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REVIEW

Scalp Psoriasis: A Literature Review of Effective Therapies and Updated Recommendations for Practical Management

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ABSTRACT

The scalp is one of the most commonly affected regions in psoriasis. However, scalp psoriasis can be difficult to treat because of challenges in the delivery of therapy. Effective therapeutic regimens for scalp psoriasis are essential to improving the quality of life of patients. Recent data on topical therapies, phototherapy, systemic agents, and complementary therapy have demonstrated that it is possible to achieve and maintain significant improvement in scalp psoriasis. In this review, efficacy data for these modalities and an algorithm for the practical management of scalp psoriasis are presented.

Keywords: Psoriasis; Scalp; Special site; Biologic; Systemic; Topical; Phototherapy

Key Summary Points

Scalp psoriasis presents as a significant burden to patients due to the difficult-to-treat nature of the site.

Data suggest discussions about patient-preferred topical formulation may be a way to improve patient quality of life and increase treatment adherence.

Additionally, UVB and excimer phototherapy via handheld device or with the addition of a blow dryer to separate the hair has been efficacious in clearing of scalp plaques.

Etanercept, adalimumab, infliximab, brodalumab, secukinumab, ixekizumab, ustekinumab, guselkumab, risankizumab, mirikizumab, ustekinumab, and apremilast all have demonstrated varying levels of efficacy in the scalp and are suitable first-line options for patients with scalp plaques plus whole-body psoriasis.

A practical treatment algorithm, derived from the most up-to-date empirical evidence, is also presented within this paper for mild-to-moderate scalp psoriasis, severe scalp psoriasis, and scalp psoriasis with moderate-to-severe whole-body involvement.

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DIGITAL FEATURES

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INTRODUCTION

Psoriasis is an immune-mediated, chronic, systemic inflammatory condition affecting the skin and other organ systems. In the United States, psoriasis affects approximately 7.4 million adults [1]. Plaque psoriasis, which is the most common subtype of psoriasis accounting for about 80–90% of cases, presents as well-demarcated, erythematous plaques with micaceous scale [2].

The scalp is the most commonly affected region of the body in psoriasis, involved in about 80% of psoriasis cases [3]. Psoriasis of the scalp requires special consideration due to the difficult-to-treat nature and disproportionate impact on quality of life [2, 4]. In addition to the physical symptoms of pain and pruritus, psoriasis, especially with involvement of the scalp, can lead to significant psychosocial impairment [5]. Due to the presence of hair, poor accessibility, and unacceptable cosmetic appeal of topical therapy, patients also tend to have poor adherence and satisfaction with treatment [3, 6]. Regimens can be complex and are highly dependent on patient preference. Recent research on scalp psoriasis treatment has focused on therapies to improve efficacy and patient satisfaction.

Effective management of scalp psoriasis is essential to improving a patient's quality of life. This article reviews the most recent efficacy data of topical therapies, phototherapy, oral and injectable therapies, and complementary therapies for scalp psoriasis. Based on these data, practical recommendations for the management of scalp psoriasis are provided.

METHODS

A literature search was conducted in PubMed and Embase in December 2020 using the search terms "scalp" AND "psoriasis" AND ("patient preference treatment" OR "topical" OR "corticosteroid" OR "intralesional corticosteroid" OR "vitamin D analogue" OR "keratolytic" OR "salicylic acid" OR "urea" OR "methotrexate" OR "cyclosporine" OR "acitretin" OR "etanercept" OR "adalimumab" OR "brodalumab" OR "ixekizumab" OR "secukinumab" OR "guselkumab" OR "infliximab" OR "certolizumab" OR "ustekinumab" OR "risankizumab" OR "mirikizumab" OR "apremilast" OR "phototherapy" OR "comb" OR "coal tar"). Studies were included if they were original, peer-reviewed studies assessing treatment for scalp psoriasis. Case studies or case series were only included if there were no other studies to support the efficacy of that treatment. Studies were excluded if the primary or secondary outcomes did not include a scalp-specific measurement or if the full text could not be obtained. Only studies written in the English language were reviewed. Comprehensive review articles were referenced to identify any additional studies that were missed. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

RESULTS

Topical Therapy

Topicals are the first-line therapy in the treatment of mild-to-moderate scalp disease. Topical corticosteroids remain a mainstay treatment in scalp psoriasis, with data supporting safety and efficacy [7, 8]. Alternative topical treatments such as topical vitamin D analogs, keratolytics, and coal tar can be a beneficial addition to the therapeutic regimen for scalp psoriasis. Highlighted below are recent data regarding patient preference, efficacy, safety, and responses for corticosteroids, topical vitamin D combination therapy, keratolytics, and coal tar.

Corticosteroids

Topical corticosteroids are an effective option for short-term treatment of scalp psoriasis. A systematic review comparing the efficacy outcomes of topical treatments in scalp psoriasis found that topical corticosteroid monotherapy was more effective in clearing scalp psoriatic lesions than vitamin D analog monotherapy [9]. Corticosteroid monotherapy also led to fewer withdrawals from treatment due to adverse events than did vitamin D monotherapy [9].

Different formulations of topical corticosteroids have emerged to improve treatment adherence, quality of life, and satisfaction regarding the cosmetic appeal [10]. Corticosteroid vehicles that are most frequently preferred for the scalp include foam, gel, solutions, shampoo, and spray [6]. Several studies have shown excellent clinical improvements using foams and sprays in the treatment of scalp psoriasis [11–13]. A foam formulation of betamethasone valerate was previously found to show significantly greater improvement ($p < 0.001$) in erythema, scaling, burning, and itching clinical global scores of the scalp when compared with standard-treatment corticosteroid lotion formulations [11]. Additionally, foam therapy was noted by patients to be more cosmetically acceptable compared with standard treatment. The most frequently reported drug-related adverse events were burning and itching at the site of application [11].

More recently, desoximetasone 0.25% topical spray was evaluated in an open-label observational study [12]. Desoximetasone 0.25% topical spray led to rapid improvement in the clearance of lesions when treated twice daily for 4 weeks. The reduction from baseline scalp Investigator's Global Assessment (IGA) and Psoriasis Scalp Severity Index (PSSI) was 65% and 82.4%, respectively. The application was transitioned to twice weekly for maintenance of an additional 12 weeks, which showed a maintained reduction of scalp IGA and PSSI of 50% and 62.5% from baseline, respectively. The most common adverse events included burning sensation of the scalp and itching [12]. Given the efficacy and convenience, desoximetasone 0.25% topical may be an effective option for short-term or maintenance scalp treatment.

However, it is important to note that patient preference for topical formulation may vary with race, as one study showed that African Americans are more likely than white-race individuals to prefer ointment and lotion formulations when treating conditions of the scalp [14].

Combination Corticosteroid and Vitamin D Analog Topical Therapy

While moderate, high, and super-potent corticosteroids are effective in the management of scalp psoriasis, there are limited data regarding the long-term safety of corticosteroid monotherapy on the scalp [3, 9]. Vitamin D analogs are therefore a useful modality for maintenance therapy and long-term control. Combination therapy of topical corticosteroids plus vitamin D analogs appears to be at least equally as efficacious as corticosteroid monotherapy, and recent research demonstrates it may offer enhanced benefit in some cases [9]. A systematic review found that combination topicals consisting of corticosteroids and vitamin D analogs were more efficacious than both topical corticosteroid and vitamin D monotherapy alone in the treatment of scalp psoriasis, although the additional benefit over corticosteroid monotherapy was small. Combination therapy also led to fewer withdrawals from treatment due to adverse events when compared with vitamin D monotherapy [9].

In 2020, a post hoc analysis of a phase II randomized clinical trial evaluated the efficacy of a calcipotriene 0.005% and betamethasone dipropionate 0.064% (Cal/BD) foam in scalp psoriasis [15]. This study demonstrated that the modified Psoriasis Area and Severity Index (mPASI) score of the scalp for those treated with the Cal/BD foam showed a significantly greater improvement after 4 weeks of treatment when compared with calcipotriene 0.005% (Cal) foam monotherapy (0.18 versus 0.38, $p < 0.001$), but was not statistically different from patients treated with betamethasone dipropionate 0.064% (BD) foam monotherapy (0.18 versus 0.26, $p = 0.058$). The mPASI75 of the scalp for Cal/BD foam, Cal foam, and BD foam was 73%, 50.5%, and 65.3%, respectively, with no

statistical difference between the Cal/BD foam and BD foam ($p = 0.25$) [15].

While the added benefit of combination therapy in the scalp may be minimal, combination therapy may be useful for long-term intermittent treatment of scalp psoriasis. Combination of calcipotriol 50 μg/g plus betamethasone dipropionate 0.5 mg/g used as needed was found to be safe and effective up to 52 weeks [16]. Additionally, this study found no increased risk of steroid-associated adverse events in the combination compound when compared with 52 weeks of treatment with calcipotriol monotherapy [16].

Keratolytics

Keratolytic agents are also a helpful adjunctive treatment by promoting the reduction of psoriatic scale. These agents are proposed to increase the absorption of topical corticosteroids, which may lead to increased efficacy and clearance. However, one review noted this benefit may be limited to clinical trials, as increasing the complexity of regimens with multiple products may lead to decreased adherence in the clinical setting [17].

Typically, salicylic acid and urea are the treatments of choice for keratolysis, yet very few studies evaluate their efficacy in the scalp. Salicylic acid 6% foam was evaluated in an open-label pilot study of ten patients and led to a significant decrease in PSSI from 15.3 to 3 after 4 weeks of monotherapy ($p < 0.001$) [18]. Sixty percent of the subjects also were noted to be "completely cleared" or "almost cleared" at week 4. No adverse events were noted, but this study was limited by size and lack of control [18]. Even though urea is a well known keratolytic, to date there are no studies solely evaluating the benefit of urea in the treatment of scalp psoriasis.

Another notable keratolytic treatment option is a dimethicone-based topical solution (Loyon) that removes scaling of the scalp in a physical rather than pharmacological mechanism, as opposed to urea and salicylic acid. The low surface tension of the solution allows penetration between and underneath the scales of the scalp, facilitating softening and removal of scale [19]. The spray solution is applied to the scalp and washed off after allowing the solution to sit on the scalp for several hours. A noninterventional clinical trial in 2017 of 40 patients with psoriasis (70% with psoriasis capitis) demonstrated that after 7 days of use, patients had a significant mean reduction of PSSI by 33.4% ($p < 0.05$) when compared with baseline [19]. There were no product-related adverse events [19]. The lack of risk for skin irritation or systemic side effects suggests this solution may be a safe and effective option for adjunctive therapy, although larger studies with active comparators and controls are needed to further define the benefit.

Coal Tar

While coal tar is a very effective treatment for full-body psoriasis, there is a paucity of data regarding its efficacy in the scalp. One study demonstrated a coal tar gel was effective in clearing or markedly improving the scalp. Following 5 days of treatment with coal tar gel, patients that switched to coal tar shampoo were able to sustain the improvement for a median time of 8 months [20]. While it may be an effective treatment option in the scalp, discoloration of the scalp and light-hair leads to issues with patient compliance and cosmetic appeal of this treatment. A novel lecithinized coal tar that was shown to be less likely to stain hair and clothes may be a more patient-acceptable option for scalp psoriasis in the future [21, 22]. A case study demonstrated the effectiveness of a topical coal tar foam in combination with topical steroids for treatment-resistant scalp psoriasis. However, at this time, no randomized clinical trials have been completed for the foam formulation [23]. Further research may prove this formulation of coal tar to be a more cosmetically appropriate treatment for the scalp.

Phototherapy

Phototherapy is an effective option for psoriasis but is limited by a lack of efficient ways to target the scalp in the presence of hair. Handheld phototherapy machines help overcome this challenge and provide a more convenient option for directed treatment of the scalp. A

targeted broad-band UVB fiber-optic comb, evaluated in a small pilot study, demonstrated improvement of scalp psoriasis, as seen through an overall improved mean mPASI score of 3.6 [24]. The method of phototherapy was also well tolerated, without patient reports of sunburns or blistering [24]. Another randomized head-to-head study of 44 patients demonstrated a UVB comb on the scalp five times a week was equally efficacious to betamethasone valerate solution five times a week after 3 weeks [25]. Treatment with the UVB comb also resulted in a statistically significant lower rate of relapse compared to the corticosteroid comparator [25].

Several studies have shown both the 308-nm excimer laser and light to be useful tools for the treatment of scalp plaques [26–28]. A 2004 study evaluated the 308 nm excimer laser for the treatment of patients who had refractory scalp psoriasis unresponsive to class I steroids and medicated shampoos [27]. A total of 13 patients were treated over half of their scalp with the excimer laser twice weekly for 15 weeks or until a mPASI of 0 was achieved. A hair blower was used to part obstructing hair and allow better access to the scalp. After the last treatment, there was a mean mPASI difference of 4.0 between the control and treated sites ($p < 0.0001$), with 12 of the 13 patients showing clinical improvement in the treated area [27]. A study in 2012 evaluated the efficacy of the xenon chloride gas 308-nm excimer laser in 23 patients with recalcitrant scalp psoriasis. After 12 weeks, the median percent improvement of PSSI from baseline was 78.57%. Improvement in PSSI was present as early as week 4 [28].

Furthermore, a novel nonlaser monochromatic excimer 308 nm light, which provides a more powerful and larger irradiation area, was evaluated for the treatment of scalp psoriasis [26]. Results from the retrospective study revealed that 11 out of 20 patients achieved more than 50% improvement after a total of ten sessions. Treatment with the excimer lamp was associated with a significant improvement in itch and PSSI. The most common adverse events reported were pain and erythema, but all adverse events resolved within 7 days [26]. While early results appear promising, device availability may be limited and further research is needed.

Although an unconventional therapy for psoriasis, one early randomized head-to-head study of 68 patients suggested UVA1 is as effective as narrowband UVB (NB-UVB) and may even lead to quicker response for the treatment of scalp psoriasis [29]. UVA1 was delivered to the scalp by a UVA1 emitting light system (Sigma, Shanghai, China), and NB-UVB was delivered to the scalp via a NB-UVB system with Philips TL-01 lamps (Philips, Einthoven, Netherlands). UVA1 led to significantly greater improvements in PSSI compared with NB-UVB at week 3, but by week 10 of treatment these differences decreased. Both UVA1 and NB-UVB significantly improved Dermatology Life Quality Index (DLQI) when compared with baseline, but this was more rapid with UVA1 [29]. UVA1 is a relatively uncommon therapy for scalp psoriasis, but it is commonly prescribed for other dermatologic conditions. While handheld UVA1 systems may not be widely available at this time, both National Biological (Houva 4/5) and Daavlin (ML24000) produce clinic-based full-body UVA1 phototherapy machines, and Daavlin also produces a home UVA1 phototherapy lamp panel (1 Series). More research is needed to further evaluate the efficacy of UVA1 in scalp psoriasis.

Systemic Therapy

Treatment with systemic agents, including methotrexate, cyclosporine, acitretin, biologics, and phosphodiesterase-4 inhibitors (PDE-4 inhibitors), is first-line therapy for patients presenting for scalp psoriasis with accompanying moderate-to-severe whole-body psoriasis. These agents are also indicated as second-line therapy in patients who have failed previous treatment with topicals or phototherapy. While there is a lack of clinical data regarding the efficacy of traditional systemic therapies, such as methotrexate, cyclosporine, and acitretin, in the treatment of scalp psoriasis, these agents are still recommended by consensus groups for scalp disease given their well-recognized success in the treatment of whole-body plaque psoriasis

[3, 30]. Several randomized control trials and observational studies have emerged in the last few years evaluating the efficacy of biologics and small molecules for scalp psoriasis, including etanercept, adalimumab, infliximab, brodalumab, secukinumab, ixekizumab, ustekinumab, guselkumab, risankizumab, mirikizumab, and apremilast. No clinical data were found regarding certolizumab pegol in the treatment of scalp psoriasis. Detailed scalp-specific study outcomes of the systemic agents are presented in Table 1. To date, the only biologic or small-molecule therapies that have efficacy data for scalp psoriasis included in their Food and Drug Administration (FDA) label are guselkumab, secukinumab, and apremilast [31–33].

TNF-Alpha Inhibitors

Etanercept

Etanercept was one of the first biologics shown to be effective for the treatment of moderate-to-severe scalp psoriasis, as demonstrated by a randomized, double-blind, placebo-controlled study in 2012. The proportion of patients who achieved PSSI 75 at week 12 was 86% in the etanercept group and 11% in the placebo group [$p < 0.0001$]. At week 12, patients treated with etanercept had a significantly greater mean PSSI improvement than patients treated with placebo (86.8% and 20.4%, respectively [$p < 0.0001$]). Both groups of patients, including patients initially on etanercept 50 mg twice weekly and patients on placebo, were switched to etanercept 50 mg once weekly at week 12. At week 24, the mean improvement of PSSI was 90.6% in the group lowered to once-weekly dosing of etanercept and was 79.1% in the group switched from placebo to etanercept. The rates of adverse events were comparable between etanercept and placebo at week 12 and between etanercept and placebo/etanercept at week 24 [34]. Etanercept has since been compared head-to-head with several biologic and small-molecule therapies for the treatment of scalp psoriasis as noted below.

Adalimumab

In a post hoc analysis of the phase III study BELIEVE, adalimumab was evaluated for efficacy of scalp psoriasis. The enrolled patients had a mean Psoriasis Scalp Severity Index (PSSI) score of 17.9 ± 14.1 at baseline. After 16 weeks of adalimumab, 77.8% of patients achieved a PSSI score of ≤ 4. Of all patients receiving adalimumab, both patients with scalp and nail disease, 61.8% experienced an adverse event. A majority of adverse events were classified as mild or moderate and headache and nasopharyngitis were the two most commonly reported events [35].

Another observational study evaluated the improvement of scalp psoriasis in patients with moderate-to-severe plaque psoriasis after treatment with adalimumab for 1 year. The 157 enrolled patients had a mean PSSI of 26.8 at baseline. After 1 year of therapy, 71.7% of patients had a PSSI of 0 representing a complete clearance of the scalp. Additionally, a mean reduction of 94.8% in PSSI was demonstrated after 1 year of adalimumab treatment. Out of all patients enrolled in the study with scalp or nail psoriasis, 9.6% reported any adverse event [36]. Adalimumab was also compared with guselkumab in a head-to-head randomized clinical trial, which is described in further detail below.

Infliximab

While there are currently no randomized controlled trials evaluating the efficacy of infliximab for the treatment of scalp psoriasis, it has been evaluated in both retrospective and prospective observational studies [37, 38].

Infliximab was compared with treatment with etanercept, adalimumab, and ustekinumab in a retrospective cohort study of patients receiving biologic treatment with baseline scalp psoriasis [38]. Patients who were treated with one of the four biologics, responded to treatment, and completed 1 year of biologic treatment were included in the study analysis. Treatment with infliximab and ustekinumab led to faster reductions in mean PSSI compared with etanercept and adalimumab at week 12 (90.8%, infliximab; 88.7%, ustekinumab; 72.2%, etanercept; 73.1%, adalimumab). By week 48, PSSI 75 was achieved by 91.4% with

Table 1 Scalp psoriasis-specific efficacy data for biologic and small-molecule agents

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
TNF-alpha inhibitors										
Etanercept	Moderate to severe plaque psoriasis with scalp involvement: a randomized, double-blind, placebo-controlled study of etanercept [34]	Placebo	Etanercept 50 mg twice weekly for 12 weeks, followed by etanercept 50 mg once weekly and placebo once weekly (etanercept) Placebo twice weekly for 12 weeks, followed by etanercept 50 mg twice weekly for 12 weeks (placebo/etanercept)	(Week 12): Etanercept: 86.6% ± 18.0**** Placebo/etanercept: 20.4% ± −39.9 (Week 24): Etanercept: 90.6% ± 13.1 Placebo/etanercept: 79.1% ± 33.6 ($p < 0.0001$)****	(Week 12): Etanercept: 86.0% **** Placebo/etanercept: 11.0% PSSI 75 (wk 24): Etanercept: 86.0% Placebo/etanercept: 72.0% ($p < 0.0001$)****				Rates of adverse events comparable between etanercept and placebo at week 12 and between etanercept and placebo/etanercept at week 24	
Adalimumab	Adalimumab for the treatment of moderate to severe psoriasis: subanalysis of effects on scalp and nails in the **BELIEVE** study [35]	None, statistical comparison was with baseline	Randomized to receive adalimumab 80 mg at week 0 and 40 mg Q2W until week 15 plus topical C/B ointment or adalimumab plus vehicle for 16 weeks/ Topical C/B treatment specifically avoided in the scalp and nails All groups combined for analysis	77.2% ± 96.9% (week 16)					Of all patients receiving adalimumab (both scalp and nail psoriasis patients), 61.8% experienced an AE Majority of AEs were classified as mild or moderate. Headache and nasopharyngitis were the most common	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
	Effectiveness of adalimumab in the treatment of scalp and nail affection in patients with moderate to severe plaque psoriasis in routine clinical practice [36]	None, statistical comparison was to baseline	Decision to treat with adalimumab was made independent of participation in the study, but the majority (96.6%) received adalimumab 40 mg Q2W dosing schedule	94.8% (1 year)			71.7% (1 year)[α]		Of all patients receiving adalimumab (scalp and nail psoriasis patients), 9.6% had an AE. Skin and subcutaneous tissue disorders and infection/ infestations were most common	DLQI scores ≤ 5: improved 94.0% (1 year)
Infliximab	Treatment effect of adalimumab and infliximab in Japanese psoriasis patients: results in a single community-based hospital [37]	Adalimumab	Patients were allocated, based on patient preference, to adalimumab 80 mg at week 0, and then 40 mg every other week from week 2 through week 24 or infliximab 5 mg/kg at weeks 0, 2, 6, 14, and 22		(Week 16) Adalimumab: 54.5% Infliximab: 90.0% (Week 24) Adalimumab: 54.5% Infliximab: 70.0%	(Week 16) Adalimumab: 45.5% Infliximab: 70.0% (Week 24) Adalimumab: 54.5% Infliximab: 70.0%			No injection-site reactions with adalimumab nor infusion reactions with infliximab Mild upper respiratory tract infection in 19.0% of patients, no serious AEs	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
	Scalp psoriasis and biologic agents: a retrospective, comparative study from a tertiary psoriasis referral centre [38]	Etanercept, adalimumab, and ustekinumab	Received infliximab 5 mg/kg (IV) at weeks 0, 2, 6, 8, and every 8 weeks after; etanercept 50 mg twice weekly for 12 weeks and once weekly after; adalimumab 80 mg at week 0, 40 mg at week 1, and 40 mg Q2W after; ustekinumab 45 mg or 90 mg at week 0 and week 4, and every 12 weeks after	(Week 12) Infliximab: 90.8% Etanercept: 72.2% Adalimumab: 73.1% Ustekinumab: 88.7% (Week 48) Infliximab: 94.35% Etanercept: 83.16% Adalimumab: 89.09% Ustekinumab: 94.91%	(Week 12) Infliximab: 91.4% Etanercept: 33.3% Adalimumab: 61.5% Ustekinumab: 92.6% (Week 48) Infliximab: 91.4% Etanercept: 70% Adalimumab: 92.3% Ustekinumab: 97.5%	(Week 12) Infliximab: 74.2% Etanercept: 20.0% Adalimumab: 43.5% Ustekinumab: 80.4% (Week 48) Infliximab: 80.0% Etanercept: 50.0% Adalimumab: 69.2% Ustekinumab: 85.3%			Minor AEs, none that required discontinuation of the study	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
Certolizumab pegol	*No specific scalp psoriasis clinical data outcomes*									
IL-17 inhibitors										
Brodalumab	Brodalumab, a human anti-interleukin-17-receptor antibody in the treatment of Japanese patients with moderate-to-severe plaque psoriasis: efficacy and safety results from a phase II randomized controlled study [39]	Placebo	Randomized to receive brodalumab 70 mg, 140 mg, or 210 mg or placebo at baseline and weeks 1, 2, 4, 6, 8, and 10	(Week 12) Brodalumab 70 mg: 38.3% ± 50.3 Brodalumab 140 mg: 73.8% ± 41.2*** Brodalumab 210 mg: 94.5% ± 14.8*** Placebo: 12.6 ± 63.0 ($p < 0.001$)***					AE reported in 44.7% of placebo, 53.8% of 70 mg brodalumab, 56.8% of 140 mg brodalumab, and 73.0% of 210 mg brodalumab Most common AEs in brodalumab group were nasopharyngitis, diarrhea, and upper respiratory tract inflammation	
	Efficacy of brodalumab in the treatment of scalp and nail psoriasis: results from three phase 3 trials (AMAGINE -1) [40]	Placebo	Received either brodalumab 210 mg Q2W or placebo through week 12	(Week 12) Brodalumab: 92.8%*** Placebo: 14.4% ($p < 0.001$)***	(Week 12) Brodalumab: 89%*** Placebo: 9.5% ($p < 0.001$)***		(Week 12)[α] Brodalumab: 63.4%*** Placebo: 3.2% ($p < 0.001$)***		No specific safety data reporting for scalp post hoc analysis	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
Ixekizumab	Improvement of scalp and nail lesions with ixekizumab in a phase 2 trial in patients with chronic plaque psoriasis [44]	Placebo	Randomized to receive ixekizumab 10, 25, 75, or 150 mg or placebo at weeks 0, 2, 4, 8, 12, and 16. In the OLE, all received ixekizumab 120 mg Q4W	(wk 20) Ixekizumab 10 mg: 16.5% Ixekizumab 25 mg: 75.3%** Ixekizumab 75 mg: 83.7%** Ixekizumab 150 mg: 82.2%*** Placebo: 18.8% OLE (week 48) Placebo/ ixekizumab: 98.1%*** Ixekizumab/ ixekizumab: 87.5%*** (Compared with baseline) ($p < 0.01$)** ($p < 0.001$)***			OLE (week 48)[β] Placebo/ ixekizumab: 81.3% Ixekizumab/ ixekizumab: 77.3%		No specific safety data reporting for scalp post hoc analysis	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
	Sustained response with ixekizumab treatment of moderate-to-severe psoriasis with scalp involvement: results from three phase 3 trials (**UNCOVER-1, UNCOVER-2, UNCOVER-3**) [45]	Placebo and etanercept	UNCOVER-1, -2, -3 Randomized to receive ixekizumab 80 mg Q2W (IXEQ2W) or Q4W (IXEQ4W) after starting dose of 160 mg, or placebo until week 12 UNCOVER -2,-3 Also included a treatment arm with etanercept 50 mg biweekly until week 12 A blinded maintenance period occurred through 60 weeks in UNCOVER -1, -2 All patients received ixekizumab Q4W in an OLE in UNCOVER -3	(Week 12) IXEQ4W: 88.5%*** IXEQ2W: 93.0%*** Etanercept: 72.4% Placebo: 2.8% ($p < 0.001$)*** versus placebo and etanercept	(Week 12) IXEQ4W: 83.6%*** IXEQ2W: 89.9%*** Etanercept: 67.6% Placebo: 12.7% ($p < 0.001$)*** versus placebo and etanercept OLE UNCOVER 3 (week 60) IXEQ4W/ IXEQ4W: 84.6% IXEQ2W/ IXEQ4W: 88.1%	(Week 12) IXEQ4W: 75.6%*** IXEQ2W: 81.7%*** Etanercept: 55.5% Placebo: 7.6% ($p < 0.001$)*** versus placebo and etanercept OLE UNCOVER 3 (week 60) IXEQ4W/ IXEQ4W: 80.1% IXEQ2W/ IXEQ4W: 83.9%	(Week 12)[α] IXEQ4W: 68.9%*** IXEQ2W: 74.6%*** Etanercept: 48.1% Placebo: 6.7% ($p < 0.001$)*** versus placebo and etanercept OLE UNCOVER 3 (wk 60)[α] IXEQ4W/ IXEQ4W: 77.4% IXEQ2W/ IXEQ4W: 80.5%		No safety evaluation completed in just scalp psoriasis study participants. AE rates were similar in all treatment arms in the three studies	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
	Efficacy and safety of continuous every-2-week dosing of ixekizumab over 52 weeks in patients with moderate-to-severe plaque psoriasis in a randomized phase III trial (**IXORA-P**) [46]	None, statistical comparison with other dosing regimens	Randomized at a 2:1:1 ratio to continuous IXEQ2W, continuous IXEQ4W, or dose adjustment per protocol, IXEQ4W/Q2W, each with a 160-mg starting dose				(Week 52)[β] IXEQ4W:70.3% IXEQ2W:76.9%* IXEQ4W/Q2W:72.6% ($p < 0.05$)* versus IXEQ4W		AE rates were similar across all three groups Most AEs were mild to moderate, and the most common AEs were upper respiratory infection, nasopharyngitis, injection-site reaction (ISR), headache, hypertension, and urinary tract infection	
Secukinumab	The effect of secukinumab on moderate-to-severe scalp psoriasis: results of a 24-week, randomized, double-blind, placebo-controlled phase 3b study (**SCALP**) [41]	Placebo	Randomized to subcutaneous secukinumab 300 mg or placebo at baseline, weeks 1, 2, and 3, and then every Q4W from weeks 4 to 20	(Week 12) Secukinumab:71.0% Placebo: 16.7%		(Week 12) Secukinumab: 52.9%*** Placebo: 2.0% ($p < 0.001$)*** (Week 24) Secukinumab: 58.8%	(Week 12)[α] Secukinumab: 35.3%*** Placebo: 0.0% ($p < 0.001$)*** (Week 24)[α] Secukinumab: 47.1%		72.5% in the secukinumab and 48.0% in the placebo group experienced an AE Most common AEs include nasopharyngitis, upper respiratory tract infection, cough, and contact dermatitis	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
	Secukinumab improves scalp pain, itching, scaling and quality of life in patients with moderate-to-severe scalp psoriasis [42]	Placebo	Randomized to secukinumab 300 mg or placebo at baseline, week 1, 2, and 3, and then every 4 weeks						No specific safety data reported for this study	Scalp pain/ itching/ scaling (Week 12) Secukinumab Pain: −1.98*** Itching: −4.07*** Scaling: −5.76*** Placebo Pain: 0.61 Itching: −0.04 Scaling: −0.95 ($p < 0.001$)***

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
	Real world data from the use of secukinumab in the treatment of moderate-to-severe psoriasis, including scalp and palmoplantar psoriasis: a 104-week clinical study [43]	None, statistical comparison was with baseline	Real-world subjects were recruited if being treated with the recommended dose of 300 mg secukinumab					98.7% (week 16) 86.0% (week 52) 100% (week 104)	During first 16 weeks, 7.2% of patients experienced an AE Safety comparable to secukinumab clinical trials All drug-related AEs were mild to moderate	
IL-12/IL-23 inhibitor										
Ustekinumab	*See ifliximab and risankizumab*									
IL-23 inhibitors										

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
Guselkumab	Efficacy of guselkumab compared with adalimumab and placebo for psoriasis in specific body regions: a secondary analysis of 2 randomized clinical trials [47]	Adalimumab	Randomized to receive guselkumab 100 mg (week 0 and 4, then every 8 weeks); placebo followed by guselkumab 100 mg, starting at week 16; or adalimumab 80 mg at week 0 and 40 mg at week 1 followed by Q2W						No specific safety data reporting for scalp post hoc analysis	Scalp-specific IGA 0/1 (Week 16) Guselkumab: 81.8%*** (compared with placebo) Placebo: 12.4% Adalimumab: 69.0% (Week 24) Guselkumab: 85%*** Adalimumab: 68.5% ($p < 0.001$)***
Risankizumab	Risankizumab versus ustekinumab for moderate-to-severe plaque psoriasis [48]	Ustekinumab	Randomized to receive risankizumab (a single 18 mg dose at week 0 or 90 mg /180 mg doses at weeks 0, 4, and 16) or ustekinumab (45 mg or 90 mg) at weeks 0, 4, and 16	(Week 12) Risankizumab 90 mg: 90.0% Risankizumab 180 mg: 94.0% Ustekinumab: 82.0%					81.0% in 18-mg risankizumab group, 80.0% in 90-mg risankizumab group, 69.0% in 180-mg risankizumab group, and 72.0% in ustekinumab group reported AEs Most common AE in all groups was nasopharyngitis	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
Mirikizumab	Efficacy and safety of mirikizumab (LY3074828) in the treatment of moderate-to-severe plaque psoriasis: results from a randomized phase II study [49]	Placebo	Randomized at a 1:1:1:1 ratio to receive mirikizumab 30 mg, 100 mg, 300 mg, or placebo				(Week 16)[β] Mirikizumab 30 mg: 43.0%*** Mirikizumab 100 mg: 75.0%*** Mirikizumab 300 mg: 51.0%*** Placebo: 6.0% ($p < 0.001$)***		Percentage of patients reporting AEs in each study group was comparable Most common AE included viral upper respiratory tract infections, injection-site pain, hypertension, and diarrhea	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
PDE4 inhibitor										
Apremilast	Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with difficult-to-treat nail and scalp psoriasis: results of 2 phase III randomized, controlled trials (ESTEEM 1 and ESTEEM 2) [50]	Placebo	Randomized (2:1) to apremilast 30 mg or placebo BID Placebo patients switched to apremilast from week 16 through week 32, followed by a randomized withdrawal phase to week 52					ESTEEM 1 (week 16): 46.5%**** Placebo: 17.5% ESTEEM 2 (week 16): 40.9%**** Placebo: 17.2% ($p < 0.0001$)****	Most AEs were mild to moderate No new significant AEs occurred with continued apremilast exposure	
	The efficacy and safety of apremilast, etanercept and placebo in patients with moderate-to-severe plaque psoriasis: 52-week results from a phase IIIb, randomized, placebo-controlled trial (LIBERATE) [51]	Placebo and etanercept	Randomized to placebo, apremilast 30 mg BID, or etanercept 50 mg QW through week 16. After week 16, all patients were continued or switched to apremilast until week 52					(Week 16) Apremilast: 44.4% ($p = 0.0458$) Etanercept: 50.0% ($p = 0.0083$) Placebo: 25.9% (Week 52) Apremilast: 53.1% Etanercept/ apremilast: 60.4% Placebo/ apremilast: 52.0%	Majority of AEs were mild to moderate Most common AEs include mild-to-moderate nausea, diarrhea, headaches, upper respiratory tract infections, and nasopharyngitis	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
	Safety and efficacy of apremilast through 104 weeks in patients with moderate to severe psoriasis who continued on apremilast or switched from etanercept treatment: findings from the LIBERATE study [52]	Placebo and etanercept	Randomized to placebo, apremilast 30 mg BID, or etanercept 50 mg QW through week 16. After week 16, all patients were continued or switched to apremilast until week 104					(Week 104) Apremilast: 59.2% Etanercept/ apremilast: 56.6% Placebo/ apremilast: 50.0%	Majority of AEs were mild to moderate Most common AEs include mild-to-moderate nausea, diarrhea, headaches, upper respiratory tract infections, and nasopharyngitis	
	Efficacy and safety of apremilast in systemic- and biologic-naive patients with moderate plaque psoriasis: 52-week results of UNVEIL [53]	Placebo	Randomized to receive apremilast 30 mg BID or placebo until week 16; then all patients were continued on (apremilast/ apremilast) or were switched to apremilast (placebo/apremilast) through week 52					(Week 16) Apremilast: 38.4% Placebo: 20.0% (p = 0.0178) (Week 52) Apremilast/ apremilast: 47.7% Placebo/ apremilast: 46.9%	Safety profile comparable to other clinical studies Most common AEs include diarrhea, nausea, headache, nasopharyngitis, upper respiratory tract infection, vomiting, and decreased appetite	

Table 1 continued

Agent	Study name	Comparison	Dosing	Mean percent PSSI improvement	PSSI 75	PSSI 90	PSSI 100[α]/ PSSI score of 0[β]	ScPGA 0/1	Safety	Other
	Efficacy and safety of apremilast in patients with moderate to severe plaque psoriasis of the scalp: results of a phase 3b, multicenter, randomized, placebo-controlled, double-blind study (STYLE) [54]	Placebo	Randomized patients to apremilast 30 mg twice daily or placebo for 16 weeks, and at week 16, all patients continued or switched to apremilast 30 mg twice daily through week 32					(Week 16) Apremilast: 43.3%**** Placebo: 13.7% ($p < 0.0001$)****	AEs occurred in 67.5% of apremilast group and 51% of placebo group Most common AEs included diarrhea, nausea, headache, and vomiting	Scalp itch NRS 4-point or greater improvement (week 16): Apremilast: 47.1% Placebo: 21.2% Mean improvement from baseline in DLQI total score (week 16) Apremilast: −6.7 Placebo: −3.8 ($p \leq 0.0001$)

PSSI Psoriasis Scalp Severity Index, *ScPGA* scalp Physician Global Assessment, *DLQI* Dermatology Life Quality Index, *PDE4 inhibitor* phosphodiesterase 4 inhibitor, *Q2W* every 2 weeks, *Q4W* every 4 weeks, *BID* twice daily, *IV* intravenous, *OLE* open-label extension, *scalp-specific IGA* Scalp-specific Investigator's Global Assessment, *AE* adverse event

nfliximab, 97.5% with ustekinumab, 92.3% with adalimumab, and 70% with etanercept. Additionally, in week 48, PSSI 90 was achieved by a greater percentage of patients treated with infliximab and ustekinumab (80% and 85.3%, respectively) than with etanercept and adalimumab (50% and 69.2%, respectively).

Another study evaluated infliximab and adalimumab efficacy in the treatment of scalp psoriasis in a cohort of 21 Japanese patients with a body surface area (BSA) greater than 10% [37]. In this prospective observational study, patients were allocated either infliximab (10 patients) or adalimumab (11 patients) based on patient preference. By week 16, PSSI 75 and PSSI 90 were achieved by a greater proportion of patients treated with infliximab than adalimumab (90% versus 54.5%, and 70% versus 45.5%, respectively). Safety data were reported to be similar to previous randomized control trials of infliximab and adalimumab. A total of 19% of patients had mild upper respiratory infections.

IL-17 Inhibitors

Brodalumab

Brodalumab was evaluated in a phase II randomized, placebo-controlled trial of Japanese patients with moderate-to-severe plaque psoriasis with a sub-analysis of the efficacy and safety for patients with scalp psoriasis [39]. Patients were randomized to receive brodalumab 70 mg, 140 mg, or 210 mg or placebo. After 12 weeks, patients achieved a mean PSSI improvement of 38.3% ± 50.3 with brodalumab 70 mg, 73.8% ± 41.2 with brodalumab 140 mg [$p < 0.001$], 94.5% ± 14.8 with brodalumab 210 mg [$p < 0.001$], versus 12.6% ± 63.0 with placebo. The most common adverse events in the brodalumab group were nasopharyngitis, diarrhea, and upper respiratory tract inflammation [39].

A post hoc analysis in 2020 of the phase III, randomized, double-blind, placebo-controlled, clinical trial, AMAGINE-1, evaluated brodalumab in the treatment of patients with moderate to severe scalp psoriasis through week 12. At week 12, PSSI 75 and PSSI 100 was achieved by a significantly higher proportion of patients treated with brodalumab (89% and 63.4%, respectively) versus placebo (9.5% and 3.2%, respectively [$p < 0.001$]). Overall, there was a significantly larger mean improvement in PSSI by week 12 in brodalumab treated patients (92.8%) than with placebo (14.4% [$p < 0.001$]). After 12 weeks, 53.8% of patients taking brodalumab and 44.7% of patients on placebo reported adverse events. The most common adverse events included nasopharyngitis, diarrhea, folliculitis, and upper respiratory tract infection [40].

Secukinumab

A recent phase III prospective, randomized, double-blind, placebo-controlled study evaluated the efficacy of secukinumab in moderate-to-severe scalp psoriasis [41]. After 12 weeks, PSSI 90 was achieved in 52.9% of secukinumab-treated patients and 2% of placebo patients [$p < 0.001$]). A significantly larger percentage of patients treated with secukinumab achieved complete clearance of the scalp represented by PSSI 100 at week 12 when compared with those treated with placebo (35.3% and 0%, respectively [$p < 0.001$]). When patients were followed until week 24, the percentage of patients treated with secukinumab who achieved PSSI 100 was 47.1%. It is important to note that this study did not allow any concomitant topical therapy or medicated shampoo, which makes comparing results with other studies that allowed adjunctive treatment difficult. In the secukinumab group, 72.5% of patients reported at least one adverse event versus 49% of patients in the placebo group. The most common adverse events reported were nasopharyngitis, upper respiratory tract infection, contact dermatitis, and cough [41].

In a randomized, double-blind, placebo-controlled study, secukinumab was also noted to have greater mean improvements of patient-reported scalp pain, itching, and scaling than placebo-treated patients at week 12. Patients also had larger improvements in scalp dermatitis-related quality of life when treated with secukinumab when compared with those treated with placebo (mean change from baseline:

−39.62 and −7.91, respectively [$p < 0.001$]) [42].

Following this randomized controlled trial, a 2-year observational study evaluating real-world data of secukinumab in the treatment of scalp psoriasis demonstrated a rapid improvement of the scalp Physician Global Assessment (scPGA) from baseline (mean scPGA at baseline: 1.8 and mean scPGA at week 4: 0.8). By week 16, the mean scPGA was 0.4, and this response was maintained at week 52 (mean scPGA: 0.5) and week 104 (mean scPGA: 0.0). The safety profile was comparable to other secukinumab clinical trials. Within the first 16 weeks, 7.2% of patients reported an adverse event [43].

Ixekizumab

Ixekizumab efficacy in the treatment of scalp psoriasis was demonstrated in a post hoc analysis of a phase II randomized placebo-controlled trial and subsequent open-label extension study [44]. The baseline PSSI score was 18.7 of the 105 patients enrolled in the study. The mean reduction in PSSI at week 12 for those treated with ixekizumab 25 mg, 75 mg, and 150 mg was 75.3% [$p = 0.001$], 83.7% [$p = 0.001$], and 82.2% [$p < 0.001$], respectively. Additionally, after 20 weeks, the proportion of patients achieving a PSSI score of 0, representing complete clearance, in those treated with ixekizumab 25 mg, 75 mg, and 150 mg was 58.3%, 66.7%, and 86.4%, respectively (versus placebo group: 10%). [44].

Ixekizumab was also evaluated for the treatment of scalp psoriasis in three phase III trials, i.e., UNCOVER-1, UNCOVER-2, and UNCOVER-3. UNCOVER-1 compared maintenance ixekizumab 80 mg at 2-week intervals or 4-week intervals versus placebo. In addition to this, the UNCOVER-2 and UNCOVER-3 studies also compared ixekizumab treatment with etanercept. Pooled data from all three phase III trials at week 12 demonstrated that PSSI 90 and PSSI 100 was achieved in a significantly higher proportion of patients treated with ixekizumab every 2 weeks (81.7% and 74.6%) and ixekizumab every 4 weeks (75.6% and 68.9%) than those treated with etanercept (55.5% and 48.1% [$p < 0.001$]) or placebo (7.6% and 6.7% [$p < 0.001$]). A subgroup of patients with severe scalp psoriasis (classified by a PSSI > 15 and > 30% scalp involvement), when treated with ixekizumab every 2 weeks, was found to achieve similar PSSI 90 and PSSI 100 at week 12 (82.2% and 69.8%). In UNCOVER-3, patients were continued in the long-term extension with treatment of ixekizumab every 4-week dosing, regardless of whether they were classified as responders or nonresponders at week 12. This study demonstrated that PSSI 90 and PSSI 100 results were maintained until week 60 in patients initially treated with ixekizumab 2-week dosing who were switched to 4-week dosing schedules (79.1% and 75.9%) as well as patients continued on a ixekizumab 4-week dosing schedule (76.2% and 73.6%) [45].

Following this study, the efficacy of ixekizumab on the scalp was also evaluated in a randomized phase III clinical trial comparing ixekizumab 80 mg at 2-week dosing intervals, 4-week dosing intervals, and 4- to 2-week interval dose adjustment groups. At week 52, 76.9%, 70.3%, and 72.6% of patients with 2-week dosing, 4-week dosing, and 4- to 2-week dosing, respectively, achieved a PSSI score of 0. A significantly greater proportion of patients achieved this outcome with the 2-week dosing versus the 4-week dosing ($p = 0.032$). Rates of adverse events were similar across all three study groups [46].

IL-23 Inhibitors

Guselkumab

A secondary analysis of two clinical randomized trials, VOYAGE 1 and VOYAGE 2, compared guselkumab and adalimumab in the treatment of scalp psoriasis [47]. The percentage of patients who achieved a scalp-specific IGA score of 0 or 1 at week 24 was significantly higher for patients treated with guselkumab compared with those treated with adalimumab (85% versus 68.5%, respectively [$p < 0.001$]). At week 24, the percentage of patients treated with guselkumab and adalimumab who reached complete clearance, represented by a scalp-specific IGA score of 0, was 69.9% and 56.3%, respectively [47].

Risankizumab

A phase II randomized clinical trial in 2016 compared treatment with risankizumab at multiple doses with ustekinumab for scalp disease. Mean PSSI at week 12 was improved by 90% in the risankizumab 90 mg group, 94% in the risankizumab 180 mg group, and 82% in the ustekinumab group. By week 48, the mean percent PSSI change from baseline was sustained above 80% in the risankizumab 90 mg and 180 mg cohorts. Nasopharyngitis was the most common adverse event occurring in all cohorts [48].

Mirikizumab

To date, mirikizumab has not been FDA approved. Data from a phase II randomized study in 2019 evaluated the effectiveness of mirikizumab in the clearance of scalp psoriasis. At week 16, PSSI 0 was achieved in 43%, 75%, and 51% of patients treated with mirikizumab 30 mg, 100 mg, and 200 mg, respectively, versus 6% of placebo. The percentage of patients reporting adverse events in each study group was comparable. The most common adverse events included viral upper respiratory tract infections, injection-site pain, hypertension, and diarrhea [49].

IL-12/IL-23 Inhibitor

Ustekinumab

Clinical data regarding the efficacy of ustekinumab in scalp psoriasis therapy is referenced in the sections above (see *infliximab* and *risankizumab*).

Oral PDE4 Inhibitors

Apremilast

The oral phosphodiesterase four inhibitor, apremilast, was evaluated in two phase III randomized controlled trials, ESTEEM 1 and ESTEEM 2, for efficacy in the treatment of a subset of patients with scalp psoriasis [50]. Treatment with apremilast led to a significantly greater proportion of patients achieving scPGA 0/1 (46.5% ESTEEM 1, 40.9% ESTEEM 2) at week 16 versus placebo (17.5% ESTEEM 1, 17.2% ESTEEM 2 [$p < 0.0001$ for both studies]). The proportion of patients with scPGA 0/1 at week 32 in patients treated with apremilast was maintained at 37.4% and 32.4% in ESTEEM1 and ESTEEM 2, respectively. Most adverse events were noted to be mild or moderate in severity [50].

Results of a subset of patients with moderate or greater scalp psoriasis at baseline treated with apremilast, etanercept, or placebo were analyzed in the phase IIIb randomized, placebo-controlled trial, LIBERATE [51, 52]. After 16 weeks, the percentage of patients with moderate-to-severe scalp psoriasis to achieve a scPGA 0/1 was 25.9% with placebo, 44.4% with apremilast [$p = 0.0458$], and 50% with etanercept [$p = 0.0083$]. After week 16, all patients were continued or switched to apremilast. Effectiveness of apremilast was sustained and slightly improved in long-term follow-up. After 104 weeks, patients who switched from placebo to apremilast at week 16, patients who continued with apremilast, and patients who switched from etanercept to apremilast at week 16 achieved scPGA 0/1 in 50%, 59.2%, and 56.6% of patients, respectively. The most common adverse events reported by $\geq 5\%$ of patients include mild to moderate nausea, diarrhea, headaches, upper respiratory tract infections, and nasopharyngitis [51, 52].

The UNVEIL study evaluated apremilast in biologic-naïve patients and demonstrated similar results to prior studies [53]. At week 16, scPGA 0/1 was achieved in 38.4% of patients on apremilast versus 20% on placebo [$p = 0.0178$]. After 52 weeks, scPGA 0/1 was achieved by 46.8% of patients switched from placebo to apremilast and 47.7% continued on apremilast. Diarrhea, nausea, headache, nasopharyngitis, upper respiratory tract infection, vomiting, and decreased appetite were the most common adverse events [53].

Most recently in 2020, STYLE, a phase IIIb multicenter, randomized, placebo-controlled study dedicated to evaluating the safety and efficacy of apremilast in patients with moderate-to-severe scalp psoriasis was published [54]. After 16 weeks, a significantly larger proportion of patients treated with apremilast achieved scPGA 0/1 (43.3%) versus placebo (13.7% [$p < 0.0001$]). In addition to clearance of the

scalp, 47.1% of patients treated with apremilast reported a 4-point or greater improvement in the Scalp Itch Numerical Rating Score at week 16, compared with only 21.2% of placebo patients [$p < 0.0001$]. Patients treated with apremilast also demonstrated a significantly greater improvement in DLQI compared with placebo at week 16 (−6.7 and −3.8, respectively [$p < 0.0001$]).The safety profile was similar to adverse events described in previous clinical trials with apremilast [54].

Intralesional Corticosteroids

While typically not considered standard treatment, the use of complementary therapies can help patients struggling with difficult-to-treat scalp psoriasis. Intralesional corticosteroids have been used in clinical practice for the treatment of localized scalp disease with good effect, although there are currently no studies regarding the efficacy of this modality in the scalp [3]. Data show that intralesional injections of corticosteroids (typically triamcinolone acetonide) in the trunk and limbs are highly effective at clearing small, localized psoriatic plaques; therefore, it likely has similar efficacy in the scalp [55]. Prior recommendations from the National Psoriasis Foundation suggested the use of intralesional corticosteroids in persistent but limited scalp psoriasis [3].

DISCUSSION

Practical Management of Scalp Psoriasis

Management of scalp psoriasis is primarily dependent on the extent of the scalp disease and presence of accompanying psoriasis on the rest of the body. As outlined by the European consensus on grading, extent of psoriasis in the scalp may be defined as mild, moderate, or severe [56]. Mild disease or moderate disease affects < 50% of the scalp with mild or moderate erythema, scaling, thickness, and pruritis, respectively. Severe disease affects > 50% of the scalp with moderate to severe erythema, scaling, thickness, and pruritis.

First-line therapy for patients with any severity of scalp psoriasis with minimal involvement of other sites is topical corticosteroids. Formulation of the corticosteroid is important, and likely a foam, gel, solution, shampoo, or spray will be preferred. However, a discussion about preference for formulations should occur with all patients, especially in African American patients, who may prefer ointments and lotions owing to differences in hair texture.

Patients may also benefit from topical vitamin D analog treatment. Combination therapy consisting of corticosteroids and vitamin D analogs has shown to be an effective long-term maintenance option. Keratolytic agents are also an effective first-line option for scalp disease with minimal body involvement and may be used as monotherapy or in combination with a topical corticosteroid. Coal tar is likely effective for scalp psoriasis, but research is lacking.

Second-line therapy for mild-to-moderate localized disease includes intralesional corticosteroids. While efficacy data in the scalp are absent for intralesional corticosteroids, anecdotal evidence suggests they are effective for localized plaques of the scalp.

Second-line therapy for any severity of scalp psoriasis with minimal involvement of the body is phototherapy. Phototherapy is best used in the form of a direct or targeted therapy, such as a laser or comb, or in combination with a hair blower. UVB and excimer laser are both effective options for scalp psoriasis. Faster improvements in both scalp severity and QoL may be seen with UVA1 therapy, but there is a paucity of data in scalp psoriasis, and use is limited by the lack of availability of handheld devices.

Systemic therapy is first line for those with scalp psoriasis and accompanying moderate-to-severe psoriasis of the trunk and extremities. Additionally, it is third-line therapy for patients with recalcitrant scalp psoriasis with minimal involvement of other sites. While it is difficult to determine the most effective biologic or small molecule in the treatment of scalp psoriasis because of varying differences in outcome measures and lack of head-to-head studies, guselkumab, infliximab, ixekizumab, and brodalumab appear, on average, to have the

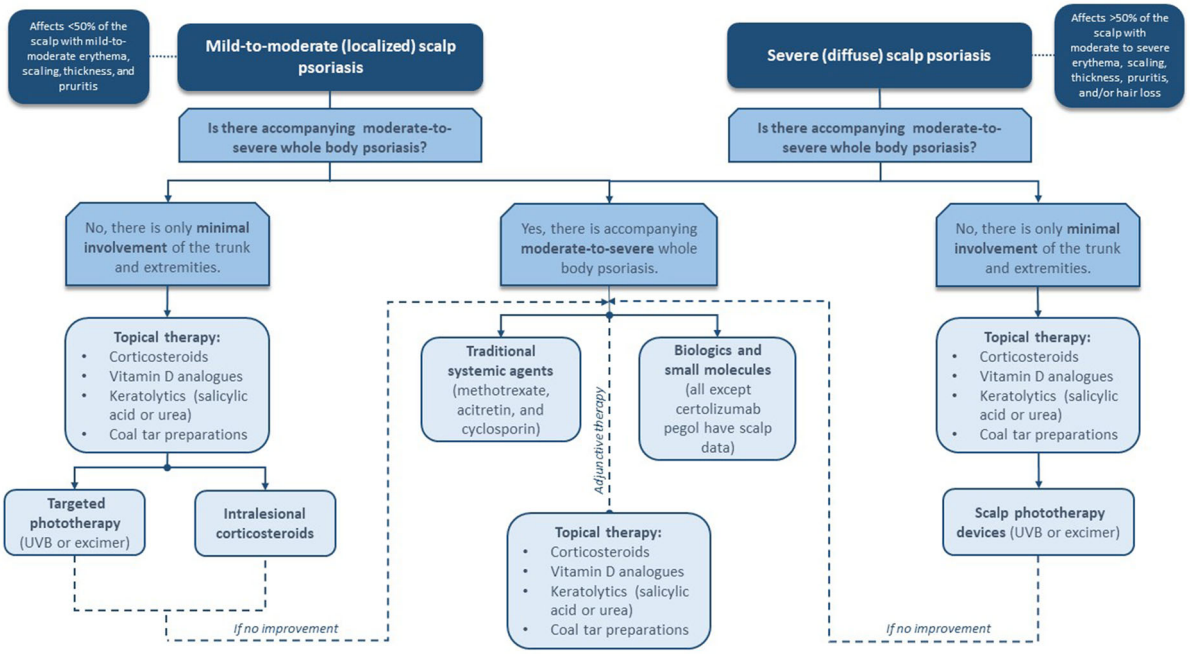

Fig. 1 Treatment recommendations for scalp psoriasis. Abbreviations: *UVB* ultraviolet B

highest efficacy in the clearance of scalp psoriasis across studies (Table 1). However, only guselkumab, secukinumab, and apremilast have scalp psoriasis efficacy evidence on the FDA label, which may be a factor in insurance approval. A treatment algorithm for scalp psoriasis based on the updated evidence in this review is presented in Fig. 1.

CONCLUSION

Scalp psoriasis presents considerable treatment challenges for the patient and practitioner. Psoriasis of this site also contributes to a significant burden on patient quality of life. Patients should be counseled that there are a number of options for this difficult-to-treat area, including biologics. Recent data have emerged regarding the newest treatments, but efficacy between treatments is difficult to compare because of the wide range of defined research outcomes. Ultimately, further head-to-head research is needed to determine the most effective options when treating scalp psoriasis.

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