Gaps in the Treatment of Psoriasis and PsA for Systemic Therapy

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Icahn School of Medicine at Mount Sinai
Mount Sinai gets dollars from:

- Abbvie
- Amgen
- Boehringer Ingelheim
- Celgene
- Eli Lilly
- Janssen / Johnson & Johnson
- Kadmon
- Medimmune/Astra Zeneca
- Novartis
- Pfizer
- ViDac.
Research gaps in psoriasis: opportunities for future studies


Psoriasis outcome measures: a report from the GRAPPA 2012 annual meeting

Gottlieb AB, Armstrong AW.

J Rheumatol. 2013;40:1428-33
Research Gaps

• Can we predict who’ll develop PsA and can we prevent it?
• Can we predict who’ll develop other comorbidities (cardiac, renal, etc) and can we prevent them?
• Can we predict who’ll respond to which therapy?
Can we predict who’ll develop PsA?

*(Can we treat to prevent joint disease?)*
Patient perspectives in the management of psoriasis: Results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey.

• 139,948 households were screened and 3426 patients
• prevalence of psoriasis/PsA ranged from 1.4% to 3.3%
• 79% had psoriasis alone and 21% had PsA
• 27% (psoriasis) and 53% (PsA ± psoriasis) of patients rated it as severe
• 45% had not seen a physician in a year;
Psoriasis and Psoriatic Arthritis: Timing of Onset

72% Psoriasis 1st
21% Arthritis 1st
7% concurrent
Subclinical Joint Involvement in Patients With Psoriasis

- Joint structural damage can occur before the appearance of clinical symptoms of PsA.
- In a study by Offidani and colleagues, which used MRI rather than conventional radiography to assess joint involvement, 68% of patients with psoriasis were found to have 1 or more arthritic signs, which appeared before patients experienced clinically evident joint symptoms.
  - Joint damage was only detected by X-ray imaging in 32% of these patients.

Treatment of psoriatic arthritis with tumor necrosis factor inhibitors: longer-term outcomes including enthesitis and dactylitis with golimumab treatment in the Long term Extension of a Randomized, Placebo-controlled Study (GO-REVEAL).

Kavanaugh A, Mease P.

Effect of certolizumab pegol on signs and symptoms in patients with psoriatic arthritis: 24-week results of a Phase 3 double-blind randomised placebo-controlled study (RAPID-PsA)


Change From Baseline in Modified Total vdhS Score Over Time (ITT)

- Placebo (n=310)
- Placebo→45 mg at Wk 24 (n=269)*
- UST 45 mg (n=308)
- UST 90 mg (n=309)

*Patients who did not receive UST are excluded
FUTURE 1: Radiographic progression in PsA patients stratified by MTX use

Baseline to Week 24 (full analysis set)
- Pooled SKB doses
- PBO

Mean change in vdH-mTSS
- Overall population:
  - MTX: Yes
  - MTX: No

*P<0.05 vs PBO
Change in mTSS >0.5 considered progression of radiographic disease

Gottlieb AB, et al. EADV 2015, P0348 Sponsored by Novartis Pharma AG

**Effect on structural disease progression**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>IXEQ4W</th>
<th>IXEQ2W</th>
<th>Adalimumab 40 mg Q2W*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LS mean change from baseline mTSS (SE)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 16</td>
<td>0.38 (0.07)</td>
<td>0.13 (0.07)†</td>
<td>0.08 (0.07)§</td>
<td>0.12 (0.08)†</td>
</tr>
<tr>
<td>Week 24</td>
<td>0.49 (0.09)</td>
<td>0.17 (0.08)§</td>
<td>0.08 (0.08)‖</td>
<td>0.10 (0.09)‖</td>
</tr>
<tr>
<td>Percentage of patients with change in mTSS at week 24</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤0</td>
<td>72.0</td>
<td>83.0</td>
<td>83.5</td>
<td>91.6‖</td>
</tr>
<tr>
<td>≤0.5</td>
<td>77.4</td>
<td>89.0**</td>
<td>94.8‖</td>
<td>95.8‖</td>
</tr>
<tr>
<td>≤0.95</td>
<td>83.9</td>
<td>94.0†</td>
<td>96.9§</td>
<td>95.8§</td>
</tr>
</tbody>
</table>
Brodalumab Phase 2 PsA study: Clinical response and improvement in psoriasis in subjects with PsA

Mease P, et al. AAD 2014, P7605
We don’t have a serologic marker that predicts psoriatic arthritis or its severity
Research Gaps

• Can we predict who’ll develop PsA and can we prevent it?

• Can we predict who’ll develop other comorbidities (cardiac, renal, etc) and can we prevent them?

• Can we predict who’ll respond to which therapy?
Risk of myocardial infarction in patients with psoriasis.

Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB.

JAMA 2006;296:1735-41
Does treatment of psoriasis reduce the risk of cardiovascular disease?
Reduction in the incidence of myocardial infarction in patients with rheumatoid arthritis who respond to anti-tumor necrosis factor alpha therapy: results from the British Society for Rheumatology Biologics Register.

Association between tumor necrosis factor inhibitor therapy and myocardial infarction risk in patients with psoriasis.

Wu JJ, Poon KY, Channual JC, Shen AY

Research Gaps

• Can we predict who’ll develop PsA and can we prevent it?
• Can we predict who’ll develop other comorbidities (cardiac, renal, etc) and can we prevent them?
• Can we predict who’ll respond to which therapy?
Cost of Biologics: Year 1

- Etanercept: ~$72,848
- Adalimumab: ~ $63,728
- Ustekinumab: ~$45,195-90,280
- Infliximab: ~$20,462-81,848 (60-120 Kg q4-8w. at 5mg/kg)
- Secukinumab: ~$133020 (300 mg)
- Ixekizumab: ~$77,860
Week 16 Partial Responders (50 ≤ PASI < 75) and Nonresponders (25 ≤ PASI < 50) That Achieved PASI 50, 75, or 90 at Week 28

<table>
<thead>
<tr>
<th>UST Combined*</th>
<th>50 ≤ PASI &lt; 75 at Week 16</th>
<th>25 ≤ PASI &lt; 50 at Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients at Week 16, n</td>
<td>98</td>
<td>48</td>
</tr>
<tr>
<td>Achieve PASI 50 at Week 28</td>
<td>98%</td>
<td>71%</td>
</tr>
<tr>
<td>Achieve PASI 75 at Week 28</td>
<td>52%</td>
<td>13%</td>
</tr>
<tr>
<td>Achieve PASI 90 at Week 28</td>
<td>13%</td>
<td>2%</td>
</tr>
</tbody>
</table>

*Combined data for PHOENIX 1 and 2 patients ≤100kg receiving 45 mg UST and >100kg receiving 90 mg UST.

Successful treatment of hand and foot psoriasis with infliximab.

Severe psoriasis pustulosa palmaris et plantaris (Barber-Königsbeck) treated successfully with soluble tumour necrosis factor receptor fusion protein (etanercept).
Safety and efficacy of Adalimumab in the treatment of moderate to severe palmo-plantar psoriasis: an open label study.

Richetta AG, et al

4/11→clear
5/11→50% improvement
Increased expression of IL-17A and limited involvement of IL-23 in patients with palmo-plantar (PP) pustular psoriasis of PP pustulosis; results from a randomized controlled trial. Bissonnette R et al. JEAADV 2013 DOI: 10.1111/jdv.12272.

• UST 45mg doesn’t work
Investigator-initiated, open-label trial of ustekinumab for the treatment of moderate-to-severe palmoplantar psoriasis.

J Dermatolog Treat. 2012 May 8. [Epub ahead of print]

7/20 → clear (90 mg:6/9; 45mg:1/11)
12/20 → ≥2point PGA approval
Apremilast, an oral phosphodiesterase-4 inhibitor, in the treatment of palmoplantar psoriasis: Results of a pooled analysis from phase II PSOR-005 and phase III Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis (ESTEEM) clinical trials in patients with moderate to severe psoriasis.

Bissonnette R, et al.