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Cal/BD IN PSORIASIS: A REVIEW

ITCHING FOR RELIEF: THE EVIDENCE OF FIXED DOSE CALCIPOTRIOL PLUS BETAMETHASONE DIPROPIONATE FOAM FOR PSORIASIS

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THE EVOLUTION OF Cal/BD FIXED DOSE COMBINATION THERAPY FOR PSORIASIS: A CASE STUDY AND DISCUSSION

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AN UPDATE ON THE FIXED-DOSE COMBINATION TOPICAL CORTICOSTEROID/VITAMIN D3 ANALOGUE (BETAMETHASONE DIPROPIONATE-CALCIPOTRIOL) FOR PLAQUE PSORIASIS

Plaque psoriasis is a chronic, recurrent, immune-mediated, inflammatory skin disease that can have a significant negative impact on patient and family quality of life. The therapeutic landscape for this condition has evolved considerably over the past two decades, with many novel treatments receiving approval in Canada and other countries around the world. Despite these advances, which include targeted systemic therapies that are allowing patients to achieve higher levels of skin clearance, topical therapies remain a mainstay in the management of plaque psoriasis.

Most, if not all, patients with plaque psoriasis will be prescribed topical therapies at some point in their treatment course. They are commonly used as first-line monotherapy to treat mild-to-moderate disease as well as moderate-to-severe disease (before initiating light and/or systemic therapy) and as adjunctive therapy to treat moderate-to-severe disease (when complete skin clearance is not achieved by light and/or systemic therapy). Although many options are available, it has been shown that patients with plaque psoriasis have different preferences for topical therapy, which ultimately impacts adherence, thereby highlighting the importance of shared decision-making and individualized treatment approaches. Factors that must be taken into consideration include efficacy, convenience, cosmetic acceptability, safety/tolerability, and access/cost of a product.

Currently approved topical therapies for plaque psoriasis include products with a single active ingredient (corticosteroid, retinoid, or vitamin D3 analogue) and products with two active ingredients in a fixed-dose combination (corticosteroid/keratolytic, corticosteroid/retinoid, or corticosteroid/vitamin D3 analogue). For close to two decades now, fixed-dose combination products featuring a corticosteroid (betamethasone dipropionate) and vitamin D3 analogue (calcipotriol) in various formulations—initially ointment, now gel and foam as well—have been widely utilized by patients with plaque psoriasis across the entire disease severity spectrum and developed a strong legacy in dermatology.

The focus of this supplement is to provide an update on the most recent clinical trial and real-world data for the fixed-dose combination topical corticosteroid/vitamin D3 analogue (betamethasone dipropionate-calcipotriol). Herein, the authors will specifically review: (1) mechanism of action; (2) efficacy in terms of physician-reported outcomes (e.g., improvements in Psoriasis Area and Severity Index [PASI] and Physician Global Assessment [PGA] scores); (3) efficacy in terms of patient-reported outcomes (e.g., improvements in itch and pain Visual Analog Scale (VAS) scores as well as health-related quality of life [HRQoL] measures, such as Children's Dermatology Life Quality Index [CDLQI]/Dermatology Life Quality Index [DLQI]); and (4) safety.

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ITCHING FOR RELIEF: THE EVIDENCE OF FIXED DOSE CALCIPOTRIOL PLUS BETAMETHASONE DIPROPIONATE FOAM FOR PSORIASIS

Introduction

Psoriasis is a chronic immune-mediated skin disease with a variety of morphological presentations, distribution patterns and severities. Psoriasis can have a profound impact on health-related quality of life (HRQoL), almost equal to that seen in patients suffering from cardiovascular disease and cancer.[1] In Canada, it is estimated that approximately 3% of the population suffers from psoriasis, equating to over 1 million people.[2] The most common presentation is 'mild-to-moderate' plaque psoriasis characterized by well-defined silver scaly plaques on extensor surfaces.[3] However, classifying severity can be challenging. In 2020, the International Psoriasis Council recommended classifying psoriasis severity with a dichotomous definition: either candidates for topical therapy or candidates for systemic therapy.[4] Regardless of severity, all patients living with psoriasis will need a topical agent as part of their treatment regimen throughout the clinical course of their disease.

Topical treatments used to treat psoriasis in Canada include steroids, vitamin D analogues, retinoids, tar, keratolytic agents and fixed dose combination products. In 2001, the fixed dose combination of calcipotriol (Cal) 50 µg/g plus betamethasone dipropionate (BD) 0.5 mg/g was approved by Health Canada in ointment form, followed by a gel in 2012 and an aerosol ointment-based foam (Cal/BD foam) in 2016. Other combination products for psoriasis include topical steroids combined with either tazarotene or salicylic acid.

Fixed dose combination products have several advantages versus topical monotherapy agents including ease of use, increased efficacy, improved adherence, and potentially fewer adverse events.[5] Specifically for Cal/BD, Cal has been shown to reduce atrophy associated with BD; whereas, BD has been shown to reduce the irritation associated with Cal.[6]

The aim of this article is to review the evidence with regards to efficacy, onset of action, itch relief and patient-reported outcomes for Cal/BD foam.

Efficacy

Cal/BD foam is approved in Canada for the topical treatment of psoriasis vulgaris in adult and adolescent patients 12 years or older for up to 4 weeks.[8] All studies to be discussed hereafter include subjects with mild-to-severe disease severity. Head-to-head studies comparing Cal/BD foam to ointment[9] and gel[10] have demonstrated superiority of the foam in achieving physician global assessment as "clear" or "almost clear" (**Figure 1**) with at least a two-point improvement (PGA success), as well as superiority in the proportion of patients achieving at least a 75% reduction in modified psoriasis area severity index (mPASI75) (**Figure 2**). The PSO-LONG study also demonstrated ongoing proactive twice weekly use

beyond the initial daily 4 weeks resulted in patients in the proactive group having an additional 41 days in remission compared with the reactive group over a 1 year period (P < .001).[11] While there are no head-to-head studies comparing Cal/BD foam to the newer fixed dose combination of halobetasol plus tazarotene lotion (HP/TAZ lotion), an anchor-based, matching adjusted indirect comparison of the two products was performed. The indirect comparison found that 4 weeks of Cal/BD foam produced greater PGA success than 8 weeks of HP/TAZ lotion (**Figure 3**) (51.4 vs. 30.7%, p < .001).[12]

Onset of Action

The PSO-FAST study involving 426 subjects looked at the efficacy and safety of Cal/BD foam versus vehicle. At 4 weeks, 53.3% of subjects achieved PGA success in the Cal/BD foam group versus 4.8% in the vehicle group (OR 30.3, 95% CI 9.7,94.3; P < .001). Similarly, 52.9% of subjects achieved a mPASI75 in the Cal/BD foam group versus 8.2% on placebo (OR 14.9; 95% CI 6.5, 34.0; P < .001). Equally important, no major safety signals were identified. Incidence of adverse events were similar between active and placebo arms with most events rated as mild or moderate in

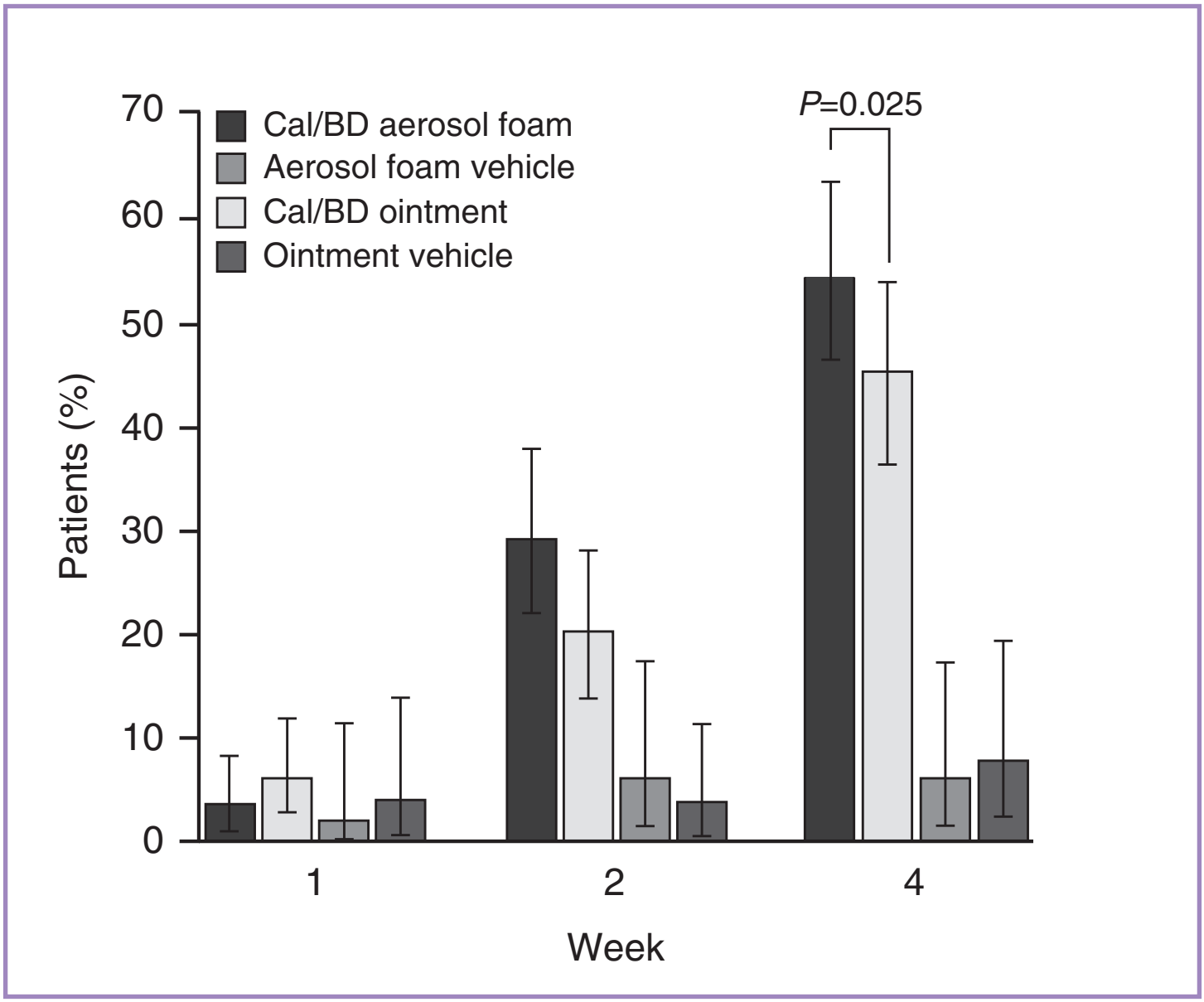


Figure 1. Proportions of patients experiencing treatment success as determined by InvestigatProportion of patients achieving PGA-assessed treatment success* over time. *Investigator assessment by PGA as ''clear'' or ''almost clear'' with at least a two-step improvement was defined as patient having achieved treatment success. Bars show 95% confidence interval. BD, betamethasone dipropionate 0.064%; Cal, calcipotriene 0.005%.

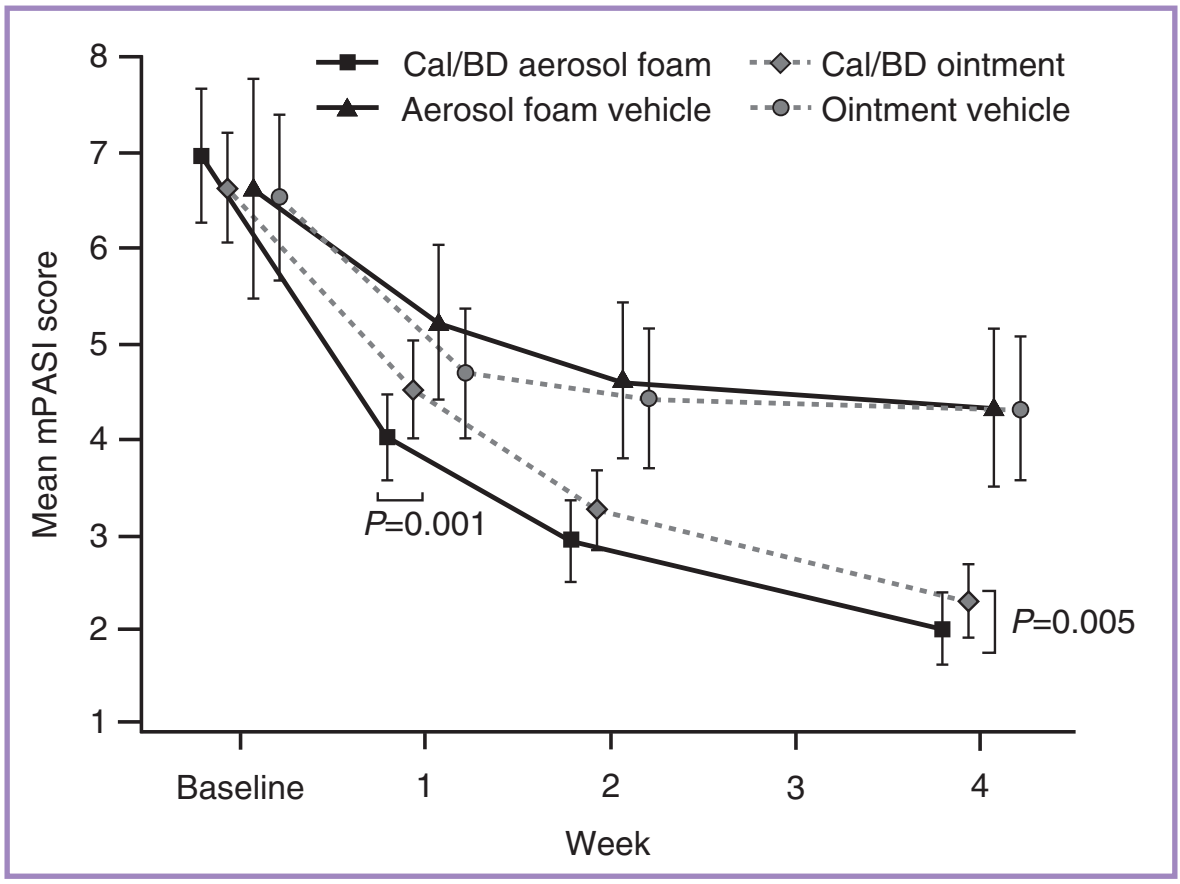


Figure 2. Change in mean mPASI over time. Bars show 95% confidence interval. BD, betamethasone dipropionate 0.064%; Cal, calcipotriene 0.005%; mPASI, modified psoriasis area severity index.

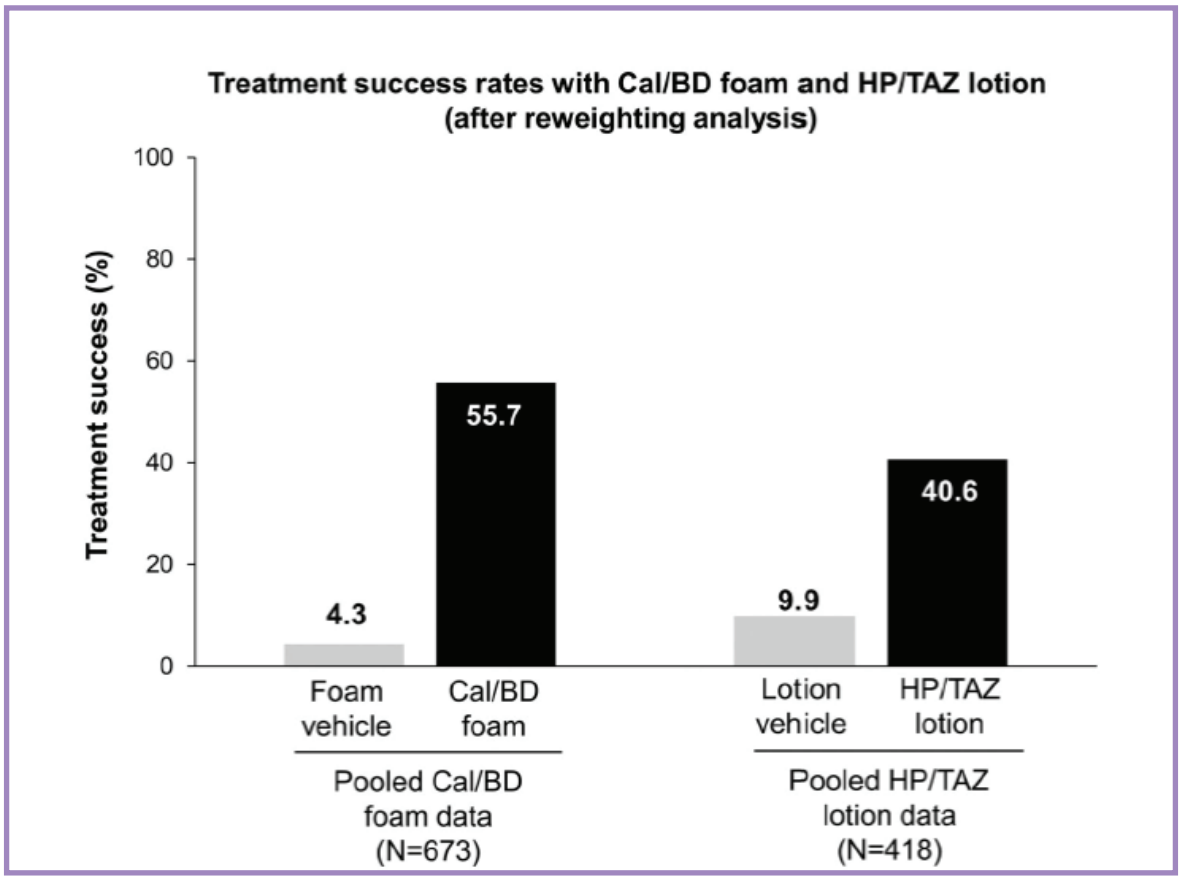


Figure 3. Matching-adjusted indirect comparison of PGA treatment success for patients treated with 4 weeks of Cal/BD foam or 8 weeks of HP/TAZ lotion. Abbreviations. Cal/BD, calcipotriene plus betamethasone dipropionate; HP/TAZ, halobetasol plus tazarotene.

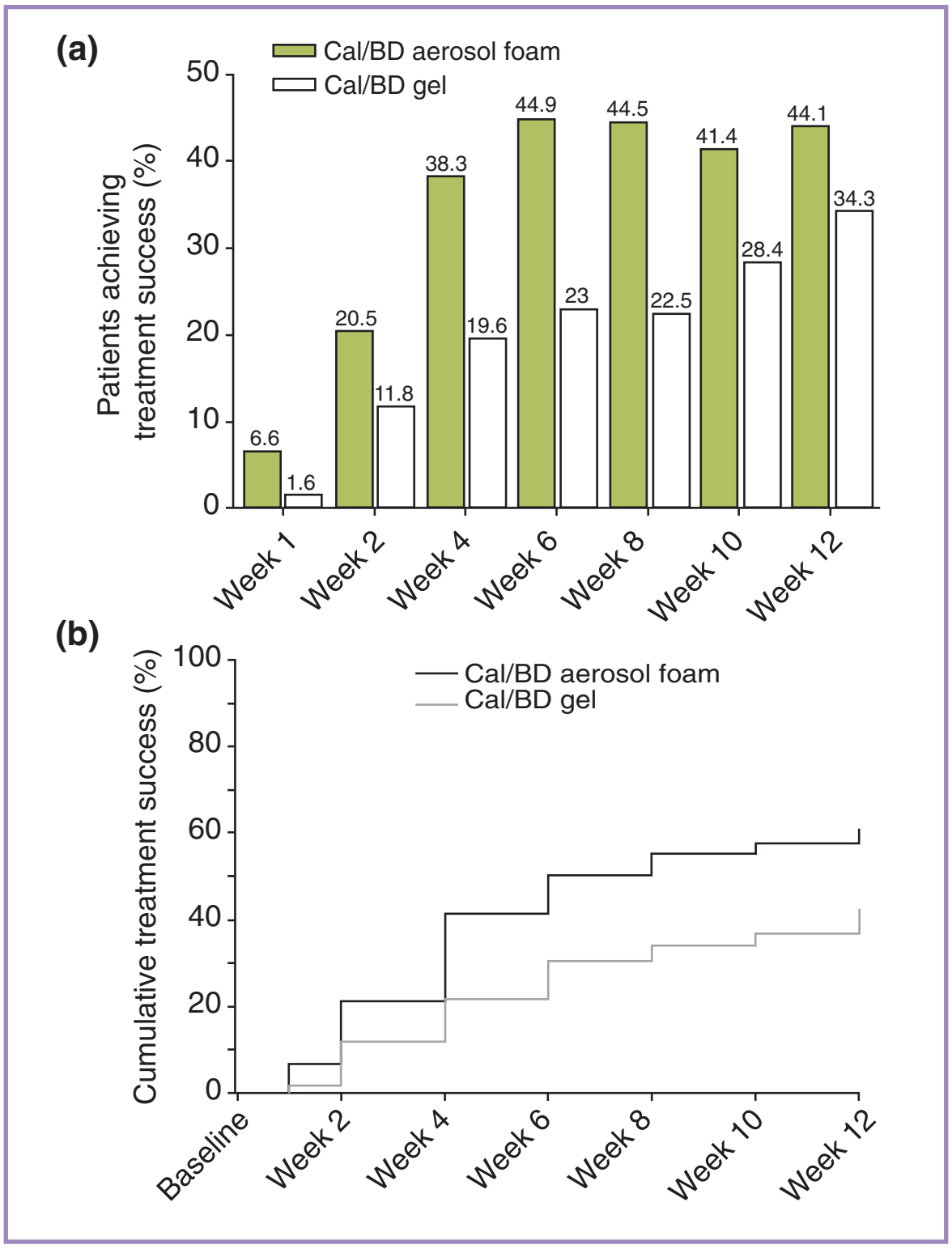
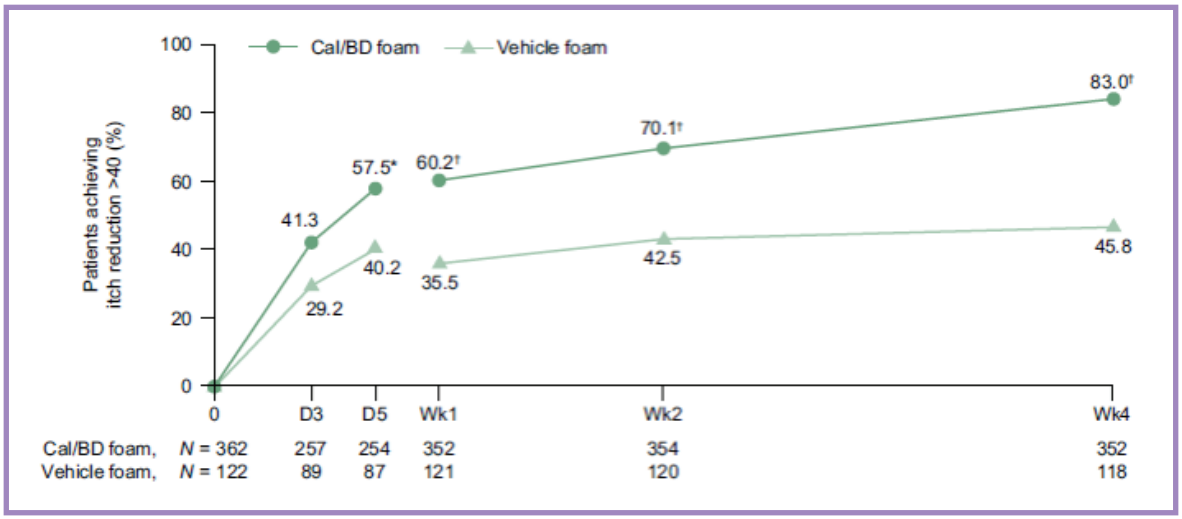


Figure 4. (a) Treatment success rates by visit (MI). (b) Time to treatment success, according to PGA (observed cases), in Cal/BD aerosol foam and gel groups. MI, multiple imputation.



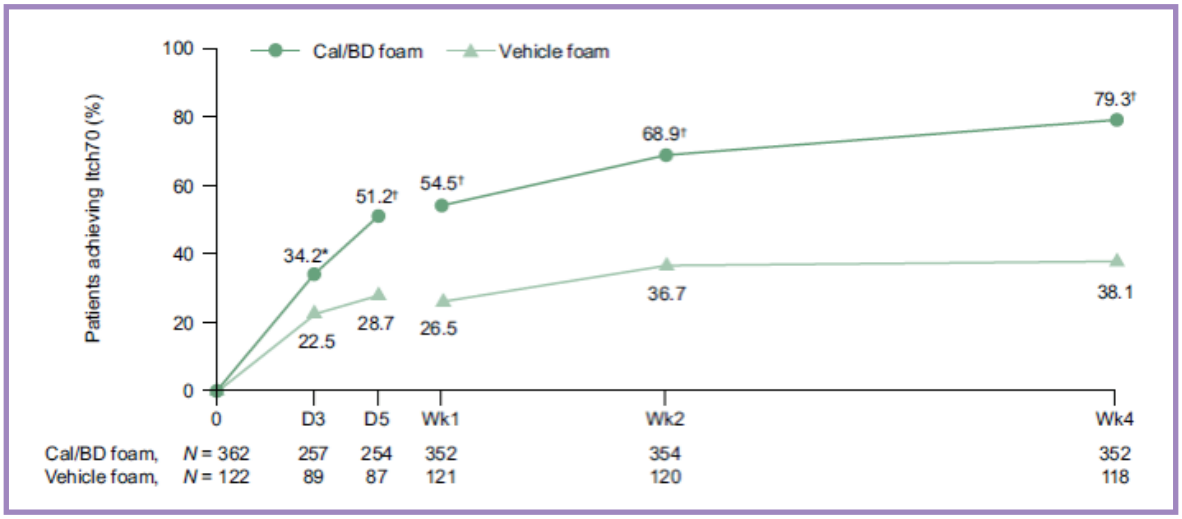


Figure 5. Proportion of patients achieving (a) absolute itch reduction >40 from baseline and (b) ≥70% improvement in itch. All patients in (a) and (b) had a baseline itch VAS >40; results for Days 3 and 5 were recorded from the Phase III pool, while results from Week 1 to 4 were recorded from the complete pool.*P < 0.05; †P < 0.001 vs. vehicle foam. The absence of symbol indicates P ≥ 0.05. The discontinuity in the figure lines in (a) and (b) indicates the use of the two different patient pools. BD, betamethasone dipropionate (0.5 mg/g); Cal, calcipotriol (50 µg/g); D, day; Wk, week.

severity. Adverse drug reactions were reported in ten Cal/BD foam patients (3.1%) and two vehicle patients (1.9%).[13] Due to the fast onset of action of Cal/BD foam, the PSO-ABLE study was designed based on the hypothesis that 4 weeks of Cal/BD foam was superior in efficacy to 8 weeks of Cal/BD gel, which was demonstrated (**Figure 4**).[10]

Itch Relief

Itch is a significant driver of health-related quality of life (HRQoL) deterioration related to psoriasis. As such, rapid and sustained improvement in itch is a valuable outcome for today's therapeutic treatments. A pooled analysis from three phase III studies examined the following outcomes: itch visual analogue scale (VAS) reduction >40 (**Figure 5a**), ≥70% improvement in itch (Itch70) (**Figure 5b**) or itch-related sleep loss, mPASI75 (excluding head) and Dermatology Life Quality Index (DLQI) scores 0/1 through 4 weeks. The results demonstrated that 57.5% of Cal/BD foam subjects achieved an itch VAS reduction of >40 from day 5 onwards versus 40.2% in the vehicle group (P < 0.05) and by week 4 this increased to 83% in the Cal/BD arm vs 45.8% in the vehicle arm (P < 0.001). A statistically significant difference in those achieving ≥70% improvement in itch was demonstrated in the Cal/BD foam group vs the vehicle group as early as day 3 (34.2% vs 22.5%, P < 0.05) and by week 4 this increased to 79.3% vs 38.1% (P < 0.001).[14]

Patient-reported Outcomes

The PSO-ABLE study also examined HRQoL wholistically in addition to itch specifically. Subjects enrolled in the study completed the Dermatology Life Quality Index (DLQI), EuroQoL-5D-5L-PSO (EQ-5D), and Psoriasis QoL (PQoL-12) questionnaires at baseline, Weeks 4, 8 and 12. At the 4-week study time point Cal/BD foam demonstrated meaningful improvement in HRQoL measures. Significantly more Cal/BD foam patients achieved DLQI scores of 0/1 at Weeks 4 (45.7% vs 32.4%; p = 0.013) and 12 (60.5% vs 44.1%; p = 0.003) than Cal/BD gel patients (**Figure 6**). Cal/BD foam significantly improved EQ-5D utility index (0.09 vs 0.03; p<0.001) and PQoL-12 scores (-2.23 vs -2.07; p = 0.029) from baseline to Week 4 versus Cal/BD gel. Itch, itch-related sleep loss, and work impairment improved more with Cal/BD foam than gel.[15]

Conclusion

Psoriasis is a chronic, relapsing, and unpredictable inflammatory disease. All patients can benefit from a safe, effective, and fast treatment whether they are candidates for topical treatments only or if they are also candidates for systemic therapies. The use of Cal/BD foam has demonstrated efficacy, quick onset of action, itch relief and overall improvement in HRQoL measures in various peer-reviewed studies of mild-to-severe plaque psoriasis. Thus, Cal/BD foam should be considered a valuable therapeutic tool for clinicians to use with psoriasis patients across all disease severities.

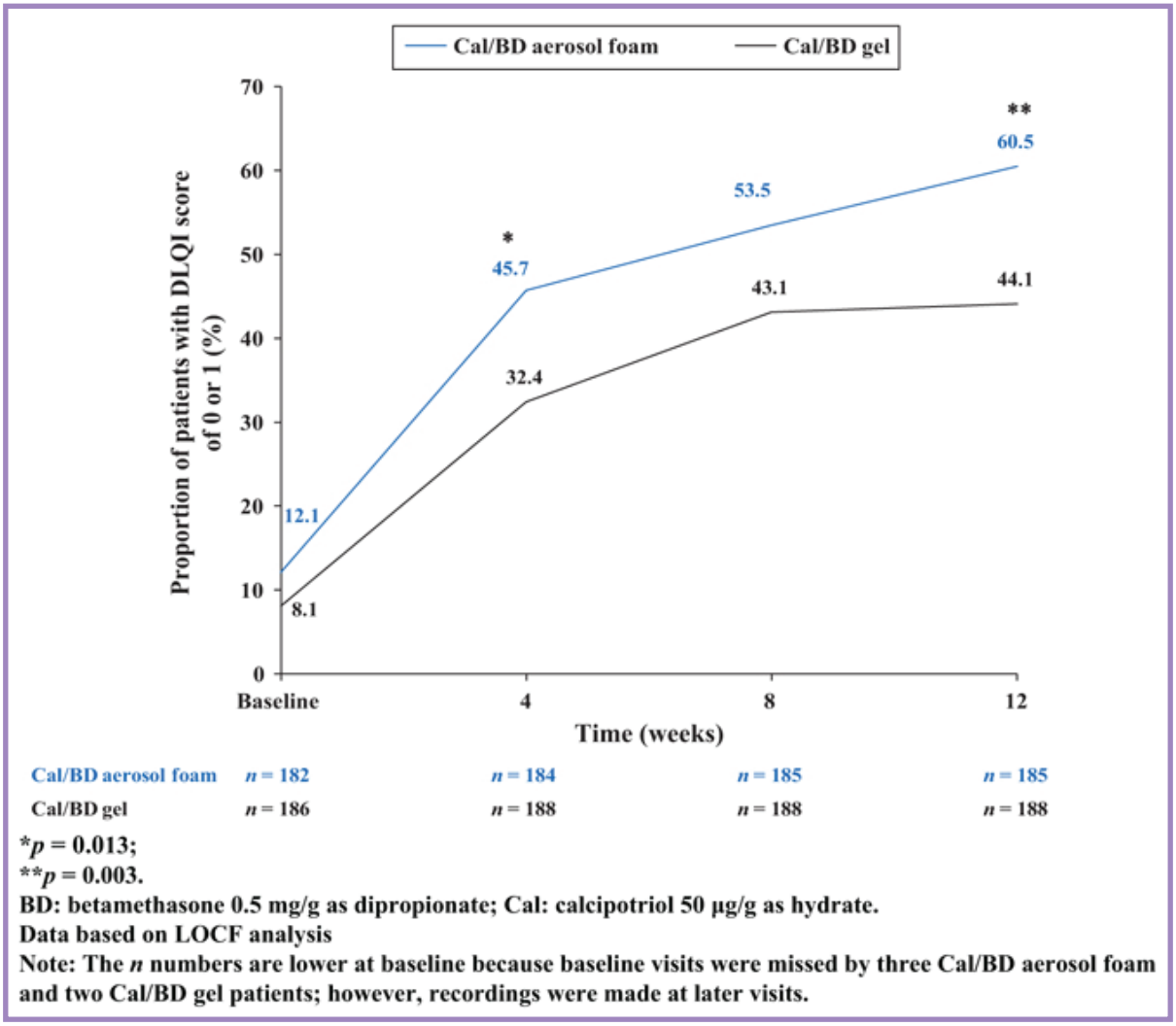


Figure 6. Proportion of patients with a Dermatology Life Quality Index score of 0 or 1 with Cal/BD aerosol foam versus Cal/BD gel at baseline and Weeks 4, 8 and 12; adapted from Griffiths et al, 2018.

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THE EVOLUTION OF Cal/BD FIXED DOSE COMBINATION THERAPY FOR PSORIASIS: A CASE STUDY AND DISCUSSION

Case Study:

A fourteen-year-old boy presented with itchy thick red scaly plaques on his scalp, arms, legs, and torso. They had been present since the age of seven. The boy hid behind his long hair and made no eye contact with me; he was accompanied by his father who did all the speaking. The itching in his scalp was more intense than other areas. His only therapy at that point had been tar shampoo as well as topical steroid creams for his body, and neither offered much improvement in symptoms.

A family history revealed that his paternal uncle had severe psoriasis and psoriatic arthritis.

On physical examination, the patient had well-demarcated erythematous plaques with a thick silvery scale throughout the scalp, on the elbows, extensor forearms, knees, shins, and lower back. He was wearing a removable cast on his left forearm for a wrist fracture that had healed months ago. He was obese with a BMI of 43 and a BP of 140/80 mmHg. Blood work revealed a FBS 5.4 mmol/L, Cholesterol 5.61 mmol/L (↑ LDL, ↓HDL), Triglycerides 8.7 mmol/L, CRP 0.8 mg/L and elevated liver enzymes with suspected non-alcoholic steatohepatitis.

After discussion about the diagnosis and possible treatment options, the boy's father asked me if I could write a note to his teacher to exempt him from gym class as his son's classmates had been ridiculing him in the change room when they saw his skin condition on his arms and legs, which is why he had continued to wear his cast.

Psoriasis can have a tremendous impact on a child's physical, emotional and social quality of life.[1] For this particular patient, having psoriasis was devastating. In addition, his father felt the guilt of having passed this gene on to his son and the frustration of not having found adequate treatment to control his son's psoriasis over the previous 7 years.

A treatment option that was effective, safe, and easy to use leading to better adherence was the desired solution. As much as the patient was interested in clearing his skin quickly, his father was equally concerned about the long-term risks of therapy given his brother's long battle with severe disease associated with arthritis and some complications from systemic therapies he had used.

Parents may underestimate the emotional burden of psoriasis in their children and the requirement for counselling and support from their child's dermatologist.[1] After a long discussion focused on the skin condition itself and treatment options, calcipotriol/betamethasone dipropionate (Cal/BD) foam was prescribed for the patient's scalp and body plaques and a 1-month follow-up was arranged to discuss potential comorbidities.

This article will review some highlights of psoriasis in children and adolescents as well as the rationale behind potential therapeutic treatment options.

Psoriasis

Psoriasis is a chronic, immune-mediated, genetic inflammatory skin disease that occurs in 2-3% of the Canadian population, which is comparable in incidence and prevalence to Europe and the USA.[3] It begins in childhood in almost a third of patients and the prevalence increases in a linear pattern from age 1 to age 18.[4] The incidence continues to increase from the 2nd decade reaching a peak in the latter half of the 6th decade. The global incidence of psoriasis has increased over the past 30 years in both adults and children, especially in North America and Western Europe.[5,6] As illustrated in this case, psoriasis is associated with comorbidities, such as hypertension, obesity, impaired glucose tolerance, hyperlipidemia, arthritis, and inflammatory bowel disease. These comorbidities occur in twice as many patients under the age of 20 with psoriasis as those without.[7]

The first line of treatment for mild-to-moderate psoriasis is topical therapy, which also complements systemic therapies in more severe disease.

Rationale for Cal/BD Fixed Dose Combination

Until recently, topical treatment options included steroids and calcipotriol as monotherapy, as well as tar, anthralin, and tazarotene. A stable formulation containing both Cal/BD in an ointment base was developed more than 20 years ago. It was thought that this combination might yield superior efficacy and that the calcipotriol and the topical steroid would have complementary effects on psoriatic inflammation. It was also hypothesized that the local irritation caused by calcipotriol might be alleviated via the anti-inflammatory effect of the steroid and that the skin atrophy from the corticosteroid might be reduced via the use of a Vitamin D analogue.[8,9] (**Box 1** and **Table 1**) Having two active ingredients in a single formulation would also improve patient adherence.

In a double-blind study, 1106 patients were randomized to receive combination Cal/BD ointment, BD ointment or Cal ointment twice daily for 4 weeks. The primary efficacy endpoint clearly demonstrated that the combination treatment was more effective than the individual active components. The mean decrease in PASI from baseline to the end of the double-blind phase was statistically significantly greater in the combination group compared to both the betamethasone and calcipotriol groups and showed a more rapid onset of action with statistically significant differences in PASI evident after 1 week.[10]

In another study, 1,603 patients randomised to one of the 4 double-blind treatments used a regimen composed of a once daily application for 4 weeks with either Cal 50 mcg/g + BD 0.5 mg/g combination ointment, or BD 0.5 mg/g ointment or Cal 50 mcg/g ointment or ointment vehicle. The results demonstrated the superiority of the combination group to the other three groups with the mean decrease in PASI being evident in the combination

Summary: Combination Therapy has Complementary Effects on the Underlying Pathophysiology of Psoriasis, Resulting in Increased Therapeutic Response

1. As well as their normalizing effect on keratinocytes, vitamin D analogs, such as calcipotriol, exert immunomodulatory effects on Th1, Th2, Th17, and T-reg cells.

2. Corticosteroids, such as betamethasone dipropionate, combined with vitamin D analogs, additively inhibit Th1 and Th17 pro-inflammatory effects.

3. Calcipotriol induces an immunomodulatory Th2/T-reg cellular response, whereas corticosteroids suppress this effect, and combination treatment yields mild induction.

4. The preclinical results support the superior anti-psoriatic effect of corticosteroid and vitamin D analog combination treatment compared with monotherapies.

Box 1. Adapted from Segaert S, Shear NH, Chiricozzi A, et al., 2017.

Table 1. Summary of the effects of corticosteroids and vitamin D analogs in skin atrophy. Adapted from Segaert S, Shear NH, Chiricozzi A, et al., 2017.

Mechanism	Effect of corticosteroids	Effect of vitamin D analogs	Overall clinical effect of combination treatment
Lipid synthesis	↓	↑	Prevents skin barrier and water loss impairment caused by corticosteroids.
AMPs, e.g., LL-37	↓	↑	
KC proliferation'	↓	=	Attenuates epidermal thinning by corticosteroid-induced reduction of epidermal cells
Change in tissue modeling and structure: - Hyaluronic acid - Matrix metalloproteinases	↓	↑	Limits epidermal thinning from corticosteroid-induced loss of cellular volume
Collagen synthesis and turnover	↓	↑	Reduces dermal thinning caused by corticosteroid induced decrease in matrix network
Glycosamine synthesis	↓	↑	Increases water-binding capacity of the skin, decreasing corticosteroid-induced dermal thinning
Elastic fiber synthesis	↓	↑	Attenuates reduced skin flexibility/elasticity observed in topical steroidal monotherapy

Downward arrow indicates downregulation; upward arrow indicates upregulation; equal sign indicates no effect; AMPs antimicrobial peptides; KC keratinocytes. * KC proliferation is psoriasis activity-dependent. The data presented here are based on non-inflamed skin.

group after only 1 week.[11] The mean decrease in PASI observed with the combination once-daily treatment in this study was similar to that seen with the combination twice-daily treatment in the previous study.

Cal/BD Fixed Dose Combination in Pediatrics

The efficacy and safety of Cal/BD has also been demonstrated in a pediatric population.[12,13] In a study from 2014, seventy-three patients (mean age 10.8 years) with mild-to-moderate plaque psoriasis were treated with Cal/BD ointment for a median time of 35·0 weeks. At week 12, the mean PASI decreased 15·4% (from 5·2 to 4·4), BSA did not change in a meaningful manner, and median CDLQI decreased significantly from 5·5 to 4·0. VAS scores for pain and itch declined. At week 24, mean PASI decreased to 4·3 (17·3%). No related serious adverse events were observed in this study.[12] Another study assessed the safety of once-daily application of fixed-combination Cal plus BD gel in adolescent scalp psoriasis. Patients in this study were aged 12-17 years with moderate-to-very severe scalp psoriasis according to Investigator's Global Assessment (IGA) (≥ 10% of the scalp area affected). Results showed that 66 patients (85%) were clear or almost clear according to IGA. There was an 80% improvement in mean Total Sign Score from baseline to end of treatment. In total, at the end of treatment, 87% of patients rated their scalp psoriasis as clear or very mild, and 75 (96%) had no or mild pruritus compared with 14 (18%) at baseline (**Figure 1**).[13]

In a third study, the safety of the two-compound product, Cal/BD was assessed with results demonstrating that treatment up to 52 weeks appeared to be safe and well tolerated whether used on its own or alternating every 4 weeks with calcipotriol treatment.[14] This is welcome news given that psoriasis is a chronic, relapsing and remitting disease that requires long-term management.[14]

Cal/BD Fixed Dose Combination in Scalp Psoriasis

Scalp psoriasis typically represents a therapeutic challenge. Itching and scaling represent the most distressing symptoms, and in some cases, scalp psoriasis can be associated with psoriatic alopecia, which can lead to scarring.[15] Patient adherence to therapy is also a challenge based on the type of vehicle (greasy vehicles are less acceptable), and ease and frequency of application.

A multicenter, randomized, double-blind study of 1504 patients with scalp psoriasis was conducted

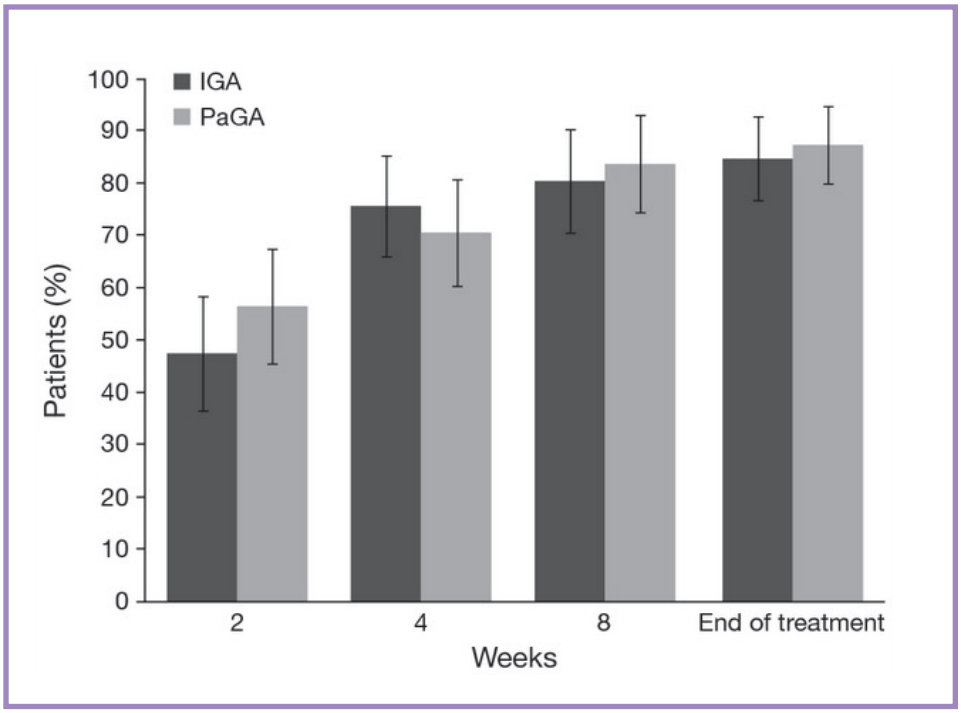

Figure 1. Proportions of patients experiencing treatment success as determined by Investigator's Global Assessment (IGA) and Patient's Global Assessment (PaGA) and 95% confidence intervals. Treatment success was defined by an assessment of clear or almost clear for IGA, or clear or very mild for PaGA. Week 8 data include only observed cases at that time point and end-of-treatment data include the last value recorded for that parameter; adapted from Gooderham et al, 2014.

to compare the clinical efficacy and safety of once-daily treatment for up to 8 weeks. The study randomized four treatments as follows: two-compound scalp formulation (calcipotriene 50 µg/g plus betamethasone 0.5 mg/g, as dipropionate) (n = 541), betamethasone 0.5 mg/g (as dipropionate) in the same vehicle (n = 556), calcipotriene 50 µg/g in the same vehicle (n = 272), or vehicle alone (n = 136). the The scalp formulation vehicle is less greasy than an ointment, which addresses patients' concerns around cosmetic acceptability. Patients who used the two-compound scalp formulation achieved "absent" or "very mild" disease more quickly than any other group, and this efficacy advantage became evident after only 2 weeks of treatment. The effect was achieved using an average of 20 g less medication over the full study period than in the BD group (p = 0.023), indicating a potential steroid-sparing effect of the two-compound scalp formulation.[16]

A 52-week, international, double-blind study of 869 patients with moderate-to-severe scalp psoriasis demonstrated a high level of safety and efficacy in long-term management of scalp psoriasis with the two-compound scalp formulation (Cal 50 µg/g plus BD 0.5 mg/g).[17]

Cal/BD Aerosol Foam Formulation

To improve drug delivery further, an alcohol-free, surfactant-free aerosol foam formulation of Cal/BD, in which the active ingredients are dissolved in a mixture of volatile propellants (butane and dimethyl ether) to build a stable, supersaturated solution after the rapid evaporation of the propellants, was developed. The medication is in a non-skin-drying emollient vehicle in a pressurized spray can. This is associated with enhanced skin penetration and increased bioavailability.[18] The foam is to be rubbed gently onto affected areas once-daily with usage not exceeding 15 g daily. Clinical studies have shown Cal/BD aerosol foam to be more efficacious than the vehicle[19], more efficacious than Cal or BD aerosol foam alone[20] and more efficacious than Cal/BD ointment in patients with psoriasis vulgaris.[21,22] In the PSO-ABLE study, 4 weeks of Cal/BD aerosol foam was significantly more effective than 8 weeks of Cal/BD gel in patients with psoriasis (with lower drug consumption)[23]. This superiority was reached by week 1 and maintained throughout the 12-week treatment period.

Although the Cal/BD foam formulation has an increased bioavailability (as a result of the supersaturation and increased skin penetration), calcipotriol/betamethasone foam was not associated with an increased risk of treatment-related adverse events compared with the individual components as foam or the fixed combination as topical gel or ointment formulations.[24] In patients with extensive psoriasis vulgaris (15%-30% of body surface area, including ≥30% of scalp) who were treated once daily for 4 weeks, Cal/BD aerosol foam exhibited no clinically relevant impact on the hypothalamic–pituitary–adrenal (HPA) axis or calcium homeostasis. Results from this multicentre, single-arm, open-label, maximal-use systemic-exposure trial demonstrated that 49% of patients achieved treatment success (clear or almost clear status) when evaluated for efficacy. Cal/BD foam also demonstrated a favourable tolerability profile.[25]

The use of Cal/BD foam in adolescents is supported by a phase II, multicentre, prospective, open-label, non-controlled, single-group, 4-week trial in patients aged 12 to <17 years with plaque psoriasis on the body and scalp.[26] Results from this study show that Cal/BD foam is generally well-tolerated in adolescent patients. Over 4 weeks of treatment with Cal/BD foam, 32 treatment-emergent adverse events (AEs) occurred in 22 patients (20.8%), all but two of which were mild in severity (no treatment-emergent AEs were serious or severe). No treatment-emergent AEs led to study withdrawal or death. The most frequently reported AEs were upper respiratory tract infection [eight (7.5%)], nasopharyngitis [four (3.8%)], and acne [two (1.9%) and expected in this age group]. There was no evidence for dysregulation of calcium homeostasis or the HPA axis in patients with moderate disease. Limitations of this study include the fact that it was not designed to determine a maximum tolerated dose and the open-label design could not exclude the possibility of investigator bias. Additionally, the lack of a placebo control group impaired the determination of the true efficacy and safety of Cal/BD foam in adolescents and no patients in the HPA-axis cohort had a PGA of severe disease.

Cal/BD Fixed Dose Combination in Elevated BMI

The use of Cal/BD foam in patients with an elevated BMI is supported by the sub-analysis from the PSO-FAST study demonstrating that Cal/BD aerosol foam, if used appropriately, is effective for the treatment of psoriasis independent of BMI and the extent or severity of disease.[27]

Case Study (Continued)

The 14-year-old patient returned after four weeks of Cal/BD foam use with marked improvement of the scalp and skin plaques; but many challenges remained and had to be discussed, including the disease's potential to affect the cardiovascular system and metabolic pathways, as well as the lifelong psychosocial impact of psoriasis. Patients with early-onset psoriasis (age < 20 years) have been observed to be more anxious and depressed than patients with late-onset psoriasis.[28] The use of Cal/BD foam may provide substantial benefit to adolescent patients and the risk-benefit profile of initiating such therapy should be discussed with patients and their families to ensure optimal outcomes considering all aspects of the disease's impact on a patient's life.

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Cal/BD IN PSORIASIS: A REVIEW

ITCHING FOR RELIEF: THE EVIDENCE OF FIXED DOSE CALCIPOTRIOL PLUS BETAMETHASONE DIPROPIONATE FOAM FOR PSORIASIS
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THE EVOLUTION OF Cal/BD FIXED DOSE COMBINATION THERAPY FOR PSORIASIS: A CASE STUDY AND DISCUSSION
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