Treating to Target—A Realistic Goal in Psoriasis?

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Abstract

For many patients, the new biologic therapies for psoriasis can improve Psoriasis Area and Severity Index (PASI) scores in a relatively short time. But when results are less than optimal, patients often become frustrated. By providing effective medical treatment using a treat-to-target strategy, clinicians can relieve symptoms and halt disease progression. Although body surface area (BSA) and PASI scores are appropriate for analyzing results of clinical trials, clinicians need to use more patient-centered assessments of patients' progress such as the Dermatology Life Quality Index (DLQI) and Psoriasis Symptom Inventory (PSI), as well as other validated patient-reported outcomes, which can enable them to set realistic and achievable goals for individual patients.

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Keywords

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Psoriasis and its comorbidities can significantly affect patients' overall health and their quality of life. To achieve optimal results from therapy, clinicians need to collaborate with patients to set long- and short-term goals: Is there a level of clearance or improvement that most patients find acceptable? Is there a target or number that accurately conveys response to therapy and that represents a realistic goal? Most important, in clinical care, are these targets—identified by analysis of populations—relevant to the patient in the office?

In psoriasis, there is a limited sense of what those endpoints are. However, the recent IHOPE study of >90,000 patients in the United Kingdom guides clinicians to reduce psoriasis so that it involves <10% of body surface area (BSA).[1] The study compared BSA and mortality rates of patients with psoriasis and those without psoriasis from a British database. When adjusted for age, sex, and comorbidities, the risk of mortality in patients with BSA >10% was higher than that of people without psoriasis (Hazard Ratio [HR], 1.79; 95% confidence interval [CI], 1.23-2.59).[1] These data suggest an initial goal of <10% BSA for all patients receiving psoriasis therapy.

Whose Target Is It?

The question remains, however: With medications that regularly attain 90% improvement in Psoriasis Area and Severity Index score (PASI) or even in complete clearance, is there any evidence-based reason to attain very high levels of improvement? The National Psoriasis Foundation recommends a treat-to-target BSA goal of 1% or less (**Table**).[2] Depending on the type and severity of a patient's comorbidities, that may be an unreasonable target. Because limited BSA psoriasis is largely a quality-of-life (QOL) disease, there is no assurance that clearing a sizeable portion of BSA will necessarily yield positive QOL scores. Clinicians cannot overestimate the toll that a chronic disease like psoriasis has on a patient's physical, social, and psychological well-being. What may matter more than the objective BSA number in assessing treatment efficacy is the subjective perspective of the patient.

The patient-reported Dermatology Life Quality Index (DLQI) assigns a score of 0 or 1 to psoriasis that does not have a significant impact on life. Studies reporting results using the DLQI reveal that different patients have varying levels of tolerance for psoriasis. For example, in studies of secukinumab, nearly 50% of patients had a PASI score of 75, which indicates that they still had substantial psoriasis, yet almost as many patients in that group also had a DLQI score of 0 or 1.[3-5] That means that if the disease is having no further effect and the patient's BSA is <10%, there would be no need to focus on a more aggressive target for therapy.

Plaque Location Matters

For a patient with psoriasis plaques on the face, any amount of surface area might be a tremendous burden. Likewise, hand or foot psoriasis can severely diminish QOL, even if the overall BSA is <10%. Because BSA does not encompass QOL, involvement of critical areas may cause BSA to underestimate the burden of the psoriasis.[2] A clinician might have a treatment target of <1%, but if the plaque remains obvious on a patient's cheek, the patient may still be dissatisfied with therapy.

Choosing Initial Therapy: Patient Preferences vs Medical Need

Jared is a 30-year-old man who presents with psoriasis and psoriatic arthritis, which require treatment with a biologic. His plaque psoriasis covers 25% of his body, and his axial psoriatic arthritis stiffens his lower back and hips in the morning. Jared is otherwise healthy, with no history of multiple sclerosis or inflammatory bowel disease (IBD).

An anti-TNF or an anti–IL-17agent would be sensible choices because both classes are efficacious in psoriatic arthritis. Due to formulary restrictions, the likely choice will be the anti-TNF agent adalimumab. Contraindications to anti-TNF medications include multiple sclerosis, because these drugs can cause or exacerbate demyelinating disease.[23]

If Jared had painful axial psoriatic arthritis, an anti–IL-17 might be faster-acting. The anti–IL-17 agents secukinumab, ixekizumab, and brodalumab provide a more predictable and rapid response than anti-TNF agents.[5,24] If he had IBD, anti–IL-17 agents would not be advisable because, in clinical trials, occasional new cases of IBD developed among patients with psoriasis.

Which Measure Is Best?

Despite its limitations, BSA for plaque psoriasis is likely the best measure of physical disease burden that currently exists. It is quick, easily estimated and recorded, and is used in almost all dermatology offices. But trying to decrease the BSA as a treatment target can be daunting. It is possible for clinicians to get to a point where they have cleared a substantial proportion of plaques, yet the patient is still bothered by itching, pain, or unsightliness. These lingering annoyances diminish a patient's QOL, and clinicians should acknowledge that at this juncture it is the *patient* who should set the treatment goals.

In a busy dermatology office, clinicians need a data point that is going to help them with decision making. The BSA, while not perfect, provides a quick and reproducible piece of information. If the patient is undressed, clinicians can derive a BSA score in a few seconds.[2,6]

Performing long, comprehensive QOL measures in the office may be more difficult. European dermatologists often use the DLQI, but in the United States few offices use it routinely because of time and logistical constraints.

Drug Selection

A common misconception is that certain psoriasis therapies, such as methotrexate, take longer to work, but mistakenly adhering to such myths can interfere with successful treatment. The multicenter METOP trial from the United Kingdom showed that subcutaneous methotrexate does not become more effective after each successive dose.[7] At week 16, 41% of methotrexate-treated patients achieved a PASI 75 response vs 10% of the placebo group (relative risk [RR], 3.93; 95% CI, 1.31-11.81; P=0.0026).[7] If patients did not achieve a PASI 50 score at week 8, they received a higher dose of methotrexate, from 17.5 mg/week for the first 16 weeks, to 22.5 mg/week. However, methotrexate appeared to reach peak efficacy around week 24 in the 52-week trial.[7]

A recent study with methotrexate found that it takes as little as 4 weeks to determine whether patients with psoriasis will respond to the systemic therapy.[8] Methotrexate-treated patients who achieved PASI 25 at week 4 were more likely to respond at week 16. In contrast, in cases where patients have a <30% probability of response at week 16, a different therapeutic strategy should be considered.[8]

The phase 3 NAVIGATE trial, in which guselkumab was introduced after patients had not responded to ustekinumab therapy, provides a clear example of why it is important to wait until the third dose is administered. Approximately 30% of patients who had not responded fully at week 16 (when the third dose would be administered) eventually did respond when they received their third injection.[9] However, patients treated with guselkumab fared better overall at week 52 than did patients treated with ustekinumab, with 50% and 24% achieving PASI 90, respectively.[9]

The National Psoriasis Foundation treat-to-target consensus recommends allowing 3 months for patients to respond to therapy.[2] Ideally, 3 months after initiating treatment, the target BSA should be ≤3% or there should a BSA improvement of 75% or more from baseline.[2] If a patient is not achieving any response, clinicians should discontinue treatment with the initial agent (**Table**).[2]

Efficacy is among the leading drivers in drug selection—and the lack of efficacy is the chief reason for therapeutic attrition. Systemic agents, and biologics specifically, are considered the go-to therapy because they treat moderate to severe plaque psoriasis as well as the common comorbidities. In systematic reviews, biologics in the aggregate can help up to 80% of patients achieve PASI 75.[10] However, PASI scores do not reflect the whole clinical outcome because the trials often focus on short-term efficacy and may not incorporate health-related QOL concerns.[10]

One such QOL study compared the efficacy of three biologics—adalimumab, etanercept, and ustekinumab—for 1 year as measured by the DLQI and European Quality of Life score-5D (EQ-5D).[10] Although there was no significant difference in the percentage of patients who received ustekinumab and adalimumab and who achieved a DLQI score of 0/1, adalimumab-treated patients were more likely than etanercept-treated patients to achieve a 0/1 DLQI score. Among the three biologics, there was no difference in the EQ-5D score. Factors most frequently associated with poor response to treatment included being female, being a current smoker, having any comorbidity, and having a higher baseline DLQI score.[10] For the EQ-5D score, each 10-year increase in age was associated with a lower EQ-5D score.[10]

TABLE Summary of National Psoriasis Foundation Consensus Targets for Plaque Psoriasis[a]

Preferred assessment instrument in clinical practice	BSA
Acceptable response after treatment initiation	Either BSA ≤3% or BSA improvement of ≥75% from baseline after 3 months of treatment
Target response after treatment initiation	BSA ≤1% at 3 months after treatment initiation
Target response during maintenance therapy	BSA ≤1% at every-6-month assessment intervals during maintenance therapy

BSA=body surface area.

[a] Treatment targets apply to plaque psoriasis, and they are to be discussed in the context of individualized evaluation of benefit-risk assessment and elicitation of patient preferences. They are not to be used to deny access to therapies.

Source: Armstrong AW, et al.[2]

Discontinuing a biologic regardless of the reason is also associated with lower health-related QOL scores.[10] Because biologics are immunomodulators, clinicians need to be alert for any infections that may arise.[11] Occasionally, patients experience side effects, the most common being an infection while on a biologic. Although patients are at an increased risk of infection with biologics, some still get infections even without being on the medications. The dosages used in clinical trials become the required dosages in clinical practice, and third party payers frequently will not allow a change in dosing in clinical practice.

Dosing Strategies

There is a dearth of evidence in prospective studies to guide clinicians on adjusting the dose of psoriasis medications.[12] A 3-year retrospective observational study found that clinicians increased the dose for 28.6% of patients and decreased the dose for 71.4%. The reason given for the increase was inadequate response in 60% of patients with plaque psoriasis and 40% of those with psoriatic arthritis. More than half of clinicians reduced the dose because of disease remission, 14% did so at the patients' request, and 18% did so for unspecified reasons.[12]

Labeling for many antipsoriatic medicines includes step-down dosing—starting with a bolus dose and then gradually decreasing it. But some patients may fare worse when the dose is reduced.[13] If there is some response, clinicians may obtain better results by increasing the dose or shortening the intervals between doses rather than switching to another agent.[14]

A systematic review of 23 studies that included 12,617 patients with psoriasis demonstrated that increasing the dose helps patients fare better overall than does decreasing the dose or switching to another agent.[14] Patient nonresponders have better outcomes with continuous vs interrupted therapy for moderate to severe plaque psoriasis.[14] Even with higher doses that are off-label, the benefits of dose escalation outweighed any adverse effects, which were mostly infections.[14] However, more and larger studies are needed to examine the effect of off-label dosing on patients with psoriasis, so as to determine a more realistic risk-benefit ratio of dose escalation.

Follow-Up Assessments

Although there is no firm, established timeline for follow-up visits, patients taking older systemic agents, such as methotrexate and cyclosporine, should be followed closely because they require routine laboratory tests, including complete blood count serum creatinine, blood urea nitrogen, uric acid, aspartate aminotransferase, alanine aminotransferase, tests for hepatitis B and C viruses, and urinalysis.[15] Indeed, long-term use of cyclosporine is not recommended because of the risk for nephrotoxicity and hypertension.[15]

When to follow up on patients taking the newer biologics is a subject of ongoing discussion. A consensus panel of the National Psoriasis Foundation has suggested that patients should undergo follow-up at 3 months after initiating a new therapy and again every 6 months during the maintenance phase.[2] Experienced clinicians say that, for most patients, 8 weeks is sufficient to assess their progress. What may also be important, especially to the patient, is the speed with which the agent works.

The follow-up for a certain medication may depend on the loading dose, subsequent doses, and the interval between dosing. A classic example is a patient who is on secukinumab and who does well in the first 5 weeks but who returns with flares 2 months later. Because the loading dosage (300 mg per week in weeks 1-4) is much higher than the follow-up dosage (300 mg every 4 weeks), some patients may be undermedicated if they receive the less-frequent maintenance dosage.[16] Such a patient for whom the anti–interleukin (IL)-17 medication works well—yet needs a more potent regimen—should probably be switched to another anti–IL-17 agent because it is mechanistically sound for the patient.[17] Finding the right drug that gets the right levels for the patient is critical. If a patient is on secukinumab and does not respond, switching to another class of agent would be prudent. Clinicians can apply the same paradigm when prescribing either the anti–tumor necrosis factor (TNF) or the anti–IL-23 classes.

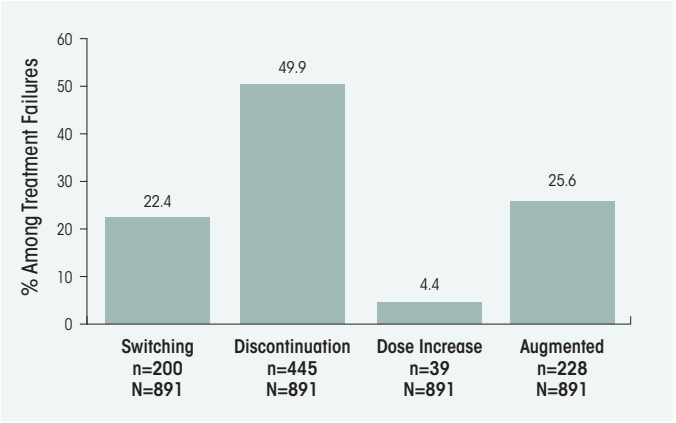

FIGURE Causes of Treatment Regimen Failures

Percentages do not add up to 100% because some patients were included in more than 1 category.

Source: Foster SA, et al.[22]

Adjusting Therapy: Dosing, Switching

For patients with moderate to severe psoriasis, clinicians change treatments due to inadequate disease control.[18] In a 5-year analysis of insurance claims, Armstrong and colleagues reported that there were frequent changes among topical agents, oral systemic medications, biologics, and phototherapy. Of the biologics studied, infliximab had the longest persistence, with a median 19 months of use.[18] Overall, more patients stopped topical agents (15.9%) or phototherapy compared with those who stopped biologic or traditional oral therapy (7.8%).[18]

The concept of changing to a therapy with a different mechanism of action was the focus of two papers in which the anti–IL-17 ixekizumab improved the signs and symptoms of psoriasis and psoriatic arthritis in patients who had originally failed on a TNF inhibitor.[19] In the SPIRIT studies, at both the 2- and 4-week dosing intervals, ixekizumab reduced symptoms in 363 patients who were nonresponders to TNF inhibitors. The safety profile was similar to that seen in previous ixekizumab studies. In the UNCOVER-2 and UNCOVER-3 studies, both the every-2-week and every-4-week doses of ixekizumab were found to be superior to etanercept and placebo in the 12-week studies. The safety profile in these studies was comparable to that seen in previous ixekizumab and etanercept studies.[20]

Likewise, the IL-23 inhibitor guselkumab was found to be superior to the TNF inhibitor adalimumab when tested in subpopulations of patients with moderate to severe psoriasis (N=1,829).[21] The subpopulations included more ethnically diverse patients, overweight and obese patients, and patients whose psoriasis had been present for a mean of 17 years. Previous studies of biologics, systemic agents, and phototherapy with these populations had lower efficacy. Among the subpopulations, guselkumab achieved an Investigator Global Assessment (IGA) score of 0/1 at week 16

vs placebo and at week 24 vs adalimumab. The VOYAGE 1 and VOYAGE 2 studies suggest that dosing based on patient characteristics such as weight and previous therapy can be effective.

No clear biomarkers exist that would enable clinicians to predict failure with biologic therapy (**Figure**).[22] One study found that those more likely to fail biologic treatment include women and those taking concomitant medications such as topical agents (67.0% vs 58.4%; $P<0.001$), methotrexate (20.2% vs 7.3%; $P<0.001$), and cyclosporine (3.1% vs 1.0%; $P<0.001$).[22] Their comorbidities included cerebrovascular disease, hypertension, chronic pulmonary disease, depression, and anxiety.[22]

Psoriasis is a multisystemic disease that affects the physical, psychological, and social well-being of patients. Clinicians need to be cognizant of these factors when initiating treatment, assessing progress, and changing regimens when patients are no longer obtaining relief. Thus long-term safe control is the ultimate goal.

Conclusion

Researchers and clinicians are increasingly aware that patient-reported outcomes are essential for managing the care of patients with psoriasis because therapy should be based on QOL concerns. Although PASI and BSA scores are easily calculated, these tools do not provide a comprehensive assessment of a patient's true progress. Location of the plaque psoriasis may be just as important as the *amount* of BSA with lesions. Clinicians should be prepared to reassess their patients' response to treatment and adjust the strategy accordingly, whether through dosage adjustments or a switch to an agent with a different mechanism of action, to achieve not just a reduction in psoriasis symptoms but to improve the overall QOL for patients.

References

1. Noe MH, Shin DB, Wan MT, Gelfand JM. Objective measures of psoriasis severity predict mortality: A prospective population-based cohort study. *J Invest Dermatol*. 2018;138:228-230.
2. Armstrong AW, Siegel MP, Bagel J, et al. From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. *J Am Acad Dermatol*. 2017;76:290-298.
3. Elewski BE, Puig L, Mordin M, et al. Psoriasis patients with psoriasis Area and Severity Index (PASI) 90 response achieve greater health-related quality-of-life improvements than those with PASI 75-89 response: Results from two phase 3 studies of secukinumab. *J Dermatolog Treat*. 2017;28:492-499.
4. Puig L, Augustin M, Blauvelt A, et al. Effect of secukinumab on quality of life and psoriasis-related symptoms: A comparative analysis versus ustekinumab from the CLEAR 52-week study [published online October 21, 2017]. *J Am Acad Dermatol*. doi:10.1016/j.jaad.2017.10.025.
5. Armstrong AW, Papp K, Kircik L. Secukinumab: Review of clinical evidence from the pivotal studies ERASURE, FIXTURE, and CLEAR. *J Clin Aesthet Dermatol*. 2016;9(suppl 1):S7-S12.
6. Wu JJ, No DJ, Amin M. BSA75, BSA90, and BSA100: New clinical tools for measuring improvement in psoriasis. *Cutis*. 2017;99:418.
7. Warren RB, Mrowietz U, von Kiedrowski R, et al. An intensified dosing schedule of subcutaneous methotrexate in patients with moderate to severe plaque-type psoriasis (METOP): A 52 week, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2017;389:528-537.
8. Gordon KB, Betts KA, Sundaram M, et al. Poor early response to methotrexate portends inadequate long-term outcomes in patients with moderate-to-severe psoriasis: Evidence from 2 phase 3 clinical trials. *J Am Acad Dermatol*. 2017;77:1030-1037.
9. Langley RG, Tsai TF, Flavin S, et al. Efficacy and safety of guselkumab in patients with psoriasis who have an inadequate response to ustekinumab: Results of the randomized, double-blind, phase III NAVIGATE trial. *Br J Dermatol*. 2018;178:114-123.
10. Iskandar IYK, Ashcroft DM, Warren RB, et al. Comparative effectiveness of biological therapies on improvements in quality of life in patients with psoriasis. *Br J Dermatol*. 2017;177:1410-1421.
11. Badavanis G, Pasmatzi E, Monastirli A, Tsambaos D. Biologic agents in systemic dermatotherapy: Cutaneous and systemic side effects [published online May 18, 2017]. *Curr Drug Saf*. doi:10.2174/1574886312666170518124014.
12. Esposito M, Gisondi P, Conti A, et al. Dose adjustment of biologic therapies for psoriasis in dermatological practice: A retrospective study. *J Eur Acad Dermatol Venereol*. 2017;31:863-869.
13. Edwards CJ, Fautrel B, Schulze-Koops H, Huizinga TWJ, Kruger K. Dosing down with biologic therapies: A systematic review and clinicians' perspective. *Rheumatology (Oxford)*. 2017;56:1847-1856.
14. Brezinski EA, Armstrong AW. Off-label biologic regimens in psoriasis: A systematic review of efficacy and safety of dose escalation, reduction, and interrupted biologic therapy. *PLoS One*. 2012;7:e33486.
15. Choi CW, Kim BR, Ohn J, Youn SW. The advantage of cyclosporine A and methotrexate rotational therapy in long-term systemic treatment for chronic plaque psoriasis in a real world practice. *Ann Dermatol*. 2017;29:55-60.
16. Cosentyx (secukinumab) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2018.
17. Kerdel F, Zaiac M. An evolution in switching therapy for psoriasis patients who fail to meet treatment goals. *Dermatol Ther*. 2015;28:390-403.
18. Armstrong AW, Koning JW, Rowse S, Tan H, Mamolo C, Kaur M. Initiation, switching, and cessation of psoriasis treatments among patients with moderate to severe psoriasis in the United States. *Clin Drug Investig*. 2017;37:493-501.
19. Nash P, Kirkham B, Okada M, et al; SPIRIT-P2 Study Group. Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: Results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial. *Lancet*. 2017;389:2317-2327.
20. Griffiths CE, Reich K, Lebwohl M, et al; UNCOVER-2 and UNCOVER-3 Investigators. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): Results from two phase 3 randomised trials. *Lancet*. 2015;386:541-551.
21. Gordon KB, Blauvelt A, Foley P, et al. Efficacy of guselkumab in subpopulations of patients with moderate-to-severe plaque psoriasis: A pooled analysis of the phase III VOYAGE 1 and VOYAGE 2 studies. *Br J Dermatol*. 2018;178:132-139.
22. Foster SA, Zhu B, Guo J, et al. Patient characteristics, health care resource utilization, and costs associated with treatment-regimen failure with biologics in the treatment of psoriasis. *J Manag Care Spec Pharm*. 2016;22:396-405.
23. Enbrel (etanercept) [prescribing information]. Thousand Oaks, CA: Amgen Inc; 2017.
24. Sawyer L, Fotheringham I, Wright E, Yasmeen N, Gibbons C, Holmen Møller A. The comparative efficacy of brodalumab in patients with moderate-to-severe psoriasis: A systematic literature review and network meta-analysis [published online January 29, 2018]. *J Dermatolog Treat*. doi:10.1080/09546634.2018.1427205.