

Treatments for Nail Psoriasis: A Systematic Review by the GRAPPA Nail Psoriasis Work Group

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ABSTRACT. Nail involvement in psoriatic diseases causes significant physical and functional disabilities. Evaluating, measuring, and treating nail involvement is important in improving the health outcomes and quality of life among patients with psoriasis and psoriatic arthritis (PsA). We performed a systematic analysis of the literature on nail psoriasis to help inform an update of treatment recommendations by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA). (J Rheumatol 2014;41:2306–14; doi:10.3899/jrheum.140881)

Key Indexing Terms:

NAIL PSORIASIS TREATMENT THERAPY PSORIASIS EFFICACY EFFECTIVENESS

We performed 2 independent comprehensive literature searches of English-language human studies, published in the Medline database between January 1, 2006, and March 1, 2014, using the following search terms: psoriasis, psoriatic arthritis (PsA), nail, and treatment. Articles from the 2 searches were combined, and reference lists from articles from the database search were manually reviewed for additional relevant publications. Inclusion criteria were the following: adults (studies with > 5 patients) with psoriasis or PsA and psoriatic nail involvement, and clinical trials, case series, or observational studies of therapies for psoriatic nail disease. Authors independently extracted the data, and any disagreements were adjudicated by consensus. Results are summarized below and presented fully in Tables 1A-1E.

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Topical Therapies^{1,2,3,4,5} (Table 1A)

Topical therapies, an initial option for patients with mild nail involvement without significant functional impairment, include calcipotriol, a synthetic analog of vitamin D3 (50 $\mu\text{g/g}$), alone or in combination with betamethasone dipropionate. Limited evidence supports modest efficacy in psoriasis limited to < 2 nails when used for ≥ 12 weeks^{1,2,3}. Moreover, twice daily calcipotriol monotherapy may have modest efficacy similar to daily calcipotriol and betamethasone dipropionate combination therapy.

Tacrolimus, a nonsteroidal topical calcineurin inhibitor that downregulates antigen-specific T cell activity and proinflammatory cytokine production, may have modest efficacy when applied once daily for ≥ 12 weeks⁴.

Tazarotene, a third-generation topical retinoid available as a cream or gel, may have a modest effect when used once daily in patients with nail bed and nail matrix lesions of moderate severity affecting > 2 nails^{1,5}.

5-fluorouracil (5-FU), an antimetabolite that inhibits pyrimidine synthesis, has been used to treat actinic keratosis and squamous cell carcinoma *in situ*. However, topical 5-FU 1% lotion was no more effective than vehicle lotion when used daily for 12 weeks in patients with severe psoriatic nail dystrophy in ≥ 1 nail¹.

Procedural Therapies^{1,2,6,7} (Table 1B)

The 595-nanometer pulsed dye laser (PDL) has been used to treat moderate-to-severe psoriatic nails monthly for ≥ 6 months with limited efficacy^{6,7}. Longer pulse durations (e.g., 6 ms vs 0.45 ms) do not appear to result in greater efficacy and may cause greater side effects, such as pain^{6,7}.

Limited evidence suggests that intralesional corticosteroid injections may be moderately effective in treating psoriatic nail dystrophies, particularly abnormalities of the nail matrix. However, studies vary on dosing and frequency, and many lack sufficient patient characteristics, e.g.,

Table 1A. Topical therapies for nail psoriasis.

Study	Therapy	Study Type and Population	Outcome Measure	Patient Disease Characteristics	Results
Rigopoulos 2009 ² , Greece	Calcipotriol-betamethasone valerate ointment (qd ×12 wks)	Open-label, uncontrolled; N = 25	NAPSI at wks 4, 8, 12	Mild cutaneous psoriasis (PASI < 10)	Mean NAPSI at baseline: 5.8 ± 1.7, wk 12: 1.6 ± 0.6, p < 0.01 c/w baseline
Tzung 2008 ³ , Taiwan	0.005% calcipotriol + 0.05% betamethasone dipropionate ointment (qd ×12 wks) vs 0.005% calcipotriol ointment (bid ×12 wks)	Randomized, single-blinded, comparator; N = 40	Investigator Global Assessment Score (IGA), NAPSI at wks 0, 4, 8, 12	Fingernail psoriasis (severity not mentioned)	IGA after 12 wks (% patients with ≥ moderate improvement): calcipotriol + betamethasone: 53%, calcipotriol: 53%, p = 0.071 btwn groups ; mean NAPSI after 12 wks: specific values NR; p = 0.649 btwn groups
De Simone 2013 ⁴ , Italy	0.1% tacrolimus ointment (qd ×12 wks) vs no treatment	Randomized, controlled, open-label; N = 21	NAPSI at wks 0, 6, 12	Fingernail psoriasis (severity not mentioned)	Mean NAPSI at baseline vs wk 12: 0.1% tacrolimus: 23.0 vs 10.0, No treatment: 19.3 vs 16.3, p < 0.001 btwn groups
Fischer-Levancini 2012 ⁵ , Spain	0.1% tazarotene ointment under occlusion (qd ×6 mo)	Open-label, observational; N = 6	NAPSI at months 0, 3, 6	Fingernail psoriasis affecting both the matrix and the bed	Mean NAPSI at baseline: 14.3 ± 6.3, 3 mo: 8.0 ± 3.3, p = 0.007 c/w bl , 6 mo: 2.3 ± 1.2, p = 0.003 c/w bl

Data in bold face are p values. bid: twice daily; btwn: between; c/w: compared with; bl: baseline; qd: every day; N: number; NAPSI: Nail Psoriasis Severity Index; PASI: Psoriasis Area and Severity Index; NR: not reported.

Table 1B. Procedural therapies for nail psoriasis.

Study	Therapy	Study Type and Population	Outcome Measure	Baseline	Results
Goldust 2013 ⁶ , Iran	Pulsed dye laser (595 nm, 7-mm spot size, 0.45 ms pulse duration, 6 j/cm ² , 20 ms cryogen spurt with 10 ms delay, qm ×6 mo) vs same, except 6 ms pulse duration, 9 j/cm ²	Randomized, double-blinded, inpatient, left-to-right; N = 40	NAPSI at mo 0, 1, 2, 3, 4, 5, 6	Mild-to-moderate plaque psoriasis and refractory nail involvement, ≤ 30% BSA of plaque psoriasis, no active PsA or pustular psoriasis of nail	Significant decrease in mean NAPSI, nail matrix NAPSI, and nail bed NAPSI at 6 mo c/w baseline in both groups; specific values NR. NS btwn groups
Treewittayapoom 2012 ⁷ , Thailand	Pulsed dye laser (595 nm, 6 ms pulse duration, 7-mm spot size, 9 j/cm ² , with 10 ms cryogen delay, qm ×6 mo) vs same, except 0.45 ms pulse duration, 6 j/cm ²	Randomized, double-blinded, inpatient, left-to-right; N = 20	NAPSI at mo 0, 1, 2, 3, 4, 5, 6	Recalcitrant, bilateral fingernail psoriasis, ≤ 30% BSA of chronic plaque psoriasis	Significant decrease in mean NAPSI at 6 mo c/w baseline in both groups; specific values NR. NS btwn groups

Data in bold face are p values; btwn: between; c/w: compared with; qm: every month; mo: month(s); BSA: body surface area; NAPSI: Nail Psoriasis Severity Index; NR: not reported; NS: not significant; PASI: Psoriasis Area and Severity Index.

severity and type of psoriatic disease¹. Typically, 0.05–0.3 ml of triamcinolone acetonide 2.5–10 mg/ml is injected at multiple sites in the proximal nailfold at weekly intervals for ≤ 5 months².

Traditional Oral Systemic Therapies^{1,8-16} (Table 1C)

Although traditional systemic therapies have not been rigorously tested, oral cyclosporine, an immunosuppressant drug that interferes with activity and growth of T cells, has modest efficacy in nail psoriasis^{1,8,9,10,11}. Oral methotrexate (MTX, ≤ 15 mg weekly), an antimetabolite and antifolate drug commonly used to treat psoriasis and inflammatory arthritis, has been tested rigorously, but is unlikely to result in significant improvement in psoriatic nail disease^{8,9,12,13,14}. Briakinumab [an interleukin 12/23 (IL-12/23) inhibitor no

longer in development] was superior to MTX in 1 study¹³. Acitretin, a second-generation retinoid and a metabolite of etretinate, had modest efficacy at doses of 0.2–0.3 mg/kg/day for 6 months^{1,9,14,15}. Leflunomide, an oral pyrimidine synthesis inhibitor, also had modest efficacy in psoriatic nail dystrophy when dosed at 100 mg/day for 3 days, then 20 mg/day for 24 weeks¹⁶.

Biologic Therapies^{1,9,11,14,17-41} (Table 1D)

Tumor necrosis factor-α (TNF-α) plays a key role in the pathogenesis of psoriasis and PsA, and can interrupt TNF signaling, thereby leading to improvements in nail dystrophy. In several controlled studies, adalimumab (ADM)^{9,11,14,17,18,19,20,21,22,23,24}, certolizumab pegol²⁵, etanercept^{9,14,22,23,24,26,27}, golimumab^{28,29}, and infliximab

Table 1C. Traditional oral systemic therapies for nail psoriasis.

Study	Therapy	Study Type and Population	Outcome Measure	Baseline	Results
Gumusel 2011 ⁸ , Turkey	CsA (initial 5-mg/kg dose PO qd ×12 wks → 2.5–3.5 mg/kg PO qd ×12 wks) vs MTX (initial 15-mg dose SQ qw ×12 wks → 10 mg SQ qw ×12 wks)	Randomized, single-blinded, comparator, N = 37	NAPSI at wks 0, 4, 8, 12, 16, 20, and 24	Psoriatic patients with nail involvement, ≥ 10% of BSA with lesions, PASI ≥ 10, NAPSI 10 or psoriatic patients with nail involvement distressed because of either their condition or their nail pathology that proved to be resistant to topical treatment regardless of BSA and PASI	Mean NAPSI score at wk 0: CsA: 42.1 ± 26.4, MTX: 39.1 ± 19.9; wk 24: CsA: 25.4, MTX: 18.3, NS btwn groups
Sanchez-Regana 2011 ⁹ , Spain	Classical treatments [acitretin (PO), MTX (PO or SQ) CsA (PO), PUVA, NB-UVB, Re-PUVA, Re-NB-UVB] vs biological treatments (IFX; IV), (ETN; SQ), efalizumab (SQ), or (ADM; SQ)	Retrospective review, N = 84	NAPSI at weeks 12, 24, and 48	Moderate-to-severe psoriasis (PASI ≥ 3), PsA, and presence of psoriasis of the nails	Mean percent change in NAPSI score: wk 48: Classical: CsA: 89.1% (p value vs CsA), Acitretin: 51.7%, p < 0.001 , MTX: 34.9%, p < 0.001 , PUVA: 69.1%, p = 0.023 , NB-UVB: 5.0%, p < 0.001 , Re-PUVA: 84.6%, p = 0.190 , Re-NUVB: 64.4%, p = 0.003 , Biological: IFX: 91.5% (p-value vs IFX), ETN: 86.7%, p = 0.423 , Efalizumab: 82.5%, p = 0.237 , ADM: 84.2%, p = 0.083 , Mean percent change in NAPSI score at wk 48: Classical: 57.2%, Biological: 86.0%, p < 0.001 btwn groups
Syuto 2007 ¹⁰ , Japan	CsA (initial 3-mg/kg dose PO bid → 1.5 mg/kg PO qd if improvement)	Open-label, uncontrolled, N = 16	Improvement	Duration of psoriatic nails ranged from 1–27 years. 13/16 patients were unresponsive to prior treatments	2/16 complete resolution; 10/16 significant improvement; 3/16 slight improvement; 1/16 no change
Kingsley 2012 ¹² , UK	MTX (initial 7.5-mg dose PO qw ×4 wks → 10 mg PO qw ×4 wks → 15 mg PO qw ×16 wks) vs Placebo	Randomized, double-blinded, placebo-controlled, N = 221	Nail disease score at months 0, 3, 6	Active psoriasis and arthritis, and presence of nail changes	No evidence of a treatment effect (specific results NR)
Reich 2011 ¹³ , Germany, Canada, France	MTX (5–25 mg PO qw ×52 wks) vs Briakinumab (initial 200-mg dose SQ at wks 0 and 4 → 100 mg SQ q 4 wks, wks 8–48)	Randomized, double-blinded, comparator, N = 317	NAPSI (target fingernail) at wks 0, 24, 52	Psoriasis for ≥ 6 months and stable plaque psoriasis ≥ 2 months, PGA ≥ 3, PASI ≥ 12, 10% BSA affected by psoriasis, Moderate-to-severe psoriasis limited to the nails	Mean NAPSI score (target fingernail) at wk 0: MTX: 4.8 ± 2.1, Briakinumab: 4.8 ± 2.0; wk 52: MTX: 3.0, Briakinumab: 1.2, p < 0.001 btwn groups
Tosti 2009 ¹⁵ , Italy	Acitretin (0.2–0.3 mg/kg PO qd ×6 months)	Open-label, uncontrolled, N = 36	NAPSI at months 0, 2, 4, 6	Moderate-to-severe psoriasis limited to the nails	Mean NAPSI score at baseline vs month 6: 31.5 (range 10–46) vs 18.6 (range 6–34); percent reduction of NAPSI score at month 6: 41%
Behrens 2013 ¹⁶ , Germany, Czech Republic, Slovenia	Leflunomide (initial 100-mg dose PO qd ×3 days → 20 mg PO qd ×24 wks)	Observational, N = 514	Clinical severity (5-pt scale)	Active psoriatic disease; no previous leflunomide treatment	Proportion of patients experiencing improvement of ≥ 1 point from baseline to final visit: 32%

Data in bold face are p values. btwn: between; PO: orally; qd: every day; qw: every week; SQ: subcutaneous; BSA: body surface area; N: number; NAPSI: Nail Psoriasis Severity Index; NR: not reported; PUVA: psoralen + ultraviolet A; CsA: cyclosporin A; MTX: methotrexate; ADM: adalimumab; IFX: infliximab; NB-UVB: narrow band ultraviolet B; PASI: Psoriasis Area and Severity Index; PGA: physician global assessment.

mab^{1,9,14,22,23,24,30,31,32,33,34,35} were highly efficacious in treating psoriatic nail disease. Larger studies are necessary to determine comparative effectiveness of these agents^{9,14,22,23,24}.

Ustekinumab, an anti-IL-12/23 monoclonal antibody, was highly effective in treating nail psoriasis, when weight-based dosing was used^{36,37,38,39,40}. Limited data

Table 1D. Biologic therapies for nail psoriasis.

Study	Therapy	Study Type and Population	Outcome Measure	Baseline	Results
Demirsoy 2013 ¹⁴ , Turkey	IFX, ADM, or ETN vs MTX, vs narrow-band UVB (NB-UVB), vs acitretin, vs no treatment	Comparative, N = 87	NAPSI at wks 0, 16	Any type of skin psoriasis with nail involvement	Mean NAPSI score at wk 0: Biologics: 36.5, MTX: 25.1, NB-UVB: 22.5, Acitretin: 23.8, Control: 21.3; wk 16: Biologics: 7.9, p = significant c/w control but specific value NR, MTX: 20.5, NS c/w control , NB-UVB: 17, NS c/w control , Acitretin: 17.9, NS c/w control ; Control: 18.3
Sola-Ortigosa 2012 ¹⁷ , Spain	ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ at wk 1, then eow)	Retrospective, N = 15	NAPSI at wks 0, 24	Moderate-to-severe plaque psoriasis, failed to respond to conventional systemic treatments or other biological agents, in which ADM therapy was indicated	Mean NAPSI score at baseline vs wk 24: 18.9 ± 12.2 vs 8.2 ± 4.7, p = 0.001
Leonardi 2011 ¹⁸ , USA, Canada	ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ eow wks 1–15; → Pbo at wk 16 → 40 mg SQ eow wks 17–27), vs Pbo (crossover to ADM 80 mg SQ at wk 16 → 40 mg SQ eow, wks 17–27)	Randomized, Pbo-controlled, double-blind (16 wks); open-label 12-wk extension, N = 72	NAPSI at wks 0, 8, 16, 28	Chronic plaque psoriasis on hands and/or feet with PGA of hands/feet of at least “moderate” severity	Mean NAPSI score (target nail): Baseline: ADM: 3.9 ± 2.0; Pbo: 3.3 ± 1.8; Mean % NAPSI improvement: Wk 16: ADM: 50%, Pbo: 8%, p = 0.02 btwn groups ; Wk 28: ADM: 54%, Pbo (switched to ADM at wk 16): 38%
Rigopoulos 2010 ¹⁹ , Greece	ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ at wk 1 → 40 mg SQ q2wks)	Open-label, N = 21	Mean NAPSI at wks 0, 12, and 24	Severe plaque psoriasis with nail involvement	Mean NAPSI score at baseline: Psoriasis patients: Fingernails: 10.57 ± 1.21; Toenails: 14.57 ± 2.50, PsA patients: Fingernails: 23.86 ± 2.00; Toenails: 29.29 ± 2.87, Mean NAPSI score at wk 24: Psoriasis patients: Fingernails: 1.57 ± 0.20; Toenails: 4.14 ± 1.58, PsA patients: Fingernails: 3.23 ± 0.32; Toenails: 10.00 ± 1.40
Van den Bosch 2010 ²⁰ , Belgium, Germany, France, UK, Norway, Denmark, Sweden, Finland, Ireland	ADM (40 mg SQ eow ×12 wks)	Open-label, N = 442	NAPSI at wks 0, 12, 20	Diagnosis of PsA, previous treatment with > 1 DMARD	Improvement > 50% in NAPSI score at wk 12 (in patients with baseline NAPSI > 10): 54.2%, Median NAPSI: Wk 12: 5, Wk 20: 1
Rudwaleit 2010 ²¹ , Germany	ADM (40 mg SQ eow ×12 wks)	Open-label, N = 442 (with PsA)	NAPSI at wks 0, 12	History of anti-TNF treatment [IFX, ETN, or both] and failure of 1 or more DMARD for PsA	Median change in NAPSI score at wk 12: No prior ETN/IFX: –6 (range –14 to –2), Prior ETN/IFX: –6 (range –15 to –1), NS btwn groups
Ozmen 2013 ²² , Turkey	ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ eow starting wk 1), vs ETN (50 mg SQ biw ×12 wks → 50 mg SQ qw), vs IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks to wk 46)	Randomized, open-label, N = 28	NAPSI at wks 0, 12, 24, 36, 48	Moderate-to-severe nail psoriasis, failed other systemic therapies	Mean improvement in NAPSI score at week 48: ADM: 53.8%, ETN: 57.3%, IFX: 40.4%, CI not reported; authors report difference NS

Table 1D. Continued

Study	Therapy	Study Type and Population	Outcome Measure	Baseline	Results
Saraceno 2013 ²³ , Italy	ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ eow wks 1–24), vs ETN (50 mg SQ biw ×12 wks → 25 mg SQ biw ×12 wks), vs IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks to wk 24)	Open-label, N = 60	NAPSI at wks 0, 14, 24	Moderate-to-severe plaque psoriasis or PsA, failed ≥ 2 systemic conventional treatments, NAPSI score > 15	Mean NAPSI score at baseline vs wk 14: ADM: 33.1 ± 14.9 vs 21.0 ± 8.91, p ≤ 0.01 , ETN: 34.8 ± 12.38 vs 23.6 ± 10.43, p ≤ 0.01 , IFX: 33.3 ± 9.76 vs 14.9 ± 4.20, p ≤ 0.01 ; Mean NAPSI score at wk 14 vs wk 24: ADM: 21.0 ± 8.91 vs 11.4 ± 4.6, p ≤ 0.0002 , ETN: 23.6 ± 10.43 vs 10.6 ± 5.25, p ≤ 0.0016 , IFX: 14.9 ± 4.20 vs 3.1 ± 3.27, p ≤ 0.00001 ; At week 14, IFX had better efficacy than ADM and ETN, p < 0.05
Kyriakou 2013 ²⁴ , Greece	ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ at wk 1 → 40 mg SQ q2wks thereafter), vs ETN (50 mg SQ biw ×12 wks → 50 mg SQ qw), vs IFX (5 mg/kg IV at wks 0, 2, 8 then q8wks to wk 46)	Open-label, retrospective, N = 12	NAPSI at wks 0, 12, 24, 48	Moderate-to-severe plaque psoriasis, PASI > 10, NAPSI > 10	Mean NAPSI score at baseline vs wk 48: IFX: 80.50 ± 45.19 vs 4.58 ± 3.67, p = 0.002 , ADM: 82.64 ± 42.35 vs 9.57 ± 4.51, p = 0.001 , ETN: 82.76 ± 48.06 vs 6.61 ± 4.29, p = 0.001
Mease 2014 ²⁵ , North America, Latin America, Western Europe, Central/Eastern Europe	CZP (200 mg SQ q2wks) vs CZP (400 mg SQ q4wks) vs Pbo (0.9% saline)	Randomized, double-blind, Pbo-controlled to week 24, dose-blind to week 48, open-label to week 216, N = 409 (73.3% with nail disease at baseline)	Modified NAPSI (target fingernail) at wks 0, 24	Patients with adult-onset PsA of at least 6 months' duration, active joint disease, failed ≥ 1 DMARD, documented history of psoriasis, nail disease at baseline	Mean NAPSI score at baseline: CZP 200 mg: 3.1 ± 1.8, CZP 400 mg: 3.4 ± 2.2, Pbo: 3.4 ± 2.2; Modified NAPSI score change from baseline at wk 24: CZP 200 mg: -1.6, p = 0.003 c/w pbo , CZP 400 mg: -2.0, p < 0.001 c/w pbo , Pbo: -1.1
Ortonne 2013 ²⁶ , Austria, France, Greece, Italy	ETN (50 mg SQ biw ×12 wks → 50 mg qw ×12 wks [biw/qw]), vs ETN (50 mg SQ qw ×24 wks [qw/qw])	Randomized, open-label, N = 72	NAPSI at wks 0, 12, 24	Moderate-to-severe plaque psoriasis, previously failed 1 form of systemic therapy for nail psoriasis	Mean improvement in NAPSI score (target nail) at baseline vs wk 24: biw/qw: 6.0 vs 1.7, p < 0.0001 , qw/qw: 5.8 vs 1.4, p < 0.0001
Luger 2009 ²⁷ , Germany, UK, Belgium	ETN (25 mg SQ biw ×54 wks), vs Interrupted ETN (initial 50-mg dose SQ biw ×12 wks max or until PGA ≤ 2; if relapse (PGA ≥ 3), 25 mg ETN SQ biw until response)	Randomized, open-label, N = 771 (564 with nail psoriasis)	NAPSI at wks 0, 12, 24, 56, or at time of discontinuation	Psoriasis with BSA ≥ 10%, PGA ≥ 3, previously failed usual care	Mean NAPSI score at baseline vs wk 12 (pooled continuous and interrupted therapy): Patients with nail psoriasis: 4.64 vs 3.30, p < 0.0001
Kavanaugh 2009 ²⁸ , USA, Canada, Belgium, Poland, Spain, UK	Golimumab (GLB, 50 mg SQ q4wks ×20 wks), vs GLB (100 mg SQ q4wks ×20 wks), vs Pbo	Randomized, double-blind, Pbo-controlled phase 3, N = 405	NAPSI at wks 0, 14, 24	Same as above	Mean NAPSI score (target nail) at baseline: GLB 50 mg: 4.7 ± 2.2, GLB 100 mg: 4.6 ± 2.1, Pbo: 4.4 ± 2.2; Median % change in NAPSI: Wk 14: GLB 50 mg: 25%, GLB 100 mg: 43%, Pbo: 0%; Wk 24: GLB 50 mg: 33%, GLB 100 mg: 54%; Pbo: 0%
Kavanaugh 2012 ²⁹ , USA, Canada, Belgium, Poland, Spain, UK	GLB (50 mg SQ q4wks ×20 wks), vs GLB (100 mg SQ q4wks ×20 wks), vs Pbo	Randomized, double-blind, Pbo-controlled phase 3, N = 405	NAPSI at wk 0, 52	Patients negative for rheumatoid factor, had active PsA and plaque psoriasis despite therapy with DMARD or NSAID, no previous treatment with TNF antagonists, rituximab, natalizumab, or cytotoxic agents	Mean NAPSI score (target nail) at baseline: GLB 50 mg: 4.7 ± 2.2, GLB 100 mg: 4.6 ± 2.1, Pbo: 4.4 ± 2.2; Mean % change in NAPSI score at wk 52: GLB 50 mg: 51.6 ± 46.8, GLB 100 mg: 65.8 ± 51.9, GLB pooled: 59.2 ± 50.0, Pbo: 56.2 ± 48.1

Table 1D. Continued

Study	Therapy	Study Type and Population	Outcome Measure	Baseline	Results
Fabroni 2011 ³⁰ , Italy	IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks to wk 38)	Open-label, uncontrolled retrospective study without comparison group, N = 121 (61 with nail psoriasis)	NAPSI at wks 0, 14, 28, 38	Moderate-to-severe psoriasis (PASI ≥ 10) or PsA for ≥ 1 year with nail involvement, previously failed ≥ 2 traditional systemic therapies	Mean NAPSI score at baseline: 49.7 ± 26.0; Mean NAPSI score at wk 14: 18.6 ± 9.4, wk 22: 9.5 ± 4.7, wk 38: 7.2 ± 4.9
Torii 2011 ³¹ , Japan	IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks to wk 46)	Open label, uncontrolled, N = 64 (56 with nail psoriasis)	NAPSI in target worst nail	Patients with plaque psoriasis, PsA, pustular psoriasis (excluding localized) or psoriatic erythroderma, PASI ≥ 12, BSA ≥ 10%	Mean NAPSI score at baseline (all underlying diseases): 4.4 ± 1.9; Mean NAPSI score (all underlying diseases) at wk 10: 3.3 ± 1.7, wk 26: 1.8 ± 1.9, wk 50: 1.9 ± 2.1
Reich 2010 ³² Germany, Netherlands, Switzerland, Canada, UK	IFX (5 mg/kg IV at wks 0, 2 and 6 → 5 mg/kg IV q8wks to wk 46), vs Pbo (crossover to IFX at wks 24, 26, 30, 38, and 46)	Randomized, double-blind, pbo-controlled, phase 3, N = 373	NAPSI at wks 0, 10, 24, 38 and 50	Moderate-to-severe plaque psoriasis ≥ 6 months, PASI ≥ 12, BSA ≥ 10%	Mean % improvement in NAPSI score (among all treated with IFX) at wk 10: 28.3%, wk 24: 61.4%, wk 50: 67.8%
Torii 2010 ³³ , Japan	IFX (5 mg/kg IV at wks 0, 2, 6, 14 then q8wks to wk 62), vs Pbo [crossover at wk 16 with IFX (5 mg/kg) IV at wks 18, 22, then q8wks to wk 62]	Randomized, double-blind, pbo-controlled, phase 3, N = 54	NAPSI at wks 0, 10, 14, 26, 42, 66	Moderate-to-severe plaque psoriasis ≥ 6 months, PASI ≥ 12, BSA ≥ 10%	Mean change in NAPSI score (change from baseline) at wk 10: IFX: 1.4 ± 2.2, Pbo: -0.3 ± 1.0; wk 14: IFX: 1.6 ± 2.0, Pbo: -0.6 ± 0.8; wk 26: IFX: 2.2 ± 2.3, Pbo → IFX: 0.7 ± 1.3; wk 42: IFX: 2.1 ± 2.0, Pbo → IFX: 1.9 ± 0.6; wk 66: IFX: 2.6 ± 2.0, Pbo → IFX: 2.4 ± 1.0
Rich 2008 ³⁴ , USA; Germany; UK	IFX (5 mg/kg IV at wks 0, 2 and 6 → 5 mg/kg IV q8wks to wk 46), vs Pbo (crossover to IFX at wks 24, 26, 30, 38, and 46)	Randomized, double-blind, pbo-controlled, phase 3, N = 373 (305 with nail psoriasis)	NAPSI at wks 0, 10, 24	Psoriasis for ≥ 6 months, PASI ≥ 12, BSA ≥ 10% with nail involvement	Mean NAPSI score at baseline: IFX: 4.6 ± 2.0, Pbo: 4.3 ± 1.9; Mean % improvement in NAPSI score: wk 10: IFX: 26.8%, Pbo: -7.7%, p < 0.001 btwn groups ; wk 24: IFX: 57.2%, Pbo: -4.1%, p < 0.001 btwn groups
Rigopoulos 2008 ³⁵ , Greece	IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks)	Nonrandomized, open-label, N = 18	NAPSI at wks 0, 14, 22, 30, and 38	Psoriasis patients with nail involvement scheduled to start IFX treatment	Mean NAPSI score at baseline vs wk 38: 55.78 ± 18.57 vs 3.28 ± 4.84, p < 0.01
Patsatsi 2013 ³⁶ , Greece	UST (45 mg at wks 0, 4 and then q12 weeks thereafter; 90 mg in patients with body weight > 100 kg)	Nonrandomized, open-label, uncontrolled, N = 27	NAPSI at wks 0, 16, 28, 40	Moderate-to-severe psoriasis (PASI ≥ 10) with nail involvement	% change in NAPSI from wk 0–wk 16: 45.3%, wk 0–wk 28: 87.6%, wk 0–wk 40: 98.0%; Friedman's ANOVA, p < 0.0001 ; Mean NAPSI score at wk 0: 76.7, wk 16: 42.6, p < 0.001 c/w bl , wk 28: 10.3, p < 0.001 c/w bl , wk 40: 2.3, p < 0.001 c/w bl
Rich 2014 ³⁷ , USA, Canada, Netherlands, Belgium	UST (45 mg SQ at wks 0, 4, 16, 28), vs UST (90 mg SQ at wks 0, 4, 16, 28), vs Pbo (crossover to UST 45 mg or 90 mg at wks 12, 16, 28). At wk 40, those with PASI75 re-randomized to continue maintenance dosing or receive Pbo	Randomized, double-blinded, Pbo-controlled, phase 3, N = 766 (545 with nail psoriasis)	NAPSI at wks 0, 12, 24	Moderate-to-severe psoriasis	Mean % improvement in NAPSI score at wk 12: UST 45 mg: 26.7%, p < 0.001 c/w pbo , UST 90 mg: 24.9%, p = 0.001 c/w pbo ; wk 24: UST 45 mg: 46.5%; UST 90 mg: 48.7%

Table 1D. Continued

Study	Therapy	Study Type and Population	Outcome Measure	Baseline	Results
Vitiello 2013 ³⁸ , USA	UST (45 mg at wks 0, 4 and then q12 weeks thereafter; 90 mg used in 5 patients with body weight > 100 kg)	Case series, N = 13	NAPSI at wks 0, 4, 12	PsA for an average 16 years, failed ≥ 4 biologics	Mean NAPSI score at wk 0: 22.3, wk 4: 19.5, wk 12: 14.8; Mean percentage reduction in NAPSI from baseline to wk 14: 31.8%
Igarashi 2012 ³⁹ , Japan	UST (45 mg SQ at wks 0, 4, then q12wks to wk 52), vs UST (90 mg SQ at wks 0, 4, then q12wks to wk 52), vs Pbo (crossover at wk 12 to either UST 45 mg or 90 mg SQ, wks 16, 28, 40, 52)	Randomized, double-blind, Pbo-controlled, phase 2/3, N = 158	NAPSI at wks 0, 12, 64	Moderate-to-severe plaque psoriasis ≥ 6 months, PASI ≥ 12, BSA ≥ 10%	Mean NAPSI score at baseline (if nail psoriasis present): UST 45 mg: 3.7 ± 1.8, UST 90 mg: 4.1 ± 2.0, Pbo: 4.6 ± 2.5; Mean % improvement in NAPSI score at wk 64: UST 45 mg: 56.6 ± 43.2%, UST 90 mg: 67.8 ± 37.5%
Rigopoulos 2011 ⁴⁰ , Greece	UST (45 mg SQ if < 100 kg or 90 mg SQ if > 100 kg at wks 0, 4, 16 and 28)	Open-label, N = 27	NAPSI at wks 0, 4, 16, 28, 40	Plaque psoriasis with fingernail involvement, failed a systemic treatment	Mean NAPSI score at wk 0: 19.59 ± 7.92 (p value c/w bl), wk 4: 16.96 ± 6.99, p < 0.001 , wk 16: 9.70 ± 4.47, p < 0.001 , wk 28: 3.85 ± 3.03, p < 0.001 , wk 40: 2.00 ± 2.34, p < 0.001
Leonardi 2012 ⁴¹ , USA, Denmark	IXE SQ (10 mg) vs IXE (25 mg) vs IXE (75 mg) vs IXE (150 mg) vs Pbo, all at wks 0, 2, 4, 8, 12, 16	Randomized, double-blind, pbo-controlled, phase 2, N = 142	NAPSI at wks 0, 1, 2, 4, 6, 8, 12	Chronic moderate-to-severe plaque psoriasis for ≥ 6 months, PASI ≥ 12, PGA ≥ 3, BSA ≥ 10%	Mean NAPSI score at baseline: IXE 10 mg: 41.9 ± 44.8, IXE 25 mg: 34.9 ± 37.7, IXE 75 mg: 45.0 ± 46.9, IXE 150 mg: 46.5 ± 51.7, Pbo: 35.0 ± 28.1; Mean % change in NAPSI score at wk 12: IXE 10 mg: 14.3 ± 97.8, NS c/w Pbo , IXE 25 mg: -24.0 ± 32.8, NS c/w Pbo , IXE 75 mg: -57.1 ± 36.7, p < 0.01 c/w Pbo , IXE 150 mg: -49.3 ± 35.9, p < 0.05 c/w Pbo , Pbo: 6.8 ± 41.1

Data in bold face are p values. btwn: between; PO: orally; qd: every day; qw: every week; SQ: subcutaneous; c/w: compared with; adalimumab (ADM); NAPSI: Nail Psoriasis Area Severity Index; narrow-band UVB (NB-UVB); MTX: methotrexate; Pbo: placebo; IFX: infliximab; ETN: etanercept; DMARD: disease modifying antirheumatic drugs; CZP: certolizumab pegol; PGA: physician global assessment; PASI: Psoriasis Area and Severity Index; BSA: body surface area; IXE: ixekizumab; UST: ustekinumab; eow: every other week; biw: biweekly; TNF: tumor necrosis factor; NR: not reported; bl: baseline.

show that IL-17 blockade with ixekizumab (> 75 mg subcutaneously) also appears to be effective⁴¹.

Combination Therapies^{11,42} (Table IE)

Literature on combination therapies for nail psoriasis is limited. In 1 single-blind, within-patient trial of PDL (595 nm, 1.5 ms pulse duration) plus topical 0.1% tazarotene cream compared to topical tazarotene alone, a significantly greater mean decrease in nail matrix modified NAPSI score was observed with PDL-tazarotene compared to tazarotene alone⁴².

In a nonrandomized, unblinded study of ADM plus cyclosporine (CSA) compared to ADM monotherapy and CSA monotherapy, 100% of patients receiving combination

therapy reported > 50% improvement in mean NAPSI score at week 12 compared to patients receiving either CSA (44%) or ADM (56%) alone¹¹.

In conclusion, nail psoriasis results in significant morbidity and warrants adequate treatment. Topical therapies may be an initial option, but their efficacy is modest. Procedural therapies require more investigation to determine their efficacy. Traditional oral therapies, e.g., MTX or CSA, may be helpful at high doses. The most rigorously studied therapies are biologic agents, with evidence suggesting that TNF- α inhibitors and IL-12/23 inhibitors are highly efficacious in treating nail psoriasis.

Table 1E. Combination therapies for nail psoriasis.

Study	Therapy	Study Type and Population	Outcome Measure	Baseline	Results
Karanikolas 2011 ¹¹ , Greece	CsA (2.5–3.75 mg/kg PO qd × 12 mo) vs adalimumab (ADM) (40 mg SQ eow × 12 mo) vs CsA + ADM (same doses as above)	Non-randomized, unblinded, N = 170	Improvement of > 50% in NAPSI score at 12 mo	PsA patients who failed MTX treatment	Improvement > 50% in NAPSI score: CsA: 44%; ADM: 56%; CsA + ADM: 100%
Huang 2013 ⁴² , Taiwan	PDL (595 nm, 1.5 ms pulse duration, 7 mm spot size, 9 j/cm ² , with 30 ms cryogen delay, qw × 6 mo) + topical 0.1% tazarotene cream (6 mo) vs topical 0.1% tazarotene cream (6 mo)	Single-blinded, inpatient, left-right, N = 25	Modified NAPSI score at mo 0, 3, 6	Psoriatic nails refractory to prior treatment (unspecified)	Mean difference of nail matrix modified NAPSI score from baseline to 6 mo: PDL + tazarotene: 2.2 ± 2.6; tazarotene: -0.1 ± 1.6, p < 0.05 btwn groups ; mean difference of nail bed modified NAPSI score from baseline to 6 mo: PDL + tazarotene: -0.6 ± 2.7; tazarotene: -0.7 ± 2.0, NS btwn groups

Data in bold face are p values. btwn: between; PO: orally; qd: every day; eow: every other week; qw: every week; SQ: subcutaneous; CsA: cyclosporine; ADM: adalimumab; MTX: methotrexate; NAPSI: Nail Psoriasis Area Severity Index; PDL: pulsed dye laser.

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