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

April W. Armstrong, William Tuong, Thorvardur J. Love, Sueli Carneiro, Rachel Grynszpan, Steve S. Lee, and Arthur Kavanaugh

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 in 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.

Topical Therapies1,2,3,4,5 (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 µg/g), alone or in combination with betamethasone dipropionate. Limited evidence supports modest efficacy in psoriasis limited to < 2 nails when used for > 12 weeks1,2,3. 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 nails1,5.

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 Therapies1,2,6,7 (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 efficacy6,7. 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 pain6,7.

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.,...
severity and type of psoriatic disease. 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 months.

**Traditional Oral Systemic Therapies** (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. 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. 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. 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 weeks.

**Biologic Therapies** (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), certolizumab pegol, etanercept, golimumab, and infliximab were superior to MTX in 1 study. 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. 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 weeks.

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**Table 1A. Topical therapies for nail psoriasis.**

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

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.**

<table>
<thead>
<tr>
<th>Study</th>
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<th>Study Type and Population</th>
<th>Outcome Measure</th>
<th>Baseline</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldust 2013, Iran</td>
<td>Pulsed dye laser (595 nm, 7-mm spot size, 0.45 ms pulse duration, 6 j/cm², 20 ms cryogen spray with 10 ms delay, qm x 6 mo) vs same, except 6 ms pulse duration, 9 j/cm²</td>
<td>Randomized, double-blinded, intrapatient, left-to-right; N = 40</td>
<td>NAPSI at mo 0, 1, 2, 3, 4, 5, 6</td>
<td>Mild-to-moderate plaque psoriasis and refractory nail involvement, ≤ 30% BSA of plaque psoriasis, no active PsA or pustular psoriasis of nail</td>
<td>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</td>
</tr>
<tr>
<td>Treewittayapoom 2012, Thailand</td>
<td>Pulsed dye laser (595 nm, 6 ms pulse duration, 7-mm spot size, 9 j/cm², with 10 ms cryogen delay, qm x 6 mo) vs same, except 0.45 ms pulse duration, 6 j/cm²</td>
<td>Randomized, double-blinded, intrapatient, left-to-right; N = 20</td>
<td>NAPSI at mo 0, 1, 2, 3, 4, 5, 6</td>
<td>Recalcitrant, bilateral fingernail psoriasis, ≤ 30% BSA of chronic plaque psoriasis</td>
<td>Significant decrease in mean NAPSI at 6 mo c/w baseline in both groups; specific values NR. NS btwn groups</td>
</tr>
</tbody>
</table>

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.
mab1,9,14,22,23,30,31,32,33,34,35 were highly efficacious in treating psoriatic nail disease. Larger studies are necessary to determine comparative effectiveness of these agents9,14,22,23,24. Ustekinumab, an anti-IL-12/23 monoclonal antibody, was highly effective in treating nail psoriasis, when weight-based dosing was used9,14,23,24. Larger studies are necessary to determine comparative effectiveness of these agents9,14,22,23,24.

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Therapy</th>
<th>Study Type and Population</th>
<th>Outcome Measure</th>
<th>Baseline Results</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gumusel 2011&lt;sup&gt;8&lt;/sup&gt;, Turkey</td>
<td>CsA (initial 5-mg/kg dose PO qd x12 wks → 2.5–3.5 mg/kg PO qd x12 wks vs MTX (initial 15-mg dose SQ qw x12 wks → 10 mg SQ qw x12 wks)</td>
<td>Randomized, single-blinded, comparator, N = 37</td>
<td>NAPSI at wks 0, 4, 8, 12, 16, 20, and 24</td>
<td>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</td>
<td>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</td>
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<tr>
<td>Sanchez-Regana 2011&lt;sup&gt;9&lt;/sup&gt;, Spain</td>
<td>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)</td>
<td>Retrospective review, N = 84</td>
<td>NAPSI at weeks 12, 24, and 48</td>
<td>Moderate-to-severe psoriasis (PASI ≥ 3), PsA, and presence of psoriasis of the nails</td>
<td>Mean percent change in NAPSI score: wk 48: Classical: CsA: 89.1% (p value vs CsA), Acitretin: 51.7%, p &lt; 0.001, MTX: 34.9%, p &lt; 0.001, PUVA: 69.1%, p = 0.023, NB-UVB: 5.0%, p = 0.190, Re-PUVA: 64.3%, p = 0.003, Biological: IFX: 91.3% (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 &lt; 0.001 btwn groups</td>
</tr>
<tr>
<td>Syuto 2007&lt;sup&gt;10&lt;/sup&gt;, Japan</td>
<td>CsA (initial 3-mg/kg dose PO bid → 1.5 mg/kg PO qd if improvement)</td>
<td>Open-label, uncontrolled, N = 16</td>
<td>Improvement</td>
<td>Duration of psoriatic nails ranged from 1–27 years. 13/16 patients were unresponsive to prior treatments</td>
<td>No evidence of a treatment effect (specific results NR)</td>
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<tr>
<td>Kingsley 2012&lt;sup&gt;12&lt;/sup&gt;, UK</td>
<td>MTX (initial 7.5-mg dose PO qw x4 wks → 10 mg PO qw x4 wks → 15 mg PO qw x16 wks) vs Placebo</td>
<td>Randomized, double-blind, placebo-controlled, N = 221</td>
<td>Nail disease score at months 0, 3, 6</td>
<td>Active psoriasis and arthritis, and presence of nail changes</td>
<td>No evidence of a treatment effect (specific results NR)</td>
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<tr>
<td>Reich 2011&lt;sup&gt;13&lt;/sup&gt;, Germany, Canada, France</td>
<td>MTX (5–25 mg PO qw x25 wks) vs Briakinumab (initial 200-mg dose SQ at wks 0 and 4 → 100 mg SQ q 4 wks, wks 8–48)</td>
<td>Randomized, double-blind, comparator, N = 317</td>
<td>NAPSI (target fingernail) at wks 0, 24, 52</td>
<td>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</td>
<td>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 &lt; 0.001 btwn groups</td>
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<tr>
<td>Tosti 2009&lt;sup&gt;15&lt;/sup&gt;, Italy</td>
<td>Acitretin (0.2–0.3 mg/kg PO qd x6 months)</td>
<td>Open-label, uncontrolled, N = 36</td>
<td>NAPSI at months 0, 2, 4, 6</td>
<td>Active psoriatic disease; no previous leflunomide treatment</td>
<td>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%</td>
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<td>Behrens 2013&lt;sup&gt;16&lt;/sup&gt;, Germany, Czech Republic, Slovenia</td>
<td>Leflunomide (initial 100-mg dose PO qw x3 days → 20 mg PO qw x4 wks)</td>
<td>Observational, N = 514</td>
<td>Clinical severity (5-pt scale)</td>
<td>Active psoriatic disease; no previous leflunomide treatment</td>
<td>Proportion of patients experiencing improvement of ≥ 1 point from baseline to final visit: 32%</td>
</tr>
</tbody>
</table>

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; Ac: cyclosporin A; MTX: methotrexate; ADM: adalimumab; IFX: infliximab; NB-UVB: narrow band ultraviolet B; PASI: Psoriasis Area and Severity Index; PGA: physician global assessment.
### Table 1D. Biologic therapies for nail psoriasis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Therapy</th>
<th>Study Type and Population</th>
<th>Outcome Measure</th>
<th>Baseline Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demirsoy 2013[^14^] Turkey</td>
<td>IFX, ADM, or ETN vs MTX, vs narrow-band UVB (NB-UVB), vs acitretin, vs no treatment</td>
<td>Comparative, N = 87</td>
<td>NAPSI at wks 0, 16</td>
<td>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</td>
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<tr>
<td>Sola-Ortigosa 2012[^17^], Spain</td>
<td>ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ at wk 1, then cow)</td>
<td>Retrospective, N = 15</td>
<td>NAPSI at wks 0, 24</td>
<td>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</td>
</tr>
<tr>
<td>Leonardi 2011[^18^], USA, Canada</td>
<td>ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ cow wks 1–15; → Pbo at wk 16 → 40 mg SQ cow wks 17–27), vs Pbo (crossover to ADM 80 mg SQ at wk 16 → 40 mg SQ cow, wks 17–27)</td>
<td>Randomized, Pbo-controlled, double-blind (16 wks); open-label 12-wk extension, N = 72</td>
<td>NAPSI at wks 0, 8, 16, 28</td>
<td>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: 5%, p = 0.02 btwn groups; Wk 28: ADM: 54%, Pbo (switched to ADM at wk 16): 38%</td>
</tr>
<tr>
<td>Rigopoulos 2010[^19^], Greece</td>
<td>ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ at wk 1 → 40 mg SQ q2wks)</td>
<td>Open-label, N = 21</td>
<td>Mean NAPSI at wks 0, 12, and 24</td>
<td>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: 23.36 ± 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</td>
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<td>Van den Bosch 2010[^20^], Belgium, Germany, France, UK, Norway, Denmark, Sweden, Finland, Ireland</td>
<td>ADM (40 mg SQ cow ×12 wks)</td>
<td>Open-label, N = 442</td>
<td>NAPSI at wks 0, 12, 20</td>
<td>Diagnosis of PsA, previous treatment with &gt; 1 DMARD Improvement &gt; 50% in NAPSI score at wk 12 (in patients with baseline NAPSI &gt; 10): 54.2%; Median NAPSI: Wk 12: 5, Wk 20: 1</td>
</tr>
<tr>
<td>Rudwaleit 2010[^21^], Germany</td>
<td>ADM (40 mg SQ cow ×12 wks)</td>
<td>Open-label, N = 442</td>
<td>NAPSI at wks 0, 12</td>
<td>History of anti-TNF treatment [IFX, ETN, or both] and failure of 1 or more DMARD for PsA Moderate-to-severe nail psoriasis, failed other systemic therapies 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 Mean improvement in NAPSI score at week 48: ADM: 53.8%, ETN: 57.3%, IFX: 40.4%, CI not reported; authors report difference NS</td>
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<tr>
<td>Ozmen 2013[^22^], Turkey</td>
<td>ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ cow 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)</td>
<td>Randomized, open-label, N = 28</td>
<td>NAPSI at wks 0, 12, 24, 36, 48</td>
<td>Moderate-to-severe nail psoriasis, failed other systemic therapies Mean NAPSI score at baseline vs wk 46: 23.8 ± 12.2 vs 8.2 ± 4.7, p = 0.001</td>
</tr>
<tr>
<td>Study</td>
<td>Therapy</td>
<td>Study Type and Population</td>
<td>Outcome Measure</td>
<td>Baseline</td>
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<tr>
<td>Saraceno 2013</td>
<td>ADM (initial 80-mg dose SQ at wk 0 → 40 mg SQ at wk 1–24), vs ETN (50 mg SQ biw x12 wks → 25 mg SQ biw x12 wks), vs IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks to wk 24)</td>
<td>Open-label, N = 60</td>
<td>NAPSI at wks 0, 14, 24</td>
<td>Moderate-to-severe plaque psoriasis or PsA, failed ≥ 2 systemic conventional treatments, NAPSI score &gt; 15</td>
</tr>
<tr>
<td>Kyriakou 2013</td>
<td>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 x12 wks → 50 mg SQ qw), vs IFX (5 mg/kg IV at wks 0, 2, 8 then q8wks to wk 46)</td>
<td>Open-label, retrospective, N = 12</td>
<td>NAPSI at wks 0, 12, 24, 48</td>
<td>Moderate-to-severe plaque psoriasis, PASI &gt; 10, NAPSI &gt; 10</td>
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<td>Mease 2014</td>
<td>CZP (200 mg SQ q2wks), vs CZP (400 mg SQ q4wks) vs Pbo (0.9% saline)</td>
<td>Randomized, double-blind, Pbo-controlled (target fingernail of psoriasis, nail c/w pbo), to week 24</td>
<td>Modified NAPSI (target nail) at wks 0, 24</td>
<td>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</td>
</tr>
<tr>
<td>Luger 2009</td>
<td>ETN (50 mg SQ biw x12 wks → 50 mg qw x24 wks)</td>
<td>Randomized, open-label, N = 72</td>
<td>NAPSI at wks 0, 12, 24</td>
<td>Moderate-to-severe plaque psoriasis, previously failed 1 form of systemic therapy for nail psoriasis</td>
</tr>
<tr>
<td>Kavanaugh 2009</td>
<td>Golimumab (GLB, 50 mg SQ q4wks x20 wks), vs GLB (100 mg SQ q4wks x20 wks), vs Pbo</td>
<td>Randomized, double-blind, Pbo-controlled phase 3, N = 405</td>
<td>NAPSI at wks 0, 14, 24</td>
<td>Same as above</td>
</tr>
<tr>
<td>Kavanaugh 2012</td>
<td>GLB (50 mg SQ q4wks x20 wks), vs GLB (100 mg SQ q4wks x20 wks), vs Pbo</td>
<td>Randomized, double-blind, Pbo-controlled phase 3, N = 405</td>
<td>NAPSI at wk 0, 52</td>
<td>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</td>
</tr>
<tr>
<td>Study</td>
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<tr>
<td>Fabroni 2011[30], Italy</td>
<td>IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks to wk 38)</td>
<td>Open-label, uncontrolled retrospective study without comparison group, N = 121 (61 with nail psoriasis)</td>
<td>NAPSI at wks 14, 28, 38</td>
<td>Moderate-to-severe psoriasis (PASI ≥ 10) or PsA for ≥ 1 year with nail involvement, previously failed ≥ 2 traditional systemic therapies</td>
</tr>
<tr>
<td>Torii 2011[31], Japan</td>
<td>IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks to wk 46)</td>
<td>Open-label, uncontrolled, N = 64 (56 with nail psoriasis)</td>
<td>NAPSI in target worst nail</td>
<td>Patients with plaque psoriasis, PsA, pustular psoriasis (excluding localized or psoriatic erythroderma, PASI ≥ 12, BSA ≥ 10%)</td>
</tr>
<tr>
<td>Reich 2010[32], Germany, Netherlands, and 6 → 5 mg/kg IV q8wks to wk 46</td>
<td>IFX (5 mg/kg IV at wks 0, 2, 6, 14 then q8wks to wk 62), vs Pbo (crossover to IFX at wks 24, 26, 30, 38, and 46)</td>
<td>Randomized, double-blind, pbo-controlled, phase 3, N = 373</td>
<td>NAPSI at wks 0, 10, 24, 38 and 50</td>
<td>Moderate-to-severe plaque psoriasis ≥ 6 months, PASI ≥ 12, BSA ≥ 10%</td>
</tr>
<tr>
<td>Torii 2010[33], Japan</td>
<td>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)</td>
<td>Randomized, double-blind, pbo-controlled, phase 3, N = 54</td>
<td>NAPSI at wks 0, 10, 14, 26, 42, 66</td>
<td>Moderate-to-severe plaque psoriasis ≥ 6 months, PASI ≥ 12, BSA ≥ 10%</td>
</tr>
<tr>
<td>Rich 2008[34], USA; Germany; UK</td>
<td>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)</td>
<td>Randomized, double-blind, pbo-controlled, phase 3, N = 373 (305 with nail psoriasis)</td>
<td>NAPSI at wks 0, 10, 24</td>
<td>Psoriasis for ≥ 6 months, PASI ≥ 12, BSA ≥ 10% with nail involvement</td>
</tr>
<tr>
<td>Rigopoulos 2008[35], Greece</td>
<td>IFX (5 mg/kg IV at wks 0, 2, 6, then q8wks)</td>
<td>Nonrandomized, open-label, N = 18</td>
<td>NAPSI at wks 0, 14, 22, 30, and 38</td>
<td>Psoriasis patients with nail involvement scheduled to start IFX treatment Moderate-to-severe plaque psoriasis (PASI ≥ 10) with nail involvement</td>
</tr>
<tr>
<td>Patsatsi 2013[36], Greece</td>
<td>UST (45 mg at wks 0, 4 and then q12 weeks thereafter; 90 mg in patients with body weight &gt; 100 kg)</td>
<td>Nonrandomized, open-label, uncontrolled, N = 27</td>
<td>NAPSI at wks 0, 16, 28, 40</td>
<td>Moderate-to-severe plaque psoriasis</td>
</tr>
<tr>
<td>Rich 2014[37], USA, Canada, Netherlands, Belgium</td>
<td>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</td>
<td>Randomized, double-blind, pbo-controlled, phase 3, N = 766 (545 with nail psoriasis)</td>
<td>NAPSI at wks 0, 12, 24</td>
<td>Moderate-to-severe psoriasis</td>
</tr>
</tbody>
</table>
show that IL-17 blockade with ixekinumab (> 75 mg subcutaneously) also appears to be effective41.

Combination Therapies41,42 (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 IE. Combination therapies for nail psoriasis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Therapy</th>
<th>Study Type and Population</th>
<th>Outcome Measure</th>
<th>Baseline</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karamikolas 201111, Greece</td>
<td>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)</td>
<td>Non-randomized, unblinded, N = 170</td>
<td>Improvement of &gt; 50% in NAPSI score at 12 mo</td>
<td>PsA patients who failed MTX treatment</td>
<td>Improvement &gt; 50% in NAPSI score: CsA: 44%; ADM: 56%; CsA + ADM: 100%</td>
</tr>
<tr>
<td>Huang 201325, Taiwan</td>
<td>PDL (595 nm, 1.5 ms pulse duration, 7 mm spot size, 9 j/cm², with 30 ms cryogen delay, qw × 6 mo) + topical 0.1% tazarotene cream (6 mo) vs topical 0.1% tazarotene cream (6 mo)</td>
<td>Single-blinded, intrapatient, left-right, N = 25</td>
<td>Modified NAPSI score at mo 0, 3, 6</td>
<td>Psoriatic nails refractory to prior treatment (unspecified)</td>
<td>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 &lt; 0.05 betwn 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 betwn groups</td>
</tr>
</tbody>
</table>

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.

## REFERENCES


