

A Major Win for the Treatment of Nail Psoriasis

Psoriasis is a chronic systemic inflammatory disease involving the skin, nails, and joints. In patients with cutaneous psoriasis, the prevalence of nail psoriasis is greater than 50%.¹ Furthermore, nail psoriasis affects 80-90% of psoriasis patients during their lifetime.² While most patients have concurrent skin and nail disease, 5-10% have isolated nail psoriasis,³ presenting with pitting, leukonychia, red spots in the lunula, and Beau's line, when the inflammation affects the nail matrix. Inflammation of the nail bed presents with subungual hyperkeratosis, onycholysis, salmon patches, oil spots, and splinter hemorrhages in the nail.¹ Nail psoriasis is also highly associated with psoriatic arthritis, which if severe and progressive, can lead to debilitation. In patients with psoriatic arthritis, nail involvement approaches 70%. Furthermore, studies have shown that the presence of nail psoriasis may predict development of psoriatic arthritis later in life.⁴ Studies have also shown that patients with psoriasis are more likely to also have onychomycosis, further worsening their nail disease.^{5,6} Psoriatic nails are not just an aesthetic concern. They can be painful, making it difficult to perform activities of daily life such as tying shoes or buttoning a shirt. Nail psoriasis may also contribute to social stigmatization and patients may have trouble with employment and with personal interactions. Numerous studies have shown that nail psoriasis has a significant impact on quality of life.⁷⁻⁹ Given the extensive symptoms, sequelae, systemic manifestations, and impact on quality of life, it is not surprising that in a survey-based study, 47% of patients with nail psoriasis expressed the desire to be treated for their disease.¹⁰

While nail psoriasis is a common and important disease, there is a paucity of randomized controlled trials that are specifically focused on nail psoriasis to guide treatment plans. Topical treatments including high-potency topical corticosteroids, tazarotene, or calcipotriol may be good options for patients with mild nail disease, but penetration is inadequate with hyperkeratotic nails. In addition, application of the medication one to two times daily for extended periods of time may limit patient compliance. Monthly intralesional corticosteroids are effective, but this treatment works better for matrix disease than bed disease and adherence may be diminished by the frequency and pain associated with injections. Oral methotrexate is another option for nail psoriasis, but nail matrix disease generally responds better nail bed disease.^{11,12} In addition, efficacy is significantly less than that of most biologics.¹³ Oral acitretin is moderately effective for both matrix and bed disease, but improvement in nail bed inflammation is typically slow.¹⁴ Oral biologics

shows some efficacy in nail matrix and bed psoriasis at 16 weeks with larger improvements seen at 32 weeks.¹⁵⁻¹⁷

Biologics have revolutionized the treatment of psoriasis and psoriatic arthritis and are the most effective agents for treating psoriatic nail disease. The inflammation can be suppressed with anti-TNF α , as well as anti-IL-17 and anti-IL-12/23 monoclonal antibodies.¹⁸ Clinical improvements in nail disease typically lag behind skin disease, but efficacy in nail psoriasis can be seen at 12 weeks with additional improvements or even completely normal nails seen at 1 year. Numerous studies have shown that conventional therapies are likely less effective and slower-acting therapies than biologics in treating nail disease.

Does the presence of nail psoriasis alone justify the use of biologic therapies that are expensive, may require frequent injections, and may be associated with side effects?

In 2015, the Medical Board of the National Psoriasis Foundation developed treatment guidelines for nail psoriasis to assist dermatologists in caring for their patients. These recommendations took into account severity of skin disease, psoriatic arthritis, nail disease, and impairment of quality of life. In sum, they suggested high-potency topical corticosteroids with or without calcipotriol for patients with nail psoriasis only. However, if this initial treatment was ineffective, they recommended adalimumab, etanercept, intralesional corticosteroids, ustekinumab, methotrexate sodium, and acitretin.¹⁹

Despite mounting evidence that biologics provide the fastest and most efficacious for nail psoriasis, it remains challenging for patients to get access to these medications, often requiring concomitant skin and/or joint involvement. Dermatologists are faced with settling for less desirable treatment options, and the disease often progresses leaving patients with loss of functionality, permanent nail dystrophy, and a negative impact on quality of life.

On March 30, 2017, the U.S. Food and Drug Administration (FDA) approved the inclusion of moderate to severe fingernail psoriasis data in the adalimumab prescribing information for patients with moderate to severe chronic plaque psoriasis.²⁰ The FDA based this decision on data from a multicenter, double-blind, randomized, parallel-arm, placebo-controlled, Phase 3 clinical trial (NCT02016482) that evaluated the safety and efficacy of adalimumab for the treatment of nail psoriasis in patients with

FIGURE 1. Nail psoriasis. Severe pitting and subungual hyperkeratosis of the nails. The patient has minimal skin involvement affecting only the penis.



chronic plaque psoriasis. Almost 50% of patients treated with adalimumab achieved an assessment of clear or minimal with at least a two-grade improvement from baseline in signs and symptoms of fingernail psoriasis compared to 7% percent of placebo patients.²¹

The treatment plan for every patient must be individualized taking into account nail psoriasis severity, involvement of the nail matrix, nail bed or both, fingernails vs. toenails, number of nails affected, concomitant skin and joint involvement, patient lifestyle, and adherence to a treatment regimen, comorbidities medications, and impact on quality of life. The recent FDA approval of adalimumab fingernail psoriasis data in the package insert for this drug is a major win for the treatment of nail psoriasis. It is hoped that this approval will improve access to biologics for our nail psoriasis patients, thus improving their functionality and quality of life.

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References

- Jiaravuthisan MM, Sasseville D, Vender RB, et al. Psoriasis of the nail: anatomy, pathology, clinical presentation, and a review of the literature on therapy. *J Amer Acad Dermatol* 2007;57(1):1-27.
- Samman PD, Fenton DA. *The Nails in Disease*. 5th edition ed. London, England: Butterworth-Heinemann Ltd, 1994.
- Salomon J, Szepletowski JC, Proniewicz A. Psoriatic nails: a prospective clinical study. *J Cutan Med Surg* 2003;7(4):317-21.
- Armesto S, Esteve A, Coto-Segura P, et al. [Nail psoriasis in individuals with psoriasis vulgaris: a study of 661 patients]. *Actas Dermosifiliogr* 2011;102(5):365-72.
- Gupta AK, Lynde CW, Jain HC, et al. A higher prevalence of onychomycosis in psoriatics compared with non-psoriatics: a multicentre study. *Br J Dermatol* 1997;136(5):786-9.
- Rigopoulos D, Papanagiotou V, Daniel R, 3rd, et al. Onychomycosis in patients with nail psoriasis: a point to point discussion. *Mycoses* 2017;60(1):6-10.
- de Jong EM, Seegers BA, Gulincx MK, et al. Psoriasis of the nails associated with disability in a large number of patients: results of a recent interview with 1,728 patients. *Dermatology* 1996;193(4):300-3.
- van der Velden HM, Klaassen KM, van de Kerkhof PC, et al. The impact of fingernail psoriasis on patients' health-related and disease-specific quality of life. *Dermatology* 2014;229(2):76-82.
- Klaassen KM, van de Kerkhof PC, Pasch MC. Nail Psoriasis, the unknown burden of disease. *JEADV* 2014;28(12):1690-5.
- Klaassen KM, van de Kerkhof PC, Pasch MC. Nail psoriasis: a questionnaire-based survey. *Br J Dermatol* 2013;169(2):314-9.
- Gumusel M, Ozdemir M, Mevlitoglu I, et al. Evaluation of the efficacy of methotrexate and cyclosporine therapies on psoriatic nails: a one-blind, randomized study. *JEADV* 2011;25(9):1080-4.
- Demirsoy EO, Kiran R, Salman S, et al. Effectiveness of systemic treatment agents on psoriatic nails: a comparative study. *J Drugs Dermatol* 2013;12(9):1039-43.
- Sanchez-Regana M, Sola-Ortigosa J, Alsina-Gibert M, et al. Nail psoriasis: a retrospective study on the effectiveness of systemic treatments (classical and biological therapy). *JEADV* 2011;25(5):579-86.
- Tosti A, Ricotti C, Romanelli P, et al. Evaluation of the efficacy of acitretin therapy for nail psoriasis. *Arch Dermatol* 2009;145(3):269-71.
- Papp K, Reich K, Leonardi CL, et al. Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, in patients with moderate to severe plaque psoriasis: Results of a phase III, randomized, controlled trial (Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis [ESTEEM] 1). *J Amer Acad Dermatol* 2015;73(1):37-49.
- Paul C, Cather J, Gooderham M, et al. Efficacy and safety of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate-to-severe plaque psoriasis over 52 weeks: a phase III, randomized controlled trial (ESTEEM 2). *Br J Dermatol* 2015;173(6):1387-99.
- Rich P, Gooderham M, Bachelez H, et al. 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). *J Amer Acad Dermatol* 2016;74(1):134-42.
- Pasch MC. Nail Psoriasis: A Review of Treatment Options. *Drugs* 2016;76(6):675-705.
- Crowley JJ, Weinberg JM, Wu JJ, et al. Treatment of nail psoriasis: best practice recommendations from the Medical Board of the National Psoriasis Foundation. *JAMA Dermatol* 2015;151(1):87-94.
- Abbvie. News release. 2017. <https://news.abbvie.com/news/us-fda-approves-addition-moderate-to-severe-fingernail-psoriasis-data-to-abbvies-humira-adalimumab-prescribing-information.htm>. Last accessed 4/11/17
- Abbvie. News release. 2016. <https://news.abbvie.com/news/abbvie-presents-initial-data-from-pivotal-phase-3-trial-evaluating-efficacy-and-safety-humira-adalimumab-for-moderate-to-severe-fingernail-psoriasis-in-adult-patients-at-psoriasis-2016-congress.htm>. Last accessed 4/11/17

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