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REVIEW ARTICLE

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Emerging paradigm shift toward proactive topical treatment of psoriasis: A narrative review

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Abstract

Psoriasis (PsO) requires safe and effective long-term management to reduce the risk of recurrence and decrease the frequency of relapse. Topical PsO therapies are a cornerstone in the management of PsO though safety concerns limit the chronic, continuous use of topical corticosteroids and/or vitamin D_3 analogs. Evidence-based guidelines on optimal treatment targets and maintenance therapy regimens are currently lacking. This review explores the evidence supporting approaches to maintenance topical therapy for PsO including continuous long-term therapy, chronic intermittent use, step-down therapy, sequential or pulse therapy regimens, and proactive maintenance therapy. Several unaddressed questions are discussed including how and when to transition from acute to maintenance therapy, strategies for monitoring long-term treatment, the role of topical maintenance therapy in the context of systemic and biologic therapies, risks of maintenance therapy, prescribing a topical preparation suitable for patients' preferences and skin type, and key concepts for patient education to maximize long-term outcomes. Overall, emerging evidence supports a paradigm shift toward proactive treatment once skin is completely clear as a strategy to enhance disease control without compromising safety.

KEYWORDS
long-term safety, maintenance therapy, psoriasis, topical corticosteroids, vitamin D_3 analogs

1 | BACKGROUND

Psoriasis (PsO) is a chronic inflammatory disease with a global prevalence between 0.14 and 2.0%[1] and commonly follows a relapsing–remitting course of disease flares interspersed with periods of quiescent disease.[2,3] Given its variability, PsO requires multifaceted long-term management that may include safe and effective therapies as well as nonmedicinal strategies: moisturizers, avoidance of triggers, treatment adherence optimization, and scheduled follow-up.[3]

"Maintenance therapy" is used interchangeably with "long-term management," and is defined as ongoing treatment to retain disease control following successful initial therapy.[2] In the context of PsO, initial therapy often includes first-line topical agents such as topical corticosteroids (TCS), vitamin D_3 analogs, or a combination of both.[4] Adherence to product labels for steroid-containing therapies generally limits use to 4 weeks of consecutive treatment, although in practice treatment duration is often longer. While most patients experience symptomatic relief during initial therapy, a significant proportion

experience a relapse or worsening (i.e., flare) of their symptoms after treatment is discontinued. Furthermore, rebounds (i.e., return of disease with greater severity after treatment discontinuation) and tachyphylaxis (i.e., decreasing response to treatment over time) remains a challenge for both physicians and patients.[2,3] It comes as no surprise that there remains a population of patients who are unsatisfied or undertreated with current topical treatment paradigms.[5]

The goals of maintenance therapy in PsO are multifaceted and include sustaining a maximal response to therapy, reducing the risk and frequency of relapses, flares, and rebounds, minimizing drug exposure, optimizing long-term safety, and managing the risk of tachyphylaxis.[2,3,6] Other important long-term management goals of PsO include enhancing patient outcomes, health-related quality of life, and treatment adherence.

Maintenance therapy is not a new concept to dermatology with several approaches commonly used in clinical practice. However, expert opinions and guidelines provide limited direction to inform clinical decisions on how and when to transition from acute to long-term therapy, and on the safety and efficacy of different approaches to maintenance treatment of PsO with topical agents.

The goal of this review is to explore evidence from controlled clinical trials that inform on strategies to optimize the many facets of maintenance PsO therapy. Notably, the recently published PSO-LONG trial suggests that a proactive approach to maintenance therapy sustains response with optimal drug exposure and without increasing the risk of adverse effects compared to intermittent reactive management.[7]

2 | METHODS

The literature was searched using PubMed for clinical trials and guidelines using the search terms "psoriasis" and "topical therapy" in combination with "maintenance" or "long-term." Articles reporting on the efficacy, safety, and/or clinical implementation of topical maintenance therapy regimens in PsO were selected for inclusion in this review.

3 | WHAT DIFFERENT TOPICAL MAINTENANCE THERAPY REGIMENS EXIST?

In contrast to atopic dermatitis where topical tacrolimus ointment is approved by regulatory agencies for maintenance therapy,[8] in PsO there are currently no topical regimens approved for maintenance therapy. Consequently, maintenance treatment decisions in PsO are based on clinical experience and on a limited number of studies reporting on long-term efficacy, safety, and acceptability of select topical therapy regimens, primarily TCS, vitamin D_3 analogs, or a combination of both, applied using a variety of maintenance approaches including continuous therapy, chronic intermittent therapy, step-down regimens, sequential or "pulse" regimens, and proactive maintenance therapy. These approaches variably meet the goals of long-term management of PsO as summarized in Table 1.

Evidence supports the efficacy of TCS for inducing remission and reducing the frequency of relapses over periods of up to 6 months of continuous twice-daily treatment (see Supplemental Table 1).[9,10] However, treatment success with TCS is variable across short-term studies, and there are relatively few longer-term studies despite PsO being a chronic disease.[11] Importantly, no severe adverse effects including hypothalamic–pituitary–adrenal (HPA) axis suppression were reported in trials of patients who used up to 20 g per week of clobetasol propionate ointment 0.05%,[9,10] betamethasone valerate 0.1% ointment[9] or fluocinolone acetonide 0.025% ointment with or without occlusion.[10] Continuous long-term treatment with vitamin D_3 analogs such as tacalcitol and calcitriol significantly decreases Psoriasis Area and Severity Index (PASI) scores within weeks and this effect was generally maintained with continued treatment, without clinically relevant disturbances in calcium homeostasis or other serious adverse effects reported in studies of up to 18 months' duration.[12–15] There is limited evidence of efficacy for continuous long-term treatment with topical therapies that are used off-label in PsO (e.g., topical calcineurin inhibitors); however, studies were generally limited to ≤12 weeks and most investigated specific body areas (e.g., genitals and nails).[16–18]

Fixed-dose products combining calcipotriol with betamethasone dipropionate (Cal/BD) are recommended as first-line agents for acute PsO treatment due to their reduced risk of adverse effects compared with either agent alone.[3] This combination exerts additive suppression of inflammatory cytokines implicated in PsO, such as tumor necrosis factor-α (TNF-α) and interleukin-23 (IL-23),[19] which may result in more efficient long-term disease control. Cal/BD is available in a variety of formulations including gel, ointment, and aerosol foam, offering flexibility with respect to patient preference and for treatment of different body areas.[20,21] Evidence suggests that the Cal/BD aerosol foam formulation is more effective than the ointment[22] or gel[23] formulations in treating PsO, and patients have reported higher levels of satisfaction.[20,21] This enhanced efficacy of the aerosol foam formulation has been attributed to the supersaturation effect of the vehicle, which provides greater bioavailability and skin penetration.[20,24,25]

.25wChronic intermittent maintenance therapy is supported by a large study of patients with scalp PsO where daily treatment with Cal/BD gel as needed for up to 52 weeks was associated with significantly fewer adverse drug reactions and was significantly more effective at controlling disease than calcipotriol alone.[26] In another study, 4 weeks of daily treatment with Cal/BD foam significantly improved skin clearing and efficacy was maintained with as needed chronic intermittent therapy for up to 26 weeks.[27] Systematic reviews on topical long-term PsO therapy suggest that fixed-dose formulations of topical vitamin D_3 analogs plus corticosteroids offer a favorable risk–benefit ratio and better cost-effectiveness than monotherapy with either class of therapy[28,29] and have been proposed as first-line agents for maintenance therapy.[30,31]

An alternative to continuous long-term therapy involves rapidly gaining disease control with daily topical therapy and then stepping down to less frequent dosing. This approach has been demonstrated effective at maintaining long-term remission. In scalp PsO, once daily induction with clobetasol propionate shampoo for 4 weeks followed by 6 months of twice-weekly maintenance therapy was shown to

TABLE 1 Summary of long-term management regimens (≥12 weeks) for the topical treatment of psoriasis

Topical agent	Label dose	Maintenance regimen studied[a]	Body area(s) treated[a]	Supporting evidence	Long-term management goal(s) fulfilled	Reference
Continuous long-term therapy						
Vitamin B_{12} ointment versus emollient cream	Not stated	Twice daily × 12 weeks	Any affected area	1 RCT (N = 24)	• Maintenance of disease control • Reduces frequency of relapse • Long-term safety and tolerability • Optimizes the patient experience (quality of life)	Del Duca et al., 2017[58]
Clobetasol propionate 0.05% ointment versus betamethasone valerate 0.1% or fluocinolone acetonide 0.025%	Two to three times daily up to 2 weeks	Twice daily × 6 months	Any affected area	2 RCTs (N = 41)	• Maintenance of disease control • Reduces frequency of relapse • Increases interval until recurrence • Long-term safety • Optimizes the patient experience	Corbett, 1976[9] Floden et al., 1995[10]
Tacalcitol 4 μg/g	Once daily (maximum duration not stated)	Once daily × 3 to 18 months	Any affected area	3 RCTs (N = 472)	• Maintenance of disease control • Long-term safety • Optimizes the patient experience and adherence	Lambert & Trompke, 2002[12] Van de Kerkhof et al., 1997[13] Van de Kerkhof et al., 2002[14]
Calcitriol 3 μg/g	Twice daily (maximum duration not stated)	Twice daily for up to 78 weeks	Any affected area	1 RCT (N = 253)	• Maintenance of disease control • Reduces frequency of relapse • Long-term safety • Optimizes the patient experience	Langner et al., 1996[15]
Tacrolimus 0.3% gel or 0.5% cream[b]	Twice daily (induction) and two to three times weekly up to 12 months	Twice daily × 12 weeks	Any affected area	1 RCT (N = 124)	• Maintenance of disease control • Long-term safety • Optimizes the patient experience	Ortonne et al., 2006[16]
Chronic intermittent therapy						
Calcipotriol 50 μg/g + betamethasone dipropionate 0.5 mg/g gel	Once daily up to 8 weeks (body) or 4 weeks (scalp)	Once daily until clearing followed by reactive treatment for up to 52 weeks	Scalp	1 RCT (N = 869)	• Maintenance of disease control • Long-term safety • Optimizes the patient experience and adherence	Luger et al., 2008[26]
Calcipotriene 0.005% + betamethasone dipropionate 0.064% foam	Once daily up to 4 weeks	Once daily until clearing followed by reactive treatment for up to 6 months	Any affected area	1 RCT (N = 134)	• Optimizes the patient experience and adherence • Maintenance of disease control	Svendsen et al., 2018[27]
Step-down therapy						
Clobetasol propionate 0.05% shampoo	Once daily up to 4 weeks	Once daily × 4 weeks (induction) + Twice weekly × 6 months (maintenance)	Scalp	1 RCT (N = 168)	• Maintenance of disease control • Reduces frequency of relapse • Increases interval until recurrence • Minimizes long-term drug exposure • Long-term safety • Optimizes the patient experience and adherence	Poulin et al., 2010[32]

(Continues)

TABLE 1 (Continued)

Topical agent	Label dose	Maintenance regimen studied[a]	Body area(s) treated[a]	Supporting evidence	Long-term management goal(s) fulfilled	Reference
Calcipotriol 50 μg/g + betamethasone dipropionate 0.5 mg/g gel	Once daily up to 4 weeks	Once daily until remission then twice weekly for 12 weeks	Scalp	1 RCT (N = 885)	• Maintenance of disease control • Reduces frequency of relapse • Minimizes long-term drug exposure • Long-term safety	Saraceno et al., 2014[33]
Calcipotriol 50 μg/g + betamethasone dipropionate 0.5 mg/g ointment	Once daily up to 4 weeks	Once or twice weekly × 3 months (maintenance in pts with stable disease)	Any affected area	1 RCT (N = 96)	• Maintenance of disease control • Minimizes long-term drug exposure • Long-term safety • Optimizes the patient experience	Zhu et al., 2016[34]
Calcipotriol 50 μg/g + betamethasone dipropionate 0.5 mg/g gel	Once daily up to 8 weeks	Once daily × 8 weeks (induction) then twice weekly (on weekends) × 8 weeks	Limbs and trunk	1 RCT (N = 117)	• Maintenance of disease control • Minimizes long-term drug exposure • Long-term safety • Optimizes patient adherence	Lee et al., 2017[35]
Sequential or pulse therapy ("weekend") regimens						
Calcipotriene 0.005% + halobetasol 0.05%	Calcipotriene: once daily (with steroids; maximum duration not stated) Halobetasol: twice daily up to 2 weeks	Calcipotriene twice daily (weekdays) + halobetasol twice daily (weekends) × 6 months	Any affected area	1 RCT (N = 40)	• Maintenance of disease control • Increases interval until recurrence • Long-term safety	Lebwohl et al., 1998[38]
Clobetasol propionate (CP) foam 0.05% + calcipotriene 0.005% ointment	Clobetasol: Twice daily up to 2 weeks Calcipotriene: once daily (with steroids; maximum duration not stated)	Twice daily combination or monotherapy × 2 weeks (induction) then calcipotriene once daily on weekdays + CP or vehicle once daily on weekends × 24 weeks (maintenance)	Any affected area	1 RCT (N = 38)	• Maintenance of disease control • Optimizes the patient experience	Koo et al., 2006[37]
Calcipotriol 50 μg/g + betamethasone dipropionate 0.5 mg/g ointment	Once daily up to 4 weeks	Once daily prn × 52 weeks (continuous OR alternating 4-week periods with calcipotriol OR 4 weeks Cal/BD ointment followed by 48 weeks calcipotriol)	Any affected area	1 RCT (N = 634)	• Maintenance of disease control • Long-term safety • Optimizes the patient experience	Kragballe et al., 2006[39] Kragballe et al., 2006[36]
Proactive management regimen						
Calcipotriene 0.005% + betamethasone dipropionate 0.064% foam	Once daily up to 4 weeks	Once daily × 4 weeks (induction) then twice weekly up to 52 weeks (maintenance) with rescue daily therapy during flares	Any affected area	1 RCT (N = 545)	• Maintenance of disease control • Reduces frequency of relapse • Increases interval until recurrence • Minimizes long-term drug exposure • Long-term safety • Low risk of rebound	Lebwohl et al., 2021[7]

Abbreviations: Cal/BD, fixed-dose calcipotriol + betamethasone dipropionate; CP, clobetasol propionate; pts, patients; RCT, randomized controlled trial.
[a]According to clinical trials.
[b]Off-label (not approved for treatment of psoriasis).

prolong time to relapse by 141 days compared to a vehicle control.[32] Studies involving fixed-dose combinations of TCS and vitamin D_3 analogs also support a step-down strategy to maintain remission in patients with stable disease. A large European and Canadian study in patients with scalp PsO demonstrated that twice-weekly application of Cal/BD gel was significantly more effective at maintaining remission and preventing relapse compared to a reactive strategy (i.e., "on demand" daily application).[33] A smaller study conducted in China compared once or twice weekly maintenance treatment with Cal/BD ointment versus calcipotriol ointment daily for 12 weeks in patients with stable body PsO.[34] The twice-weekly Cal/BD maintenance regimen provided comparable efficacy as daily treatment with calcipotriol, and both regimens were significantly more effective than once weekly Cal/BD ointment. Patients with limb or trunk PsO who achieved disease control after 8 weeks of daily treatment with Cal/BD gel were randomized to either maintain once daily treatment continuously or as needed, or to twice weekly treatment on weekends for a further 8 weeks in a small Korean study.[35] Long-term daily treatment used either continuously or as-needed was significantly more effective at maintaining remission than weekend-only therapy. It should be noted that this study had a relatively short duration of maintenance therapy (i.e., 8 weeks) compared to other long-term trials.

Sequential regimens (i.e., alternating between two different topical agents) have been investigated as a long-term approach for the management of PsO. A 52-week study showed that alternating between 4-week cycles of once daily treatment with Cal/BD ointment and calcipotriol ointment was similarly effective as continuous treatment with Cal/BD ointment or 4 weeks of Cal/BD followed by 48 weeks of calcipotriol alone, although there was a trend favoring continuous Cal/BD from both the physician's and patient's perspective.[36] "Pulse" therapy or "weekend" regimens involve an induction or clearing phase with daily treatment followed by a maintenance phase of cycling between two treatments with different modes of action.[37] For example, after an induction phase, alternating daily treatment with a vitamin D_3 analog on weekdays and a TCS on weekends has been shown more effective for maintaining remission than a single therapy regimen applied only on weekdays or weekends.[37,38] Importantly, these long-term fixed-dose combination strategies were not associated with risk of HPA axis suppression or disturbances in calcium homeostasis;[7,26,39,40] in one study, Cal/BD was associated with a lower rate of adverse effects such as local skin irritation compared to either agent used alone.[26]

Proactive maintenance therapy has been employed in real-world management of PsO for several years, but it has not been an evidence-based approach—until now. The PSO-LONG study explored the efficacy and safety of a proactive maintenance approach to the management of PsO using Cal/BD foam twice-weekly.[7] This strategy involves proactively applying topical agents to target lesions that have cleared to prevent relapses instead of reactively treating flares, and it has been successfully implemented in other dermatological conditions such as atopic dermatitis.[41] PSO-LONG was a Phase III trial with a 4-week open-label lead-in phase followed by a 52-week double-blinded randomized maintenance phase comparing proactive management (i.e., Cal/BD foam twice weekly during remission and Cal/BD foam rescue treatment during relapse) versus reactive management (i.e., vehicle foam twice weekly during remission and Cal/BD foam rescue treatment during relapse) (Figure 1).[7] The risk of relapse was significantly reduced by 43% with the proactive versus reactive regimen, and patients spent 41 additional days in remission (Supplemental Table S1). The incidence of adverse effects was similar in both groups, and maintenance therapy with Cal/BD foam over 52 weeks was not associated with increased risk of skin atrophy, HPA axis suppression, or disturbances in calcium homeostasis.[7] Evidence from the PSO-LONG study considerably strengthens the observation that proactive maintenance therapy is an effective and well-tolerated approach that has a favorable safety profile. Overall, this study provides reassuring evidence to support the extended use of a proactive topical maintenance strategy in PsO for at least 1 year.

4 | UNANSWERED QUESTIONS

4.1 | How should we transition to maintenance therapy to maintain disease control?

A prominent unanswered question concerns the optimal way to transition from acute care to maintenance therapy to preserve remission and avoid relapses. The authors suggest that maintenance therapy should begin when a clinical response is reached, likely after approximately 4 weeks of acute topical treatment. A 4-week acute treatment period has been used successfully in a scalp PsO maintenance study[32] and in the PSO-LONG proactive maintenance study of Cal/BD foam,[7] while other studies have used induction phases as short as 2 weeks[37,38] or as long at 8 weeks.[35] Overall, 4 weeks of acute treatment is likely realistic for most patients, but decisions should be individualized since some patients may benefit from earlier or later transition from acute to maintenance therapy.

Based on the natural relapsing–remitting course of PsO, symptoms eventually re-appear in most patients if left untreated. This introduces the discussion about the optimal duration of maintenance therapy. Current evidence on extended use of Cal/BD is limited to 52 weeks, but there are no reasons to suggest this duration cannot be extended based on its favorable efficacy and safety. In PSO-LONG, only a minority of patients had no relapses at their target lesion through 52 weeks of maintenance Cal/BD foam treatment; however, the overall relapse rate was significantly lower in the proactive versus reactive group (i.e., 3.1 vs. 4.8 per year, respectively; $p < 0.001$).[7] This suggests that proactive long-term treatment with Cal/BD foam is associated with important benefits for patients. Clinical judgment should be used to individualize the duration of maintenance therapy.

4.2 | How should maintenance therapy be monitored?

The concept of "treating to target," or the practice of tailoring treatment to achieve specific and measurable targets, has been used successfully in several fields, such as cardiovascular disease and rheumatoid arthritis. This approach is relatively new in PsO

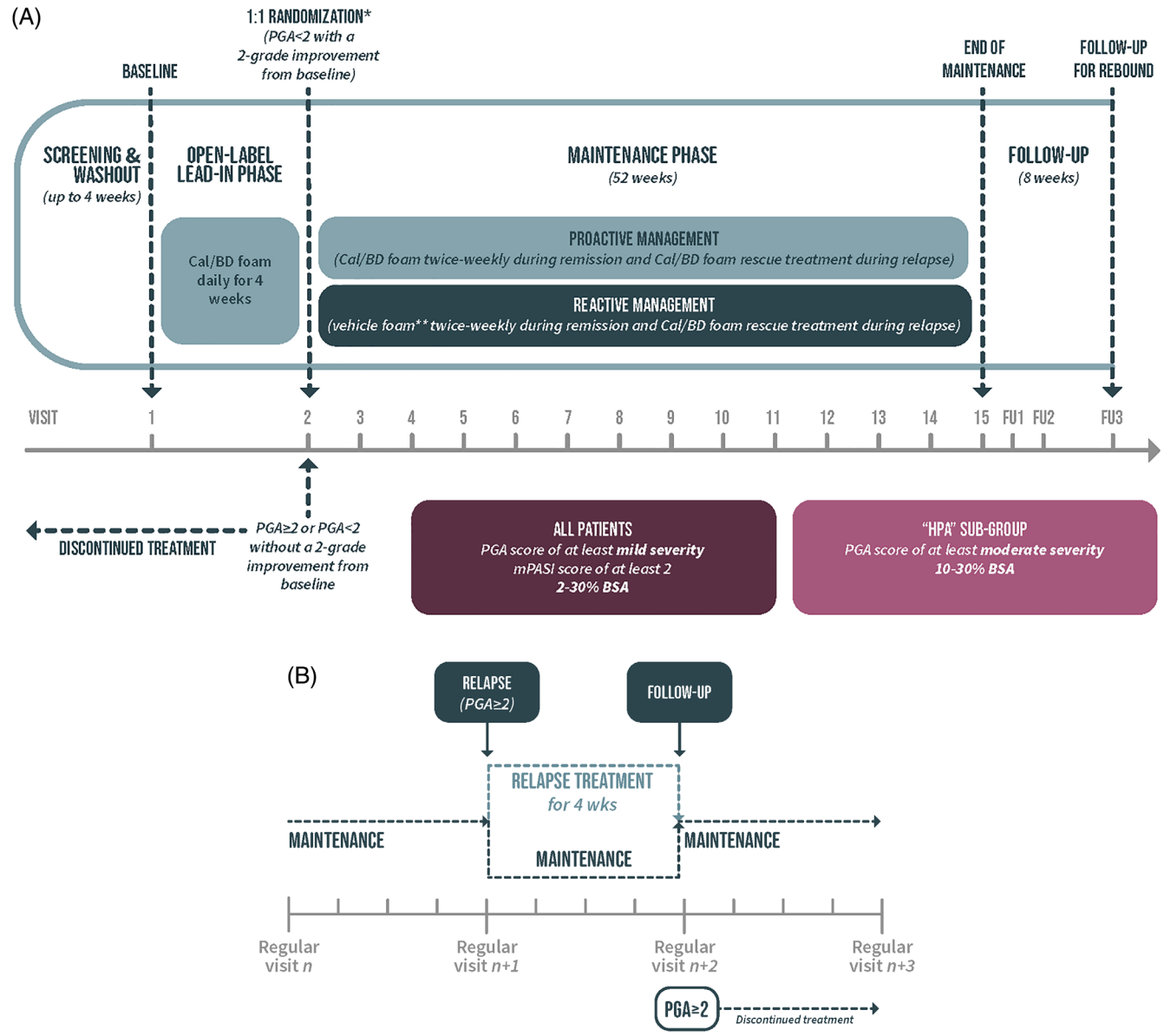

FIGURE 1 PSO-LONG trial design (A) and relapse management throughout the maintenance phase (B). Adapted from Lebwohl et al. (2021).[7] *Only patients achieving PGA <2 with a 2-grade improvement from baseline were randomized; those not meeting this threshold response were discontinued from the trial. **Vehicle foam is foam without any API. Relapse treatment is Cal/BD foam once daily (provided as separate relapse bottles) for both proactive and reactive management groups. BSA, body surface area; Cal/BD, calcipotriene/betamethasone dipropionate; mPASI, modified Psoriasis Area and Severity Index; PGA, Physician's Global Assessment

management and is limited by the lack of clear and established targets. A variety of treatment targets have been suggested across different PsO guidelines and expert consensus groups, mostly pertaining to systemic therapies. For example, the National Psoriasis Foundation (NPF) recommends BSA as the preferred assessment tool for PsO: they characterize target response—both for induction and maintenance phases—as BSA < 1%.[42] A Canadian expert group suggested an optimal target of Physician's Global Assessment (PGA) x BSA <1; however, BSA poorly reflects the patient's disease burden and there is low-interrater reliability for this outcome measure.[43] An Asian consensus statement highlights "satisfactory control of the disease and prevention of relapses" as main goals of maintenance therapy.[6] In PSO-LONG, a PGA score of 0 to 1 (i.e., "clear" or "almost clear") at the target lesion was used to define maintenance of response.[7] Similarly, Canadian expert groups have suggested treating lesions to achieve clear skin (i.e., PGA score = 0),[44] while an international group of experts suggests PGA score of 0 or 1.[2] European experts define treatment success as 90% improvement or more in baseline PASI scores (PASI 90 response).[45] Objective measures should be considered in parallel with patient-centered reports of health-related quality of life to truly assess the impact of treatment on patients' everyday lives.[3,45] Noninvasive imaging modalities such as dermoscopy and reflectance confocal microscopy have been shown to be sensitive to treatment response and could thus be used for monitoring response to topical therapy[46,47] and for the early detection of TCS-related side effects including atrophy and telangiectasias.[48]

We suggest that the goals of maintenance therapy should be based on two objectives: (1) preservation of the clinical effect at the target area, and (2) minimize drug utilization. By extension, treatment failure should be defined by disease flares that force patients to either increase frequency of topical treatment use or require an increase in the quantity of medication required for disease control. In their recent guidelines, the NPF recommended that maintenance therapy be monitored by biannual medical visits.[42] While this suggestion was originally devised with systemic PsO therapies in mind, follow-up every 6 months provides a reasonable starting point for many patients, including those treated exclusively with topical agents. Follow-up frequency should be adjusted according to physicians' clinical judgment in association with patients' needs and preferences. It is well documented that adherence with PsO therapy is suboptimal[49] and may be even lower when symptoms are well-controlled, such as during successful maintenance therapy.[50] Although more frequent follow-up may increase adherence and enhance long-term treatment success, this is impractical in the real-world clinical setting. For patients on potent or super-potent TCS either alone or as part of a fixed-dose combination product, it is suggested that the presence or absence of corticosteroid-induced skin atrophy should be documented at every follow-up visit so that this side effect can be managed at the earliest opportunity.

4.3 | Where does topical maintenance therapy fit with respect to systemic and biologic therapies?

The REFINE trial showed that the addition of a TCS to etanercept helped maintain remission at week 24 while concurrently decreasing the dosage of the biologic agent.[51] The addition of once daily Cal/BD foam in a 4-week acute phase followed by a 12-week maintenance phase of twice weekly application in patients with suboptimal response to biologics significantly reduced disease activity, increased quality of life, and was associated with higher satisfaction at both week 4 and week 16.[52] Treatment plans that include both systemic and topical agents appear to be efficacious and safe and may improve drug sustainability and cost-effectiveness. Based on the current evidence, proactive maintenance treatment with topical agents is a strategy that can be used irrespective of background therapy. Indeed, we believe that PsO maintenance treatment with topical agents can be used as a stand-alone therapy or as a complementary strategy to other systemic or biologic therapies. Nonetheless, there remains an important clinical need to formally examine the optimal modalities with which topical therapies can be used in conjunction with diverse systemic medications in the long-term treatment setting.

4.4 | Is there a rebound effect when maintenance therapy is discontinued?

Withdrawal of medication, especially if abrupt, has been associated with the risk of PsO rebound. Canadian PsO guidelines define rebound as PASI scores increasing to at least 125% of baseline or when patients experience new generalized pustular, erythrodermic, or more inflammatory PsO within 3 months of discontinuing an anti-psoriatic agent.[3] PSO-LONG is one of the only maintenance studies that analyzed rebounds as a safety outcome. There were few rebounds when patients transitioned from once daily to twice weekly application or within 2 months of discontinuing recue medication, and none during 2 months of follow-up after the end of the active study period, whereas more patients in the reactive management group experienced rebounds after the end of rescue treatment than patients in the proactive maintenance group (Table 2). These observations suggest that topical Cal/BD foam is infrequently associated with disease worsening when discontinued and proactive maintenance therapy appears to carry a lower risk of rebound compared to a reactive approach. Nonetheless, data quantity and quality remain limited on this front and additional evidence, including from real-world clinical settings, could deepen our understanding of rebound effects associated with proactive maintenance use of topical agents.

4.5 | Is there a specific patient profile or lesion type that is more amenable to maintenance therapy?

PsO is associated with heterogeneous symptoms that include scaling, erythema, and thickness and the extent and location of lesions can vary greatly between patients. At this point, it is not possible to predict a specific patient phenotype that will be responsive to maintenance therapy. From a practical perspective, patients whose quality of life is greatly impacted by PsO, those who experience seasonal disease exacerbations (e.g., in winter), those completing phototherapy, or patients who tend to experience disease recurrence shortly after stopping topical therapy, could be reasonable candidates for proactive maintenance therapy.

TABLE 2 Number of patients who experienced rebounds[a] during the PSO-LONG trial[7]

	Proactive management (n = 272)	Reactive management (n = 273)
Rebounds within 2 months of discontinuing open-label acute treatment	6	7
Rebounds within 2 months of discontinuing once-daily rescue medication	4	17
Rebounds within 2 months after the end of maintenance treatment	0	1

[a]Rebounds were characterized by a modified PASI (mPASI) score ≥ 12 and increase from baseline in mPASI of ≥125% or the development of more inflammatory disease.

4.6 | What type of patient education and support are necessary to promote optimal outcomes?

The chronic nature of PsO and its associated psychological and physical burden make patient-centered care critical to optimize outcomes. Patient concerns, worries, and preferences should be taken into account in the development of a treatment plan, especially in the current context where strong evidence is lacking to support definitive answers to several maintenance treatment-related questions. Most patients with PsO and dermatologists share similar safety concerns including treatment-related adverse effects such as HPA axis suppression and disturbances of calcium homeostasis, and risk of rebounds, flares, and tachyphylaxis. These concerns should be addressed with patients at the earliest opportunity. Tachyphylaxis is a rare occurrence in PsO patients who are treated with TCS either as monotherapy or with Cal/BD foam.[7,53] The transition between acute and maintenance therapy regimens should be explained to patients; this could be facilitated by the development of a PsO action plan, similar to action plans that are used for proactive maintenance therapy of atopic dermatitis.[54] Some patients, especially those concerned with exposure to corticosteroids, may be tempted to scale down the frequency of application as soon as they notice improvements in their lesions. However, patients should be encouraged to only decrease treatment frequency once clinical response is optimal, ideally when skin is totally clear, since premature reduction in treatment frequency when skin in "almost clear" could be expected to hasten disease recurrence.

Patient-centered care may encourage the development of desirable patient behaviors with respect to long-term adherence. A program that included patient education about the benefits of therapy, regular two-way dialog between patients and healthcare professionals, and patient involvement in the design of treatment plans led to greater clinical response rates than standard care.[55] The positive outcomes derived from patient education programs may be mediated by increased treatment adherence, a factor that is particularly problematic with topical PsO therapy.[4,49] European guidelines state that patients' active involvement in the choice of product, formulation, and mode of application enhances empowerment and treatment adherence.[31] Adherence during maintenance therapy may be especially challenging since patients tend to decrease medication usage when lesions are well-controlled[50] and with longer duration of therapy.[56] In contrast, adherence to topical therapy is maximized around medical office visits and when treatment schedules are simple.[57] Highlighting practical benefits associated with long-term therapy, including potential cost reduction to patients, may provide additional incentives to adhere to the management plan. There is also emerging evidence supporting the utility of smartphone apps to support long-term adherence to topical PsO therapies.[27]

5 | CONCLUSIONS

PsO is a chronic remitting–relapsing disease that requires long-term management over an individual's lifetime. Despite this need, current guidelines do not provide explicit recommendations on the ideal choice, frequency, and duration of topical agents that can be used safely for long-term disease control, and when to transition from acute to maintenance therapy. As such, a significant population of patients is unsatisfied with their current treatment. These unmet needs highlight the opportunity to reconsider our clinical practice with regards to PsO maintenance therapy. Recent clinical trial evidence offers reassurance to clinicians that it is no longer necessary to discontinue topical TCS-containing therapies after an initial 4-week acute treatment phase. Instead, proactive maintenance treatment for up to 1 year, even when skin is clear and clinical parameters indicate remission, is emerging as a new paradigm that may enhance long-term disease control. To maximize the potential benefits of such an approach, step-down to a maintenance regimen should only occur once the skin is clear, since premature reduction in treatment frequency could hasten disease recurrence.

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CONFLICT OF INTEREST

The authors were clinical investigators for the PSO-LONG trial. Kim A. Papp has served as an advisor/consultant for AbbVie, Akros, Amgen, Arcutis, Astellas, Bausch Health/Valeant, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite Biopharma, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Evelo, Galapagos, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, LEO Pharma, Meiji Seika Pharma, Merck (MSD), Merck-Serono, Mitsubishi Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi-Aventis/Genzyme, Sun Pharma, Takeda, and UCB; has received clinical research grants/honoraria from AbbVie, Akros, Amgen, Anacor, Arcutis, Astellas, Bausch Health/Valeant, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite Biopharma, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Evelo, Galapagos, Galderma, Genentech, Gilead, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, LEO Pharma, Medimmune, Merck (MSD), Merck-Serono, Mitsubishi Pharma, Moberg Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi-Aventis/Genzyme, Sun Pharma, Takeda, and UCB; has served as a speaker for AbbVie, Amgen, Astellas, Bausch Health/Valeant, Celgene, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, LEO Pharma, Merck (MSD), Novartis, Pfizer, and Sanofi-Aventis/Genzyme; is a scientific officer for Akros, Acutis, Astellas, and Kyowa Hakko Kirin; and a steering committee member for AbbVie, Amgen, Bausch Health/Valeant,

Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Kyowa Hakko Kirin, Merck (MSD), Merck-Serono, Novartis, Pfizer, Regeneron, and Sanofi-Aventis/Genzyme. Gurbir Dhadwal has served as a consultant and a speaker for LEO Pharma. Melinda Gooderham has served as a consultant for Amgen, Arcutis, Akros, AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Eli Lilly, Galderma, Janssen, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Valeant/Bausch Health, and SUN Pharma; has received research funds from Amgen, Arcutis, Akros, AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, Dermavant, Eli Lilly, Galderma, Janssen, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, UCB, Valeant/Bausch Health, and SUN Pharma; has received payment for lectures and/or development of educational presentations from Amgen, AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, UCB, and Valeant/Bausch Health; and reimbursement for travel/accommodations/meeting expenses from Amgen, AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, UCB, Valeant/Bausch Health, and SUN Pharma. Lyn Guenther has been a consultant, investigator, and speaker for AbbVie, Amgen, Bausch, Celgene, Eli Lilly and Company, Janssen, LEO Pharma, Merck, and Pfizer; has been a speaker and consultant for Tribute; and has been an investigator for Roche, UCB and Sun Pharmaceuticals. Irina Turchin has been a board member/consultant, speaker bureau member, and has received payment for development of educational presentations from LEO Pharma. Marni Wiseman has been a consultant/advisor and/or speakers bureau member for AbbVie, Janssen, Eli Lilly, Sanofi, Novartis, Galderma, Bausch Health, Amgen, LEO Pharma, Pfizer, UCB, and La Roche-Posay; has received grants/honoraria from the Canadian Dermatology Foundation; and a clinical investigator for 3 M Pharmaceuticals, AbbVie, Akros, Allergan, Amgen, Arcutis, Asana Biosciences, Astellas, AstraZeneca, Bausch Health, Biogen Idec, Bristol-Myers Squibb, Celgene, Cipher, Dermira, Dow Pharmaceuticals, DS Biopharma, Eli Lilly, Hoffman-La Roche, Fujisawa, Galderma, GlaxoSmithKline, Glenmark, Incyte, Janssen, LEO Pharma, Merck-Frosst Canada, Novartis, Paddock Laboratories, Pricipia, PRCL Research, Regeneron, Stiefel, UCB Biopharma, Valeant, Vical, and Xenon. Jensen Yeung has been a speaker, consultant, clinical investigator, and/or has received honoraria from AbbVie, Amgen, Anacor, Astellas, Bausch, Baxalta, Boehringer Ingelheim, Celgene, Centocor, Coherus, Dermira, Eli Lilly, Forward, Galderma, Janssen, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, Takeda, UCB, and Xenon.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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