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Management of Psoriasis and Nail Disease

HIGHLIGHTS OF CLINICAL SYMPOSIA

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Long-Term Benefit-Risk: Interpreting the Evidence

Psoriasis is a chronic, recurring autoimmune disease that typically involves the skin but may also have nail and joint manifestations.[1,2] Because of the chronic nature of psoriasis, agents used to treat it must demonstrate efficacy and safety in long-term clinical trials.[3] Evidence from long-term outcome trials is essential for making reasonable treatment decisions for patients with psoriasis.[3,4]

For reasons that are not clearly understood, patients with psoriasis can present with very different signs and symptoms and may experience widely different outcomes. Skin lesions are typically the earliest manifestation of psoriasis, and the primary goal of treatment is to control skin disease. In those patients who develop psoriatic arthritis, approximately 1 out of 4 usually develops joint disease 5 to 10 years after the onset of the skin disease. A second goal of psoriasis treatment is to prevent progression of psoriatic arthritis. No patient with psoriasis should develop crippling arthritis, dactylitis, or sacroiliitis, which may also be present at disease presentation. A significant proportion of patients with psoriasis also have nail disease that should be treated when possible, while considering the lack of response to topical therapies. Finally, quality of life is a major consideration in patients with psoriasis and should be monitored with a validated tool during physician office visits. One of the ultimate goals of psoriasis treatment should be to improve quality of life to a level similar to that in people without psoriasis.

Given these treatment goals, we can define the qualities that a biological treatment should have. First, we need a positive benefit-to-risk ratio: the drug must be both beneficial and safe. Second, the efficacy of the drug must be robust to justify the significant cost of these agents.[5] Finally, psoriasis is a chronic disease that should be treated with an agent that is safe and effective over a long period of time.[3]

The articles in this supplement deal with various aspects of psoriasis and its management. The concept of psoriasis as a systemic disease is reviewed and the consequences of this observation in terms of disease management considered. The special challenges associated with long-term management of a chronic disease such as psoriasis are addressed. Finally, clinical data related to the use of biologics for the treatment of psoriasis from a large infusion clinic are assessed.

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Psoriasis as a Systemic Disease: Benefit-Risk Considerations

Alan Menter, MD

Psoriasis is a complex, systemic, genetic autoimmune disease that primarily presents as skin lesions but may also have joint and nail manifestations.[1] Like other systemic autoimmune diseases, psoriasis of the moderate to severe variety rarely exists by itself and is frequently associated with a variety of comorbid conditions that may be the result of systemic inflammation.[2] Examples are obesity/metabolic syndrome, psoriatic arthritis, autoimmune diseases, psychiatric diseases, cardiovascular diseases, sleep apnea, personal behaviors, cancer/lymphoma, steatohepatitis, chronic obstructive pulmonary disease, and increased mortality.

Not all of the comorbidities are independently related to psoriasis. Obesity is more common in psoriasis patients than the general population—the average body mass index of patients enrolled in phase II and phase III clinical trials of biologics in North America for moderate-severe psoriasis is more than 30 kg/m^2 and likely contributes to other comorbidities, such as cardiovascular disease, metabolic disease, and fatty liver.[3] Other comorbidities include personal behaviors, such as increased smoking and alcohol use, and diseases, such as lymphoma, steatohepatitis, and chronic obstructive pulmonary disease.[4] The incidence of lymphoma, particularly Hodgkin's in psoriasis patients at baseline, is approximately 1.8 times that of patients without psoriasis.

Figure 1 summarizes the issues faced by patients with psoriasis. Proper treatment of psoriasis should be aimed at more than just reducing skin disease and should improve disability, quality of life, and comorbidities. Early intervention, especially in younger patients, can prevent disease progression, including dactylitis and severe joint disease, and is also important for maintaining quality of life and preventing serious depression in patients with psoriasis.

Recent Clinical Trials of Biologic Agents

A number of biologics have recently been evaluated over the past decade for their ability to clear psoriasis. The results of these trials are generally expressed in terms of Psoriasis Area and Severity Index (PASI) improvement. The most effective drugs achieve PASI75 (75% reduction of initial skin lesion area) quickly and maintain the reduction for a long period of time (up to 1 year in clinical trials).

In a randomized, double-blind placebo-controlled trial of the efficacy of infliximab for the treatment of psoriasis, PASI75 responses were monitored through week 50 in patients with moderate-to-severe psoriasis (**Figure 2** on page 4).[4] In this trial, the US Food and Drug Administration (FDA) required testing of a lower dose (3 mg/kg) of infliximab in addition to the standard 5-mg/kg dose. Induction therapy was initiated with both doses at weeks 0, 2, and 6. Thereafter, both doses were given either continuously or on an as-needed basis at the induction dose. At week 10, 75.5% and 70.3% of patients in the infliximab 5-mg/kg and 3-mg/kg groups, respectively, achieved PASI75, and 45.2% and 37.1% achieved PASI90, respectively (vs 1.9% for PASI75 and 0.5% for PASI90 in patients treated with placebo; $P<0.001$). Through week 50, PASI responses with each dose were better maintained with continuous therapy

Figure 1: Psoriasis: A Systemic Disease

COPD=chronic obstructive pulmonary disease; QoL=quality of life.

than with intermittent therapy and with 5-mg/kg than with 3-mg/kg continuous therapy. These results suggest that continuous therapy at the 5-mg/kg dose level or above, as needed, is best for maintaining response to infliximab.[4]

Adalimumab, a fully human monoclonal antibody that binds tumor necrosis factor (TNF), has also been tested for its efficacy in improving the skin lesions of psoriasis. The Randomized Controlled Evaluation of Adalimumab Every Other Week Dosing in Moderate to Severe Psoriasis Trial (REVEAL) randomized 1,212 patients to receive either adalimumab or placebo every other week for 15 weeks.[5] At week 16, 71% of the patients treated with adalimumab and 7% of placebo-treated patients had a PASI75 response.[5] At week 33, patients who maintained a PASI75 response were re-randomized to continue treatment with adalimumab or switch to placebo. At week 52, 79% of the patients treated with adalimumab continuously had a PASI75 response, whereas only 43% of the patients who were switched to placebo retained a PASI75 response.[5] These findings reinforce the need for maintenance therapy for this chronic lifetime disease.

Etanercept, a first-generation TNF antagonist, has also demonstrated efficacy for the treatment of psoriasis.[6] In a randomized, double-blind, phase III trial, 1,324 patients with psoriasis were randomized to receive placebo, low-dose (25 mg once weekly), medium-dose (25 mg twice weekly), or high-dose (50 mg twice weekly) etanercept for 24 weeks. Placebo-treated patients were switched to etanercept 25 mg twice weekly after 12 weeks. At week 12, a PASI75 response was seen in 4% of the placebo patients and 14%, 34%, and 49% of the patients on low-, medium-, and high-dose etanercept, respectively. Respective values after 24 weeks of treatment were 25%, 44%, and 59%.[6]

The most recent biologic approved for the treatment of psoriasis is ustekinumab, a human monoclonal antibody directed against interleukins 12 and 23, which are thought to play a major role in the pathogenesis of psoriasis.[7] The efficacy of ustekinumab has been tested recently in two randomized, double-blind phase III trials.[7,8] In both trials, patients were randomized to receive ustekinumab 45 mg or 90 mg at weeks 0, 1, and 4 and every 12 weeks thereafter. A placebo group was treated on the same schedule. In both trials, a PASI75 was achieved in approximately 80% of patients by week 20 and maintained for up to 40 weeks (**Figure 3**).[7,8]

Safety of Biologic Agents

More than 1 million patients have been exposed to infliximab worldwide across all indications; more than 500,000 to etanercept, and more than 300,000 to adalimumab.[9] Although the majority of these patients have indications separate from psoriasis, the large numbers do reflect considerable experience with these agents. No drug is completely safe, however, and several safety issues should be considered. Patients should not receive biologic agents if they have latent tuberculosis, other active infections, demyelinating disease, malignancy or a premalignant condition, congestive heart failure (New York Heart Association Functional Classification III/IV), or wherever possible if they are pregnant or breast-feeding.[10] All patients who receive biologic agents should be monitored regularly for the development of infections, malignancy, and injection or infusion-site reactions; both clinical efficacy and quality of life should be formally assessed over the long term.[10]

Important safety issues should be monitored in patients who receive TNF antagonists (**Table**), including the risk of developing opportunistic infections, such as tuberculosis and histoplasmosis.[10] Absolute risk varies by region of the country. Texas, for example, has one of the highest incidences of tuberculosis in the United States, whereas histoplasmosis is an important risk in the southern and northeast sections of the United States. Coccidiomycosis is prevalent in the southwestern United States, and blastomycosis is a risk in several areas in the eastern United States. The FDA recently required manufacturers of anti-TNF agents to strengthen package insert warnings concerning the risk of developing histoplasmosis and other invasive fungal infections. Patients must be screened rigorously at baseline for these infections, monitored during treatment, and, of course, treated appropriately if an infection develops. Hepatotoxicity is also a risk, particularly in our psoriasis population with a higher incidence of fatty liver.

Table: TNF Antagonists: Safety Considerations

- Injection-site reactions
- Infusion reactions (infliximab)
- Infections
  – Mild, Moderate, Severe
- Opportunistic infections
  (eg, tuberculosis, histoplasmosis)
- Antibodies, with decrease in response over time
- Lymphoma
- Hepatotoxicity

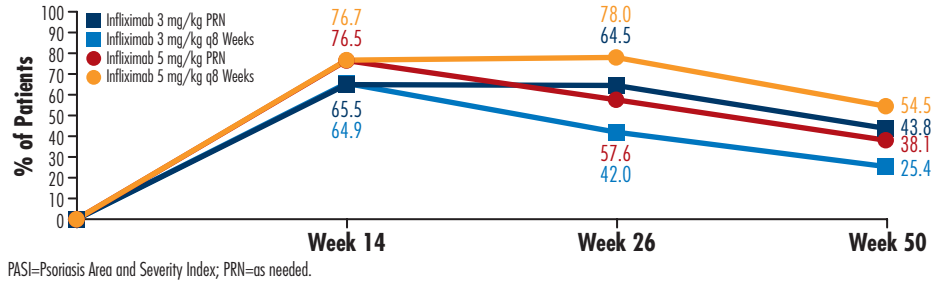
TNF=tumor necrosis factor.

The risk of developing lymphoma during treatment with a TNF antagonist also continues to be a topic of interest. In August 2009, the FDA warned of an increased risk of leukemia, lymphoma, and other cancers in children and adolescents receiving TNF antagonists. Most lymphomas associated with TNF antagonists in patients with other disease such as rheumatoid arthritis, Crohn's, and irritable bowel disease are non-Hodgkin lymphomas, with a mean time to onset of 10 to 21 months.[11] Postmarketing report rates of lymphomas with TNF antagonists are extremely low, approximately 0.01 to 0.03 events per 100 patient-years.[12] This can be compared to the expected rate of 0.07 event per 100 patient-years in a normal population of subjects aged 65 years or older as reported in the Surveillance, Epidemiology, and End Results database of the US National Cancer Institute. In the majority of cases involving biologic agents, patients have received additional systemic therapy, including methotrexate or azathioprine, which may also contribute independently or collectively to the increased risk of lymphoma.

Hepatitis B virus (HBV) infection is another risk that requires careful patient assessment at baseline and monitoring during treatment with a biologic agent.[13-15] Latent HBV reactivation has been reported from 3 weeks to 20 months after initiating therapy. In the majority of cases, patients have been treated with other immunosuppressants in addition to a biologic agent, including methotrexate, azathioprine, and corticosteroids. Several cases of HBV infection with fatal outcomes have been reported in TNF-α treated patients, again predominantly in the non-psoriasis population.[13-15]

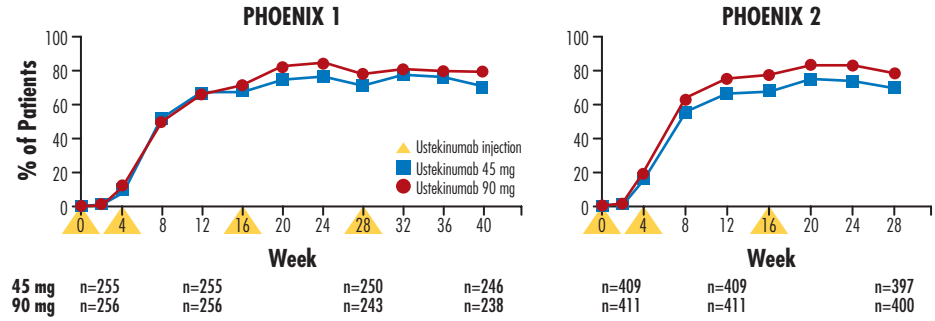
continued on page 12

Figure 2: PASI75 Response to Infliximab Through Week 50[4]



PASI=Psoriasis Area and Severity Index; PRN=as needed.

Figure 3: PASI75 Response During Phase III Trials of Ustekinumab[7,8]



PASI=Psoriasis Area and Severity Index; PRN=as needed.

Long-Term Efficacy: What Do We Really Know?

Kristian Reich, MD

Psoriasis is a chronic disease that requires long-term treatment. Both the design and the interpretation of studies looking at the efficacy and safety of long-term maintenance therapy can be challenging. In order for physicians to facilitate the understanding of the results of such studies, they need to be aware of the assumptions and limitations of the analyses that are used to produce the data. Evidence-based medicine can be effective only if we understand the trial data that form its basis.

Basic Goals for Psoriasis Treatment Trials

While a 50% improvement in Psoriasis Area and Severity Index (PASI50) and Dermatology Quality of Life Index (DLQI) <5 have been proposed as potentially useful minimum efficacy goals, both European and US guidelines for the treatment of psoriasis note that the PASI75 is the most commonly used index of efficacy in clinical trials of psoriasis treatment and is now widely accepted as being clinically meaningful.[1,2] In clinical trials of psoriasis treatments, the PASI75 is most often measured 10 to 16 weeks after the initiation of therapy.[1]

Efficacy data are usually assessed in the most conservative way, using an intention-to-treat (ITT) analysis in which all randomized patients are included in the analysis. The handling of data from the long-term endpoints in trials is more complex. Analysis is complicated by the lack of a placebo control and differences in trial designs and statistical methods. In particular, the manner in which missing values are treated can be a potential source of bias.[3,4]

Statistical Strategies for Dealing With Discontinued Patients

Three approaches to handling data from discontinued patients are frequently used in long-term studies.[3] The first and most conservative approach is called nonresponder imputation, intention-to-treat (NRI-ITT). In this analysis, an ITT approach is used, and subjects dropping out for any reason are considered nonresponders. In the approach known as "last observation carried forward" (LOCF), data from the last measurement of a subject who discontinues the study are carried forward for the remainder of the study. Another method is the "as-observed" approach, in which subjects are included only if they complete the study.[3]

The analytic consequences of these three approaches can be considered in turn using the same hypothetical scenario. Ten patients enroll in the study at baseline; there are seven responders and three nonresponders at 6 months, the primary endpoint. Subsequently, two patients drop out of the study, one a responder and one a nonresponder. After 1 year, all remaining patients are assessed and grouped into responders or nonresponders.

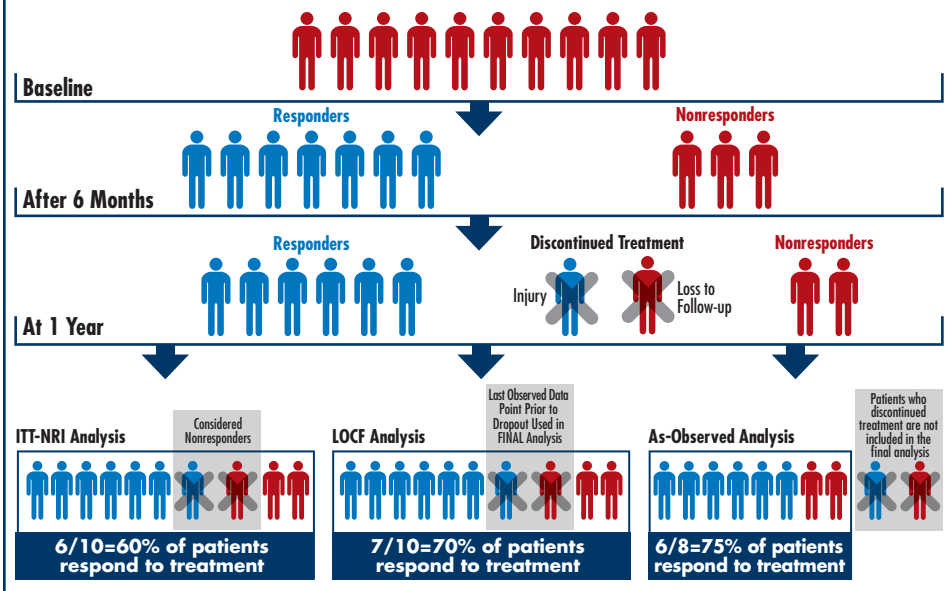
NRI-ITT considers subjects who have been lost to follow-up as nonresponders to prevent overestimation of response.[3] The baseline population of the study is the total number of patients enrolled in a study to determine response to treatment. If two patients drop out of the study, they are considered nonresponders, regardless of the reason they dropped out. Even if one of those patients has been a responder and dropped out because of injury, and the other is a nonresponder who dropped out because of illness, the response rate is still calculated without these two patients; that is, the response rate is 60% after 1 year (**Figure 1**).

Based on the LOCF analysis criteria, patients who withdrew from the study, regardless of reason, are still included in the final analysis. Their classification is based on the last observed data point at 6 months. Based on this form of analysis, 7 out of 10 total patients are considered to have responded to treatment, for a response rate of 70%.

The as-observed analysis, also called "as-treated" analysis, considers only subjects who have completed the study in the determination of response. Analysis of the hypothetical scenario using as-observed analysis criteria is also shown in **Figure 1**. Patients who withdrew from the study, regardless of reason, are not included in the final analysis, reducing the total number of patients from 10 to 8. Responder rates are calculated using the new population size; therefore, the responder rate is 6/8 or 75%.

Thus, using the same clinical data, responder rates of 60%, 70%, or 75% will be calculated depending on the method that is used to analyze the results of the study. A real-life example is shown in **Figure 2**, which shows PASI75 responses over 3 years of infliximab treatment.[5] After 3 years of treatment, the PASI75 response rates range from 41% to 75% simply based on the method of calculation. Therefore, it is particularly important to pay attention to the type of analysis used in reporting results from clinical trials.

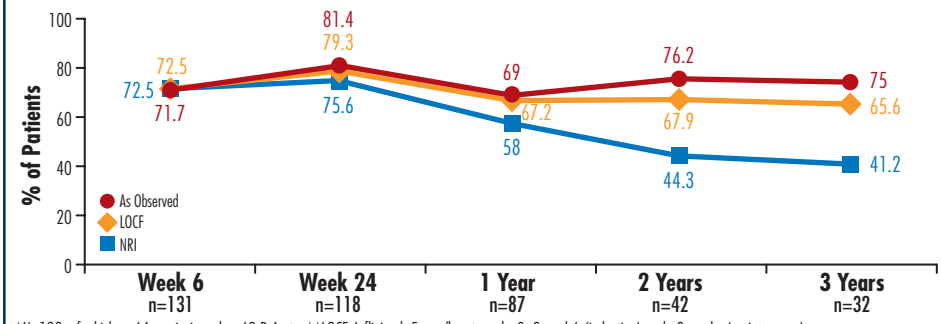
Figure 1: NRI, LOCF, and As-Observed Analyses[3]



NRI=nonresponder imputation; LOCF=last observation carried forward. Adapted from Papp KA et al. *Curr Med Res Opin.* 2008;24:2001-2008.

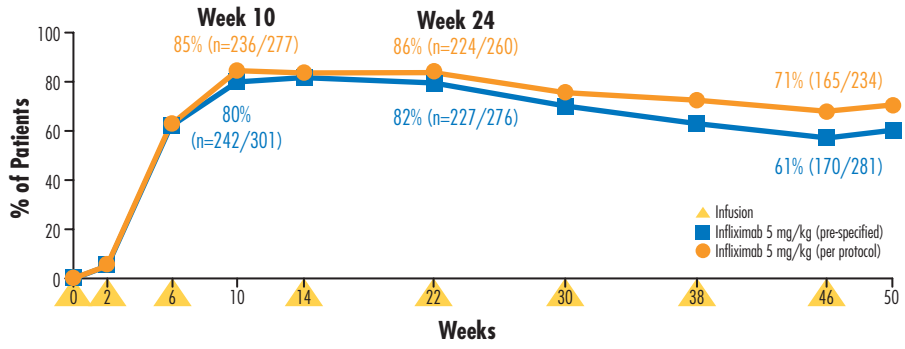
Figure 2: NRI, LOCF, and As-Observed Analyses of Infliximab Treatment Data[5]

PASI response through 3 years of infliximab treatment.



*N=133, of which n=64 psoriasis and n=69 PsA pts; **LOCF. Infliximab 5 mg/kg at weeks 0, 2, and 6 (induction) and q8 weeks (maintenance).
NRI=nonresponder imputation; LOCF=last observation carried forward; PASI=Psoriasis Area and Severity Index; PsA=psoriatic arthritis; pts=patients. Reprinted with permission.

Figure 3: PASI75 Response to Infliximab Through Week 50 in the EXPRESS Trial[11]



PASI=Psoriasis Area and Severity Index; EXPRESS=European Infliximab for Psoriasis Efficacy and Safety Study; NRI=nonresponder imputation.

PER PROTOCOL ANALYSIS

- NRI was used for patients who discontinued because of lack of response, lack of efficacy, or disallowed medication
- Analysis was limited to patients who completed the induction phase
- For subjects who missed more than 2 infusions, the data after the 2nd missed infusion were excluded

PRE-SPECIFIED ANALYSIS

- Same nonresponder imputation
- All data were used irrespective of whether drug was given

Clinical Trials of Biologic Agents

Published clinical trial data can be used to demonstrate how differences in analytic method can affect the outcome of the trial. In a multicenter, randomized, double-blind, placebo-controlled study of 147 patients with psoriasis treated with adalimumab, the primary endpoints were the percentage of patients achieving at least a 75% improvement in PASI score relative to baseline at week 12 (for the initial blinded trial) and at week 24 (for the extension trial).[6] The data were analyzed using the NRI-ITT approach; a patient with missing data was counted as a nonresponder at that visit. Patients who became eligible for dosage escalation were considered nonresponders in the primary analysis. Based on this analysis, the PASI75 responder rate of patients treated with 80 mg adalimumab at baseline followed by 40 mg every other week was 64% after 20 weeks of treatment and 56% after 60 weeks.

In a larger study of adalimumab, the Randomized Controlled Evaluation of Adalimumab Every Other Week Dosing in Moderate to Severe Psoriasis Trial (REVEAL), a complicated design was used to answer some specific questions.[7] Patient handling was different from that in the previous adalimumab trial. At least 75% improvement in the PASI score was required for subjects to advance to the second (at week 16) and third portion (at week 33) of the multiphase study.[7] The disqualification of patients who had a lower response rate complicated the discussion of long-term response and raised concerns with the European Medicines Agency as to whether the generated data were appropriate for assessment of long-term efficacy.

An alternative method of analyzing the REVEAL data is to limit the analysis to only those patients who responded at weeks 16 and 33. When this method is used, retention graphs start at 100%—because all of the patients included are PASI75 responders—and can only go down with time. The patients were then followed for 148 weeks, and retention of response was analyzed using the LOCF method.[8] The PASI75 rate for patients treated with adalimumab after 148 weeks was 78% when analyzed in this way.[8]

In a phase II trial of etanercept, the PASI75 response rate was 60% at week 24, and when analyzed using LOCF, fell off thereafter to 51% at week 96.[7] However, 127 of 591 patients dropped out between weeks 24 and 96, meaning that responses from 127 patients were being carried forward.[9] Given the large number of presumed values included in the analysis, the responder rate at week 96 must be viewed with caution.

In the PHOENIX 1 trial of ustekinumab, an ITT analysis was used until week 28.[10] At week 40, patients with a PASI75 response at week 28 and week 40 were re-randomized either to further treatment with ustekinumab or to placebo. This portion of the trial was designed to see how long response can be retained if ustekinumab is withdrawn.[10] The final design was similar to that of REVEAL. The response rate at week 40 started at 100% because nonresponders were excluded. The final retention graph showed that patients with a PASI75 response at week 26 and 40 who continue with ustekinumab had a PASI75 response rate of over 80% at week 76.[10] It is important to remember, however, that the absolute response rate is strongly influenced by the type of analysis used.

Another example of how the method of analysis can affect trial outcome is provided by the European Infliximab for Psoriasis Efficacy and Safety Study (EXPRESS) trial.[11] PASI75 responses to infliximab in this trial have been analyzed in two ways, resulting in a difference of 10% in response rates after 50 weeks (**Figure 3**).[11] The prespecified analysis of the EXPRESS data included all patients who were still in the trial at week 50 (n=281). The original cohort included 302 patients, indicating that 20 patients were lost to follow-up at week 50.[11] Next, nonresponders were defined as patients who discontinued treatment because of lack of efficacy, lack of response, or use of disallowed medication during the 50 weeks of treatment.[11] The resultant PASI75 response rate at 50 weeks was 61%.[11]

To be included in the per-protocol analysis, a patient had to finish the induction period of infliximab therapy and miss no more than two infusions. Patients who failed to achieve either or both of these goals were excluded from analysis, which contained 234 patients at week 50.[11] This less conservative analysis provided a response rate that is 10% higher than the percentage generated in the prespecified analysis (71% vs 61%).[11] This analysis again highlights the need to carefully define the denominator when calculating response rates.

A final important point that should be made and should be evident from the preceding discussion is that response rates from different trials should not be directly compared. Differences in patient selection and treatment and in analysis of the data preclude a meaningful comparison of trial results. Meaningful comparison can only come from head-to-head trials.

Conclusions

Reading trial data and preparing guidelines require a basic understanding of statistics. In long-term clinical studies, choice of analysis method can greatly affect the response rate that is calculated. Dermatologists should remember these considerations when reading the literature. To date, use of biologics to treat patients with psoriasis has produced impressive response rates, but there are still patients who fail to have a sustained response. The next challenge is to determine the optimal treatment for these patients. ■

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Six Years of Infusion Therapy: What Have We Learned?

Sergio Chimenti, MD

PSOCARE is a national registry of psoriasis patients in Italy, designed by the Italian Medicines Agency in collaboration with Italian dermatologic societies and patient groups and technically coordinated by the Italian Epidemiology Study Group. PSOCARE performs postmarketing evaluations of the effectiveness and safety of psoriasis therapies with the intention of establishing the long-term effects of treatment.[1] A recent publication, for example, reported an effect of body mass index on the clinical response to systemic treatment.[2]

As a member of PSOCARE, the Department of Dermatology, University of Rome Tor Vergata, has accrued considerable experience with infusion therapy for psoriasis. The first patient was treated with infliximab at the center in 1999, and the center has now accumulated data on 325 patients (200 men and 125 women), with a mean disease duration of 20.1 years. Of these, 168 were affected by plaque-type psoriasis, and 157 with psoriatic arthritis.

Considerations During Treatment With Infliximab

Before assigning a patient to treatment with infliximab, dermatologists should consider several important questions. What is the likelihood that the patient will respond to treatment with infliximab? What is the likely efficacy for patients who remain on infliximab long term? How can therapy be optimized? Screening of patients prior to selecting treatment is critical and should include routine blood exams, antinuclear antibody and extractable nuclear antigen profiles, purified protein derivative test or (better) QuantiFERON-TB Gold test for tuberculosis, chest x-ray, electrocardiography, and hepatitis B and C markers. Once patients begin to receive long-term treatment with infliximab, they should have a chest radiograph, testing for tuberculosis twice a year, and blood exams at every infusion. If there is loss of response or an infusion reaction, premedication should be modified. Physicians should also look for infections or paraneoplastic conditions if patients experience a loss of response to treatment.[3,4]

Representative Cases

Case 1: This male patient had a Psoriasis Area Severity Index (PASI) of 39.2 at baseline, but it dropped almost immediately after treatment with infliximab and was 0 (skin clearance) after 2 years of treatment. After 4 years of infliximab treatment, the PASI was 4.6, but the disease was well controlled with topical treatment.

Case 2: This patient, a 25-year-old man, had a PASI of 25 at baseline. After 22 weeks of treatment with infliximab, the PASI dropped to 8.8. After 1 year, however, the patient experienced a loss of efficacy. Eventually, his treatment was shifted to infliximab every 6 weeks as opposed to the standard regimen of every 8 weeks. After 1.5 years, the PASI was 0.8. It dropped to 0 at year 3, and the patient's treatment schedule was shifted back to every 8 weeks. This case demonstrates the need to consider a change in dosing frequency if efficacy deteriorates.

Case 3: This adult male patient presented with a PASI of 35 at baseline. He had an excellent response to infliximab, and the PASI dropped to 0 after the induction period. This particular patient has had a sustained response to infliximab and has been disease free for more than 6 years.

Case 4: This 51-year-old woman with psoriatic arthritis had been diagnosed with psoriasis at age 18 years and with psoriatic arthritis at age 25 years. She had received many types of treatment previously, including oral and local corticosteroids, keratolytics, vitamin D derivatives, methotrexate, acitretin, and fumaric acid esters. She had been receiving cyclosporin A since 2002 and had experienced side effects, including hypertension and the onset of several basal cell carcinomas. When she began treatment with infliximab, her PASI was 22. She was placed on infliximab (5 mg/kg) and her PASI dropped to 0 at 6 weeks, an excellent result considering the length of her disease and the number of treatments that had been tried with limited success. The PASI was still 0 at 1 year after initiating infliximab treatment, although it rose to 9.2 after 2 years, when the patient experienced a worsening of psoriasis during a time of emotional stress. By year 3 of infliximab treatment, the PASI returned again to 0 and it has continued at 0 through year 6. This case demonstrates the need for the physician to also consider the patient's mental and emotional status if the disease worsens.

Treatment Recommendations

Several possible reasons should be considered for the loss of response to infliximab, including latent infections (ie, tonsillitis, pharyngitis, genitourinary infections), induction of psoriasis by concomitant drugs, development of autoantibodies against treatment, associated comorbidities (eg, depression, anxiety, metabolic syndrome), and paraneoplastic conditions. Recommendations for responding to a loss of response are to monitor the patient for the next two infusions to ensure that loss of response is not transitory; to combine—if the patient shows a persistent loss of efficacy—a drug such as methotrexate or cyclosporin with infliximab for a short period until efficacy is regained, and to reduce the infliximab dosage interval from 8 to 6 weeks or 4 weeks.

A Delphi survey was conducted to assess key treatment decision points regarding the use of infliximab for psoriasis.[5] Based on the recommendations of the Delphi survey, PASI75 response should always be the treatment goal.[5] Similarly, an average decrease of 10 points on the Dermatology Life Quality Index should be the standard goal for treatment.[5] This is a guideline, however, and the specific goals and needs of the individual patient should be kept in mind during all treatment decisions. The report also calls for robust, data-based investigations into long-term clinical use of infliximab to strengthen these expert-based recommendations.[5] A treatment algorithm based on this report is shown in the **Figure**.[5]

Conclusions

The cumulative experience of the Italian psoriasis registry indicates that infliximab has a rapid onset of action with a sustained response (PASI75, PASI 90) after 6 years of continuous treatment. A temporary reduction in efficacy may be observed, even after the sixth year, but may be regained in some patients. Treatment with infliximab is safe and well tolerated, especially if physicians are watchful in preventing and diagnosing infections and infusion reactions early. Loss of efficacy is a problem with all biologic agents and is not specific to infliximab. Treatment optimization for waning response is possible, but this area needs further study. Long-term treatment should be managed based on sustained achievable efficacy and on the specific demands of individual patients. ■

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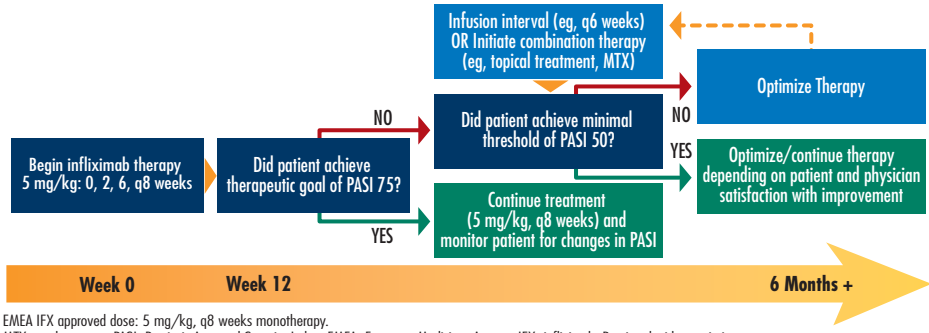
Figure: Algorithm for Long-Term Treatment of Psoriasis With Infliximab[5]



EMEA IFX approved dose: 5 mg/kg, q8 weeks monotherapy.
MTX=methotrexate; PASI=Psoriasis Area and Severity Index; EMEA=European Medicines Agency; IFX=infliximab. Reprinted with permission.

New Views on Nail Psoriasis and Treatment

Psoriasis is not just a skin disease. Up to 50% of patients can have nail involvement,[1] and one third of patients with the disease suffer from psoriatic arthritis.[2] Psoriasis is also linked to the metabolic syndrome, high blood pressure, dyslipidemia, insulin-resistant diabetes, obesity, and increased risk of cardiovascular disease.[2] A connection between psoriasis, Crohn's disease, and ulcerative colitis has also been identified.[3] Many patients with psoriasis may have a form of uveitis that may be a distinct disease entity.[4] In addition, psoriasis imposes a large psychosocial burden on patients.[2] Psoriasis is a very severe disease that produces more severe functional and mental impairment than cancer, diabetes, and myocardial infarction.[5]

In the following articles, the impact of nail psoriasis on patients is considered. The articles include results from studies using a recently developed tool to measure the effect of nail psoriasis on quality of life. The connection between nail psoriasis and psoriatic arthritis is also discussed. Nail psoriasis is positively associated with longer duration and greater extent of the skin disease, and psoriatic arthritis is much more common in people who have nail psoriasis. Severe nail psoriasis is correlated with enthesitis, polyarticular disease, and unremitting and progressive arthritis, suggesting that nail pathology may provide a mechanistic link between skin disease and joint disease in psoriasis. In particular, enthesitis may link nail psoriasis and distal interphalangeal arthritis.

In addition to reviewing the pathology of nail psoriasis, the expanding treatment armamentarium for psoriasis is discussed, including topical agents, intralesional injections, systemic agents, and biologics. Important questions to consider are whether these treatments can produce both skin and nail clearance and whether they also inhibit the radiographic progression of psoriatic arthritis.

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The Magnitude and Impact of Nail Psoriasis

Robert Baran, MD

When considering the full impact of nail psoriasis, one may find it useful to begin with a discussion of anatomy of the healthy nail. The nail is derived from an invagination that has the proximal infold as its roof and the matrix as a floor.[1] The lunula is the only visible part of the matrix. In front of the lunula lies the nail bed, which adheres tightly to the nail plate, and in front of the nail bed is the eponychium, which is the area where the nail detaches from the subungual tissue.[1]

Clinical Impact of Nail Psoriasis

Roughly 50% of patients with psoriasis have nail involvement, and, over a lifetime, between 80% and 90% of patients with psoriasis will suffer nail disease.[2] When evaluating patients with psoriasis, clinicians should consider the key points of age and gender, site of the pathology, signs of nail involvement, associated skin and/or joint lesions, and integrity of body systems. It is also important to know whether a patient has had a positive purified protein derivative test for tuberculosis, any previous treatments for psoriasis, and any side effects or factors that may have limited prior therapy.[3]

The main clinical findings of nail psoriasis include pitting of the nails, an increased thickness of the horny layer of the nail, separation of the nail from the nail bed, brownish-yellow spots ("oily spots") caused by collection of skin debris and fluid often collecting in the space left by nail separation, inflammation of the folds of skin surrounding the nail, and abnormal whitening of the nails (**Figure 1**).[1] Other patterns include subungual distal hematoma, multiple transverse grooves, and trachyonychia, a condition where the nails are rough, like sandpaper (**Figure 2**).[1]

Anatomic and Imaging Considerations in Nail Psoriasis

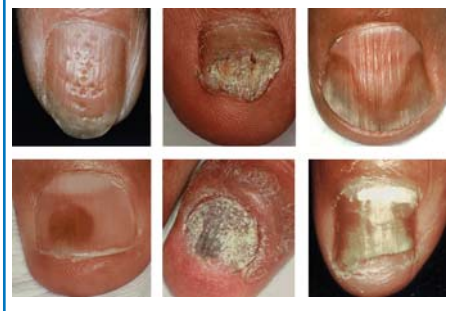
The nail is a musculoskeletal appendage, and nail psoriasis affects the nail entheses, the sites of insertion of a tendon, a ligament, or joint capsule to bone. Historically, inflammation at insertion sites has been viewed as focal, but many entheses form a larger functional unit with adjacent bone, tendon, and ligament. These structures have been termed the "enthesis organ." An enthesis is composed of both soft tissue components and hard tissue components.[4,5] Ultrasound is used to image soft tissue components of entheses, whereas magnetic resonance imaging (MRI) is used to image adjacent osteitis (bone inflammation).[6] Both techniques are used where entheseal-related new bone formation and erosion may be discerned.[7]

The collateral ligaments, which help stabilize and anchor the distal interphalangeal joint (DIP), extend along the bone shaft and are intimately associated with the nail plate. It is important to note, however, that not all nail abnormalities in psoriasis are necessarily dependent on the entheses around the DIP and nail. For example, subungual hyperkeratosis clearly appears to be related to perturbation of keratinocyte function as occurs elsewhere in psoriasis.[1,8]

Scintigraphic studies showed that bone-seeking isotopes were taken up in a periarticular distribution in patients with psoriasis without joint symptoms, demonstrating subclinical joint involvement early in the course of the disease (**Figure 3**).[9] Therefore, early detection is likely to be the key to identifying psoriasis and, most probably, to initiating treatment in time to prevent clinically apparent joint damage. Skin lesions are now known to precede arthritic symptoms in 75% of cases.[2] Typically, cutaneous manifestations of the disease develop 10 years prior to the onset of joint symptoms. This natural history of disease progression provides a potential window of opportunity for early diagnosis of psoriatic arthritis and the initiation of effective and aggressive therapies to alleviate pain and prevent longer-term damage.[10]

continued on page 10

Figure 1: Main Clinical Patterns of Nail Psoriasis



Source: Courtesy of Prof Baran.

Figure 2: Main Clinical Patterns of Nail Psoriasis

Multiple Transverse Grooves

Trachyonychia

Source: Courtesy of Prof Baran.

Understanding the Link Between Psoriasis and Arthritis

Dennis McGonagle, PhD, MB, FRCPI

The historical model for the link between psoriasis and arthritis is a paradigm that involves autoreactive T cells attacking an unknown antigen in the skin and another unknown antigen that lines the synovial membrane, the joint cavity membrane.[1] However, many of the manifestations of disease, including bone lysis and bone fusion, occur at sites that are not necessarily associated with synovium. In fact, up to 40% of patients with psoriatic arthritis develop spinal disease often at sites that are completely devoid of synovium.[1] In addition, x-rays are usually normal in early psoriatic arthritis, but studies have clearly shown prominent new bone formation in chronic disease at entheses (sites of ligament and tendon attachment).[2]

Imaging Studies of Enthesitis and Psoriatic Arthritis

The question of whether enthesitis was in fact the primary lesion in psoriatic arthritis led to a decade-long investigation using magnetic resonance imaging (MRI), ultrasound, histology, positron emission tomography scanning, animal models, and tissue microanatomy.[3,4] The use of fat suppression MRI offered an improved way to show sites of bone and enthesis inflammation. This technique is used to show that the enthesitis lesion in patients with psoriatic arthritis is pathologically diffuse and common at virtually every site of disease.[3]

Evaluation of a large group of patients with early rheumatoid, psoriatic, and other seronegative diseases confirmed that clinically unrecognized enthesitis was common in psoriatic arthritis and related conditions. Entheses were found to be frequently juxtaposed to the synovium, and they were often associated with microdamage, including both degenerative and inflammatory changes.[5] These inflammatory changes can extend to the immediately adjacent synovium.

Similarly, some patients with early psoriatic arthritis of the spine were found to have unilateral severe enthesitis and osteitis, Achilles enthesitis, and psoriasis with enthesitis involving the finger joints.[6] The various imaging techniques suggested that the unifying pathologic process associated with psoriatic arthritis was very diffuse enthesitis and associated osteitis.[5]

Link Between Enthesitis and Osteitis

Extensive diffuse osteitis was observed in patients with plantar fasciitis and in the sternum and sacroiliac of patients with a rare psoriatic arthritis variant of SAPHO syndrome, the combination of synovitis, acne, pustulosis, hyperostosis, and osteitis.[7] The presence of bone microdamage, vascularity changes, and tissue repair at attachments in normal entheses suggests a functional link between bone stress and subsequent MRI determined osteitis.[8] Also the bony thickness at insertions is equivalent to that of trabecular bone, and the bone forms part of the "enthesis organ," hence the presence of diffuse osteitis adjacent to insertions.[9] The basis for the nature of this osteitis and the involvement of cells including osteoprogenitors is now being explored at the cellular and molecular levels.[10] This anatomical knowledge of the true nature of enthesitis is essential for understanding the nature of nail disease in psoriatic arthritis as further outlined in this article.

Nail Psoriasis

In 1956, Verna Wright, MD, of Leeds University, first described the link between psoriasis and arthritis.[5] He noted that 90% of patients with psoriatic arthritis had nail disease. We asked the question whether distal interphalangeal (DIP) joint and nail disease had the same MRI appearance of psoriatic arthritis at other skeletal sites. This was demonstrated in the case of a 16-year-old girl with swelling, nail dystrophy, and onycholysis, but no pain or stiffness or tenderness of the joint, demonstrated on high-resolution MRI.[11] The finger had a normal appearance on x-ray, but significant enhancement of the distal phalange on high-resolution MRI showed diffuse severe osteitis, the hallmark of enthesitis (**Figure 1**).[11,12] Osteitis is not seen at all in rheumatoid arthritis and not to the same extent in osteoarthritis.[11] Findings such as this verified that the diffuse enthesitis-osteitis pathology of psoriatic arthritis was also common in DIP joint disease and thus linked it with enthesitis.

The basis for this link between the nail and the joint can be explained better by looking at the histological studies carried out with Dr Ai Lyn Tan and Professor Michael Benjamin (**Figure 2**). This sagittal section reveals that the extensor tendon is not only attached to the dorsal aspect of the base of the distal phalanx but also extended more distally as the superficial lamina of dense fibrous connective tissue to connect with the nail root.[13]

Further studies have demonstrated that the nail has a very complex anchorage structure. It is anchored to the enthesis at multiple levels, and the whole structure is functionally integrated.[12] The structure is formed of enthesis fibrous attachments interdigitated with blood vessels.[12]

It therefore appears that nail disease may be a forerunner or a predictor of the clinical development of psoriatic arthritis. Indeed an epidemiological study from the United States has confirmed the importance of nail disease as a predictor of psoriatic arthritis.[14] It is already known that psoriasis is associated with subclinical enthesopathy, and studies show that, on average, up to 50% of patients with psoriasis have subclinical skeletal disease. Nail disease thus appears to link into the unifying basis for psoriatic arthritis.[2,12]

Unifying Concept for Psoriatic Disease

The emerging microanatomical features of what is now termed psoriatic disease is also underpinned by emerging immunogenetic concepts.[15] The presence of the HLA-Cw0602 allele is closely associated with type 1 psoriasis. In contrast, HLA-Cw0602 does not appear to be associated with psoriatic arthritis and psoriasis

Figure 1: High-Resolution Magnetic Resonance Imaging of Patient With Psoriatic Nail Changes of the Index Finger: 5-Month Distal Interphalangeal Joint Symptoms[12]

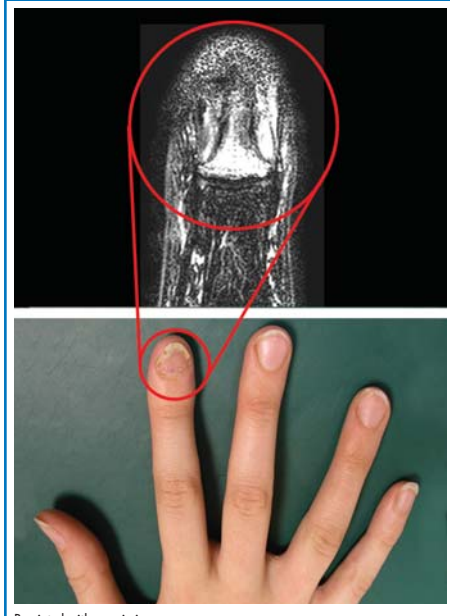


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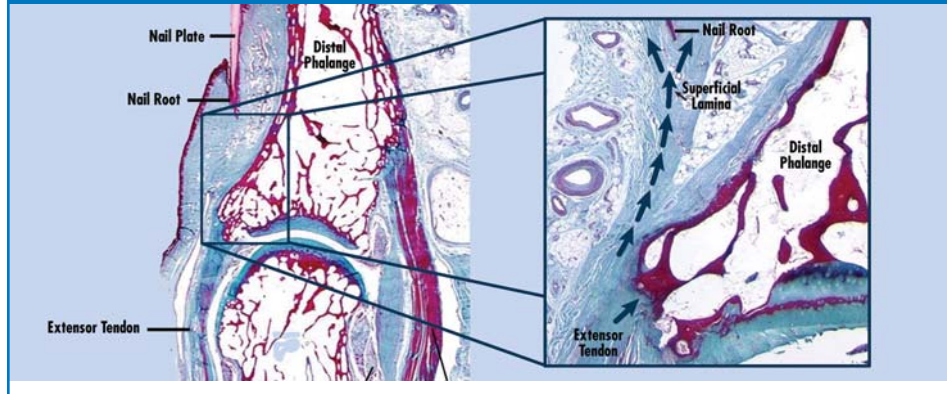
Figure 2: Extensor Tendon Enthesis[13]



Adapted from Tan AL et al. *Rheumatology (Oxford)*. 2007;46:253-256.

of the nails is actually inversely associated with the Cw6 antigen.[16,17] This indicates a differential immunopathology that is shared by the nails and the joints that is fundamentally different from type 1 psoriasis.[17]

Collectively, these data suggest that the microanatomic basis for nail disease is linked to enthesitis and to joint disease. In fact, the skin and the enthesis share microanatomic similarities. In both cases, an avascular tissue (epidermis, fibrocartilage, respectively) is attached to a vascular tissue (dermis, bone, respectively) at an irregular interface that protects against shear.[1] Observations of this sort have led to the concept that there is a group of diseases such as psoriatic arthritis and nail psoriasis that can be referred to as innately immune driven or autoinflammatory where disease localization is primarily related to tissue-specific factors including focal microdamage, microtrauma, and altered permeability at sites of high tissue stress.[18,19] These stand in contrast to type 1 psoriasis, which appears to have a secondary autoimmune component.[20]

Conclusions

Enthesitis and associated osteitis represent the unifying lesion across the entire psoriatic arthritis spectrum.[13] Entheses are sites of microtrauma, and subclinical enthesitis is very common in psoriasis.[1] The nail is functionally integrated into the skeleton, and nail psoriasis has anatomic and immunogenetic properties that are very similar to those of psoriatic arthritis.[13] These observations led to a new way of thinking about nail disease and how it is anatomically and immunogenetically associated with enthesitis, which has important implications for a better understanding of psoriatic disease.[18,20] ■

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The Magnitude and Impact of Nail Psoriasis

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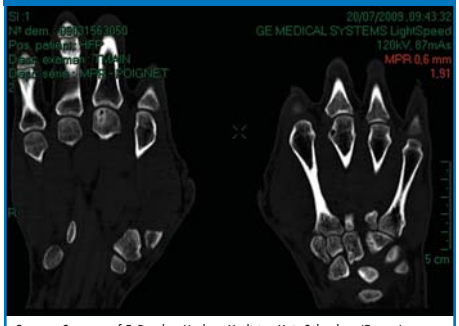
Figure 3: Scintigraphic Study in a Patient With Psoriasis Without Joint Symptoms, Demonstrating Subclinical Joint Involvement



Source: Courtesy of F. Paycha, Nuclear Medicine Unit Colombes (France).

Pain is a common feature of patients with onycholysis, separation of the nail from the plate.[1] The question that needs to be addressed is to what extent clinical nail disease with or without regional pain may, in fact, represent subclinical enthesitis and osteitis.[11] Although MRI is well suited for depicting the adjacent osteitis that may accompany enthesitis, ultrasound is the imaging modality of choice for looking at the soft tissue components of the enthesitis and the bone surface, where both entheseal-related new bone formation and erosion may be discerned.

Impact of Nail Psoriasis on Quality of Life

Although there are scoring systems available for psoriasis disease severity, no validated tool existed to measure the impact of nail psoriasis on patient quality of life (QoL) until recently, when Ortonne and colleagues developed and validated the NPQ10, the first QoL scale for patients with nail psoriasis.[12] The scale score is obtained by adding together responses to 10 questions, and the result indicates the functional difficulty experienced by the patient. The authors' validation study confirmed a serious negative change in the QoL of patients with nail psoriasis.[12] These individuals reported an adverse impact of the disease in several areas of living assessed by the questionnaire, including changes in function such as manual dexterity and limitations on activities, effects on employment (in interaction with others and difficulty performing tasks at work), and serious psychosocial disability, including anxiety and depression.[12] The impact extends to difficulties in being hired for or retained in certain types of jobs, limitations on the types of social activities in which a patient may feel comfortable engaging, and potential effects on personal relationships.

Conclusions

A wide range of tools exist to manage nail psoriasis, from nail enamel (ridging fillers) to biologic agents. Traditional systemic therapies are not likely to be abandoned as new targeted biologics are introduced. Rather, they will be used to precede biologic therapy or concurrently with the newer therapies. The recent advent of targeted biologic therapeutics will offer physicians and their patients treatment options with improved safety profiles that may permit continuous disease control with one drawback, the cost. Combination, rotational, and sequential therapeutic strategies offer the potential advantages of reduced side effects and increased efficacy, while maintaining long-term control and reducing the frequency of inevitable relapses. Finally, the choice of therapy will depend on the disease characteristics of the individual patient and, as always, on the clinician's judgment. ■

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Current Management of Psoriasis With Nail Involvement

Dimitris Rigopoulos, MD

Psoriasis is a chronic, recurring autoimmune disease that typically involves the skin but may also have nail and joint manifestations.[1] Involvement of psoriasis with the nails has a particularly strong effect to reduce quality of life. The involvement of nails should definitely influence the choice of therapy for patients with psoriasis.

A step-by-step approach is recommended for treating nail psoriasis, starting with topical treatments (**Figure 1**).[2] Topical treatment is quick and simple, but topical drugs are not well absorbed by the nail plate. Their use in the treatment of nail psoriasis has produced limited results and is poorly documented.[3]

The next step, intralesional treatment, involves injecting a small dose of the drug directly into or near the psoriatic portion of the nail; this is often painful. This approach is not widely recommended and should be used only as a last resort.[3]

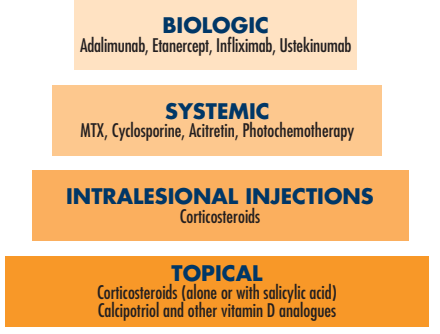
If topical and intralesional treatments are not sufficient to treat the nails, then systemic treatment should be considered. These are often used when the nail psoriasis has been resistant to other therapies, but they are not usually prescribed for patients who have psoriasis that affects only the nails. Although many nonbiologic systemic therapies have demonstrated efficacy in nail disease, more studies are still needed, especially over longer periods of time.[3]

The goal of any new treatment for nail psoriasis, either of the skin or of the nails, is to be more effective for clearing the nails, to produce a better improvement of patient quality of life, and to have fewer side effects than existing therapies. The introduction of systemic biologic therapies has greatly increased the potential for effective treatment of nail psoriasis.

Systemic Biologic Therapies for the Treatment of Nail Psoriasis

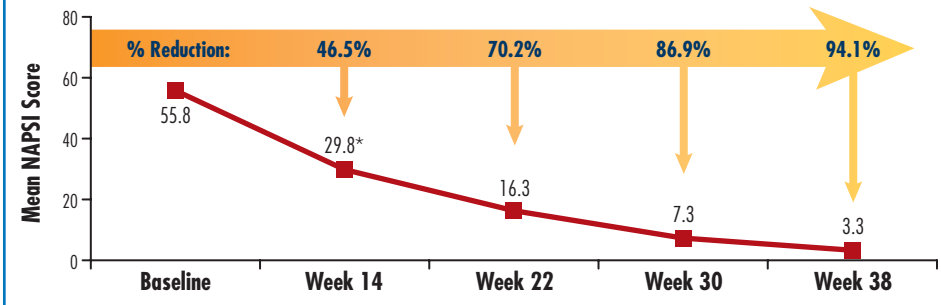
Clinical data suggest that nail clearance is an achievable goal and can be maintained once clinical remission is reached with the use of biologic agents available today.[4] Recent trials with a variety of biologic therapies have verified their effectiveness for the treatment of nail psoriasis.

Figure 1: Current Treatment Options for Nail Psoriasis: An Overview[2]



MTX=methotrexate.

Figure 2: Efficacy of Infliximab for the Treatment of Nail Psoriasis[10]



Significant improvement in mean NAPSI was seen after 3 IFX 5-mg/kg infusions, week 14 (P<0.01). Almost complete remission after 6 IFX 5-mg/kg infusions at week 38.
*P<0.01. Friedman test: λ^2=71.5. d.f.:4. **13 patients with PsA and 5 with psoriasis.
NAPSI=Nail Psoriasis Severity Index; IFX=infliximab; PsA=psoriatic arthritis. Adapted from Rigopoulos D. *Br J Dermatol.* 2008;159:453-456.

Adalimumab

Two recent publications present data for adalimumab in the treatment of nail psoriasis. The first study was an open-label trial that involved 442 subjects. Treatment with adalimumab 40 mg/wk in addition to standard therapy resulted in a 44% decrease in the mean Nail Psoriasis Severity Index (NAPSI) score by week 12, an important improvement for such a short period of time.[5] In a second open-label trial, 21 patients with psoriasis were treated with the same adalimumab regimen that is used for treatment of cutaneous psoriasis, and NAPSI was measured at weeks 12 and 24. At week 24, NAPSI score was decreased by 85.2% in fingernails and 67.4% in toenails in patients with severe plaque-type psoriatic arthritis (n=7). In patients with psoriatic arthritis (n=14), NAPSI score for the fingernails and toenails was reduced by 86.5% and 65.9%, respectively.[6]

Etanercept

A study of etanercept for nail psoriasis included 711 subjects with moderate-to-severe psoriasis randomly assigned in an open-label study to receive etanercept either continuously for 54 weeks or paused in a treat-to-response fashion.[7] Nail psoriasis was noted in 79% of the patients at baseline. Patients treated with etanercept had a 51% mean reduction in NAPSI score and a 63% improvement of quality of life, as measured by the Dermatology Life Quality Index after 54 weeks of treatment. Thirty percent of subjects reported complete nail clearance at 1 year.[7]

Ustekinumab

Rich and colleagues[8] examined the efficacy of ustekinumab for the treatment of nail psoriasis in 500 subjects. In this double-blind placebo-controlled trial, patients with moderate-to-severe psoriasis (n=766) were randomly assigned to receive ustekinumab or placebo. After 24 weeks of treatment, the median reduction in NAPSI score was 50% compared with placebo.

Infliximab

Infliximab has been shown to be effective in nail psoriasis in three studies.[4,9,10] In a phase III randomized, double-blind, placebo-controlled trial in patients with moderate-to-severe psoriasis (n=378), 305 (80.7%) had baseline nail psoriasis.[9] After 50 weeks of treatment with infliximab (5 mg/kg at weeks 0, 2, and 6 and then every 8 weeks up to week 46 with placebo crossover to infliximab at week 24), a NAPSI score improvement of 57.2% was noted at week 50 versus 5.1% improvement in patients treated with placebo at week 24. Complete clearance was observed in 44.7% of patients treated with infliximab at week 50.

In a smaller open-label trial, 25 subjects with plaque psoriasis and nail involvement received 5 intravenous doses of 5 mg/kg infliximab over 22 weeks.[4] By week 22, all patients achieved clearance of nail disease (NAPSI score=0). Clinical remission of nail psoriasis was maintained during a 12-week follow-up period after the last infusion.[4]

In another open-label trial, 18 patients with psoriasis and nail involvement were treated with 6 infusions of 5 mg/kg infliximab over 38 weeks (**Figure 2**).[10] The mean NAPSI score was reduced from 55.8 at baseline to 3.3 at week 38, indicating almost complete clearance of nail disease. This study also assessed improvement in quality of life using an index in which a lower score indicates better quality of life. The mean quality-of-life score was reduced from 66.3 at baseline to 19.1 at week 38.[10]

An additional prospective study presented as an abstract in 2008 compared three anti-tumor necrosis factor (TNF)-α agents (adalimumab, etanercept, and infliximab) in 42 patients with nail psoriasis.[11] The NAPSI score was used to assess severity of disease at baseline through week 22. Infliximab demonstrated the highest efficacy and earliest time of resolution, with significant improvement observed as early as week 6 (mean NAPSI score=8.43, P<0.001 vs baseline of 22.6). Overall, 71% of subjects treated with infliximab (10 out of 14) had a 75% or greater improvement in NAPSI score at week 22. By comparison, 50% of subjects treated with adalimumab and 50% of those treated with etanercept (7 of 14 in each group) had similar results at week 22. All subjects treated with

infliximab showed some response to treatment, but one of the adalimumab-treated subjects (7%) and five subjects in the etanercept group (36%) showed no response at week 22.[11]

Other Considerations When Selecting Treatment

Whereas treatment should be guided to a significant extent by nail disease and quality-of-life concerns, skin lesions are the primary target for therapeutic management in patients with both skin and nail manifestations of psoriasis. A meta-analysis of trials of several biologic agents for treatment of psoriasis of the skin revealed that patients receiving infliximab have an excess chance of 77% over placebo to achieve 75% reduction in the Psoriasis Area and Severity Index [PASI75] versus placebo at week 10.[12] Similarly, 30% and 47% of patients receiving etanercept (25-mg and 50-mg doses, respectively) achieved PASI75 at week 12, and 64% of those receiving adalimumab achieved it at week 16. In a randomized, double-blind, placebo-controlled phase III study of ustekinumab, 66.7% of patients who received ustekinumab 45 mg, 75.7% of patients treated with ustekinumab 90 mg, and 3.7% of patients treated with placebo achieved PASI75 at week 12 ($P<0.0001$ for both comparisons with placebo).[13]

Joint disease should also guide treatment in patients with nail psoriasis and psoriatic arthritis. Based on 2008 guidelines for the management of psoriasis, anti-TNF-α agents with or without methotrexate comprise the recommended first-line treatment in patients with psoriatic arthritis.[14] Head-to-head trials have not been performed. A comparison of effects of treatment with either an anti-TNF-α agent (infliximab 5 mg/kg)[15] or an anti-interleukin-12/23 agent (ustekinumab 90 mg)[16] in patients with psoriatic arthritis suggests that infliximab may be more effective than ustekinumab in terms of both arthritis management and skin treatment. After 16 weeks of treatment, 46.2% of patients treated with infliximab 5 mg/kg achieved 50% improvement of arthritis symptoms from baseline by American College of Rheumatology (ACR) criteria. In contrast, only 25% of patients treated with ustekinumab 90 mg achieved ACR 50 after 12 weeks of treatment.[15,16] Similarly, 68% of patients treated with infliximab achieved PASI75 after 16 weeks of treatment, whereas 52% of the patients treated with ustekinumab achieved PASI75 after 12 weeks of treatment.[15,16]

Based on a comparison of non–head-to-head trial data, anti-TNF agents may not be equally effective for the treatment of psoriasis and psoriatic arthritis. Infliximab[17] but not adalimumab[18] seems to improve enthesitis and dactylitis in psoriatic arthritis.

Members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) have developed comprehensive consensus recommendations for the treatment of clinical manifestations of psoriatic arthritis.[19] Infliximab received a Grade A, meaning that GRAPPA found category 1 evidence of its effectiveness for treating both dactylitis and enthesitis.

Conclusions

Nail involvement is highly prevalent in both psoriasis and psoriatic arthritis, and it places a significant burden on patients. Clearing the nail disease should be a treatment goal in the management of moderate-to-severe psoriasis. In the past, this was not an easily achievable goal, but the advent of biologic agents has changed this. Currently, infliximab is the most effective agent among the biologics for achieving this goal. ■

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Psoriasis as a Systemic Disease: Benefit-Risk Considerations

continued from page 4

Conclusions

Patient characteristics are an important consideration when deciding which patients with psoriasis should be treated with a biologic agent. Biologic therapy can be very effective for controlling the long-term skin manifestations of psoriasis. Continuous rather than intermittent therapy with biologics appears to be more effective. Patients with psoriasis who are treated with biologics should be followed carefully to ensure that the treatment is safe and effective for controlling any of the manifestations of psoriasis that may arise. ■

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