serum total cortisol level of ≤ 18µg/dL, was noted in 6 of 23 patients at Day 15 and resolved by the post-EOS study visit, ~4 weeks later. None of these had any clinical features of adrenal suppression and only 3 had measurable HBP plasma trough levels. In these 3 patients, no correlation was found between %BSA treated or average amount of product used and adrenal suppression or measurable HBP plasma trough levels. Overall, 9 patients of 23 had measurable plasma trough HBP levels at Day 15. The %BSA treated and average amount of product used was comparable for all study patients, including those with laboratory evidence of HPA suppression and measurable HBP plasma trough levels. By Day 15, 95.5% of patients had at least a 1-grade improvement in IGA, 50% had at least a 2-grade improvement, and 22.7% at least a 3-grade improvement from baseline. The mean %BSA affected with disease showed a 1.9% decrease from baseline at Day 8 and a 6% decrease by Day 15. All patients met the dosing compliance criterion of at least 80% and no more than 120% of the expected number of applications being applied. No serious safety issues were noted from AE/LSR evaluations, and mean changes for all clinical laboratory values were within expected limits of normal variation.

Figure 1: % Patients with IGA Reduction at Each Study Visit

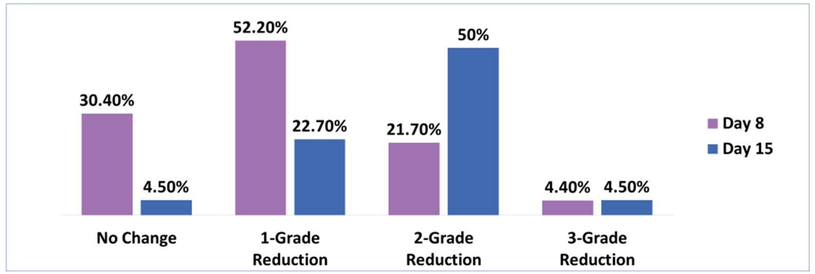

Figure 2: % BSA Affected at Each Study Visit

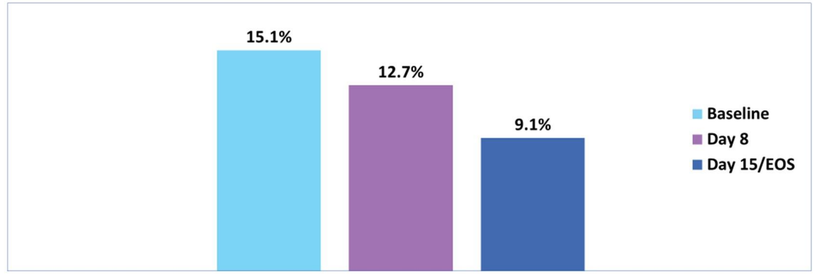

Table 1: Dosing Compliance

Compliant	n(%)
Yes	23(100)
No	0(0)
Dosing	**Mean (min, max)**
Number of Days Dosed	14.1 (9,17)
Number of Applications	28.3 (18,43)
% of Expected Doses Applied	100.6 (92.9, 107.1)

Patient compliance was monitored via diaries and weighing of product cans, and compliance was determined to be completion of at least 80% of expected applications.

Table 2: Localized Skin Reactions (LSRs)

LSRs	Day 1 – pre dose n(%)	Day 8 n(%)	Day 15 n(%)
Telangiectasia	6 (25)	6 (25)	6 (26.1)
Skin atrophy	6 (25)	6 (25)	4 (17.4)

Burning/stinging and folliculitis were absent for all subjects at all visits. With the exception of 1 case of severe telangiectasia at Baseline prior to test article application, all other cases of telangiectasia and skin atrophy were moderate or mild in severity during the study. Telangiectasia and skin atrophy were observed in 6 subjects; all from the same study site. There were no subjects who had an LSR that worsened during the study.

Table 3: Treatment Emergent Adverse Events (TEAEs)

TEAEs	n(%)	Relationship to Treatment	Seriousness
Abnormal ACTH stimulation test	1 (4.2)	Related	mild
Abnormal ACTH stimulation test	5 (20.8)	Possibly Related	mild
Gastritis	1 (4.2)	Not related	moderate
Hematuria	1 (4.2)	Not related	mild

None of the TEAEs were serious, none were within the Treatment Area, none required a change in test article dosing or discontinuation from the study, and all TEAEs recovered/resolved by EOS

***One patient was excluded from the evaluable and PK populations due to use of prohibited medication.**

Conclusions

HBP foam was well tolerated with improvement in both IGA and BSA and good patient compliance. No serious adverse events were reported and no patients discontinued due to side effects. Laboratory evidence of adrenal suppression was seen in few patients and was transient, with no accompanying clinical signs of HPA axis suppression. Systemic exposure to HBP was minimal and did not correlate to adrenal suppression, BSA treated, nor the amount of product used. Results of this study support the safety, tolerability, and efficacy of HBP foam, 0.05% in treating psoriasis in adolescent patients.

References

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Disclosures & Affiliations

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