Evaluating Psoriasis: Patient Reported Outcomes and Impact of Disease

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DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY

Evaluating Psoriasis: Patient Reported Outcomes and Impact of Disease F029
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Consultant and Advisory Boards – AbbVie, Amgen, Astra Zeneca, Celgene, Dermira, Janssen, Leo, Eli Lilly, Cutanea-Maruho, Medac, Novartis, Pfizer, Sun Pharma, Boehringer Ingelheim, UCB

Investigator – AbbVie, Amgen, Boehringer Ingelheim, Galderma, GlaxoSmithKline, Novartis, Eli Lilly, Janssen, Merck, Sun Pharma, Celgene

Scientific Director – CORRONA Psoriasis Registry

Grant Support to the University of Connecticut for Fellowship Program – AbbVie, Janssen
Advances in Research have Resulted in a Decade of Rising Expectations

Response goal

<table>
<thead>
<tr>
<th>Year</th>
<th>PASI ≤50</th>
<th>PASI 75</th>
<th>PASI 90</th>
<th>PASI 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 2004</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2004</td>
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Is going from *almost clear* to *clear* MEANINGFUL?

Do you believe that patients consider higher levels of clearance in psoriasis clinically meaningful?

1. **Yes**; the efficacy of drugs does play the predominant role for patients. Higher levels of clearance are very important.

2. **No**; patients worry most about side effects related to drugs. Robust efficacy is a secondary concern.
### Dermatologists and Patients View Psoriasis Differently

<table>
<thead>
<tr>
<th>Importance rank for dermatologists (%)</th>
<th>Importance rank for patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Side effects (87%)</td>
<td>1. Efficacy (78%)</td>
</tr>
<tr>
<td>2. Cost (80%)</td>
<td>2. Availability (55%)</td>
</tr>
<tr>
<td>3. Route of administration (68%)</td>
<td>3. Convenience (52%)</td>
</tr>
<tr>
<td>4. Availability (52%)</td>
<td>4. Side effects (52%)</td>
</tr>
<tr>
<td>5. Duration of response (38%)</td>
<td>5. Duration of response (50%)</td>
</tr>
<tr>
<td>6. Time required for treatment (35%)</td>
<td>6. How fast treatment works (46%)</td>
</tr>
</tbody>
</table>

- Patient preferences are often elicited but not subsequently used in decision-making\(^2\)
- A well-informed; shared decision-making process is important for effective disease management\(^1,2\)

Psoriasis Patient Expectations

- Clearance of psoriasis: the more the better
- After a patient is cleared; the standards change
  - Worsening disease after initial response is an extremely negative event
- Patient-reported outcomes (PROs) complement and qualify objective (“observer only”) tools
  - Not all PROs are equal
  - Certain symptoms of psoriasis are universal
- Not all body areas are equal
- Gender and age biases are strong
How do we Assess Patients with Psoriasis?

**Clinical Assessments**

- Psoriasis Area and Severity Index (PASI)
- Physician’s or Investigator’s Global Assessment (PGA or IGA)
- Body surface area (BSA)

**Patient-reported Outcomes**

- Dermatology Life Quality Index (DLQI)
- Psoriasis-specific PROs
  - Psoriasis Symptom Assessment (PSA) Scale
  - Psoriasis Symptom Diary (PSD)
  - Psoriasis Symptom Inventory (PSI)

References:
1. Fredricksson T; et al. Dermatologica. 1978;157:238-244.
Clinical Assessments Provide Information on the Extent and Severity of Psoriasis Lesions

<table>
<thead>
<tr>
<th>Features Assessed/Measured</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PASI</strong>¹</td>
<td>Presence and severity of redness; thickness; and scaling; weighted by involvement of specific body areas</td>
</tr>
<tr>
<td><strong>PGA</strong>¹</td>
<td>Overall disease severity</td>
</tr>
<tr>
<td><strong>IGA</strong>²</td>
<td>Overall disease severity</td>
</tr>
<tr>
<td><strong>BSA</strong>³</td>
<td>Percentage of body surface covered with psoriasis lesions</td>
</tr>
</tbody>
</table>

Clinical improvements in these measures do not necessarily translate into patient-perceived benefit

### DLQI: Widely Used in Clinical Trials

<table>
<thead>
<tr>
<th>Item*</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Symptoms: itchy; sore; painful; or stinging</td>
<td>0 = Not at all</td>
</tr>
<tr>
<td>2  Feelings: embarrassment or self-consciousness due to skin</td>
<td>1 = A little</td>
</tr>
<tr>
<td>3  Domestic activities: shopping or looking after home or garden</td>
<td>2 = A lot</td>
</tr>
<tr>
<td>4  Clothing choice</td>
<td>3 = Very much</td>
</tr>
<tr>
<td>5  Social or leisure activities</td>
<td></td>
</tr>
<tr>
<td>6  Participation in sports</td>
<td></td>
</tr>
<tr>
<td>7  Work or study</td>
<td></td>
</tr>
<tr>
<td>8  Relationships</td>
<td></td>
</tr>
<tr>
<td>9  Sexual interactions</td>
<td></td>
</tr>
<tr>
<td>10 Treatment (degree of mess or time necessary)</td>
<td></td>
</tr>
</tbody>
</table>

*All items rated over the preceding week

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DLQI Correlates with PASI Decrease

Correlation analysis of mean percent reduction in PASI vs mean reduction in DLQI

Mean reduction in DLQI score

Mean reduction in PASI (%)

$R^2 = 0.8055$

Increased Skin Clearance Leads to Greater Improvement in Quality of Life

Mean improvement in DLQI according to PASI response

- PASI < 75 (n = 65)
  - Mean reduction from baseline DLQI at Week 16: -2.9

- PASI 75 to < 90 (n = 15)
  - Mean reduction from baseline DLQI at Week 16: -6.9

- PASI 90 to < 100 (n = 29)
  - Mean reduction from baseline DLQI at Week 16: 9.3

- PASI 100 (n = 32)
  - Mean reduction from baseline DLQI at Week 16: 9.8

Proportion of patients achieving DLQI 0 or 1 according to PASI response

- PASI < 75 (n = 65)
  - % of patients with DLQI 0/1 at Week 16: 12.7

- PASI 75 to < 90 (n = 15)
  - % of patients with DLQI 0/1 at Week 16: 33.3

- PASI 90 to < 100 (n = 29)
  - % of patients with DLQI 0/1 at Week 16: 79.3

- PASI 100 (n = 32)
  - % of patients with DLQI 0/1 at Week 16: 84.4

*P = 0.0015 or lower vs PASI < 75.
Other between-group differences P = NS

¶P < 0.05 for pairwise comparison vs PASI < 75 and P < 0.05 for pairwise comparison vs PASI 75 to < 90

NS = not significant

In terms of improvement in QoL; is there a difference between almost clear skin and completely clear skin?

1. **No** – *almost clear* is adequate and no different from *clear*.
2. **Yes** – but the difference is insignificant for most patients.
3. **Yes** – the difference is substantial → *clear* is much better than *almost clear*. 
Almost Double the Number of Patients with ‘Clear’ Skin Have DLQI 0 than Those with ‘Minimal’ Psoriasis

CHAMPION and REVEAL
Secondary analysis from two phase III studies of adalimumab (combined n = 1469)
Percentages of patients with DLQI total score = 0 by physician’s global assessment of disease activity at week 16

Patients (%) with DLQI 0

<table>
<thead>
<tr>
<th>Physician’s global assessment of disease activity</th>
<th>Clear (n = 228)</th>
<th>Minimal (n = 408)</th>
<th>Mild (n = 220)</th>
<th>Moderate (n = 333)</th>
<th>Severe (n = 167)</th>
</tr>
</thead>
<tbody>
<tr>
<td>64.9</td>
<td>34.8</td>
<td>16.8</td>
<td>3.6</td>
<td>1.2</td>
<td></td>
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</tbody>
</table>

Quality of Life Worsens Out of Proportion to Worsening in the Objective Signs of Disease

• REVEAL subanalysis: Patients who received adalimumab from baseline and had a ≥ PASI 75 response at week 16 and week 33 were re-randomized 1:1 at week 33 to receive blinded therapy with adalimumab 40 mg EOW or placebo EOW from week 33 to week 52.

• The DLQI and PASI relationship was compared for adalimumab-treated patients while on therapy versus after protocol-mandated treatment discontinuation.

Quality of Life Worsens out of Proportion to Worsening in the Objective Signs of Disease

N = 1212

Adalimumab n = 814*
Placebo n = 398

≥ PASI 75 responders required to continue to Period B

Adalimumab n = 580

≥ PASI 75 responders required to continue to Period C

Adalimumab n = 261

Placebo n = 240

Adalimumab n = 22

REVEAL week
0  16  33  52


*40 mg EOW from Week 1 after 80 mg at Week 0; ‡40 mg EOW from Week 17 after 80 mg at Week 16
Quality of Life Worsens out of Proportion to Worsening in the Objective Signs of Disease

Week 33
n = 240

Week 52
n = 237

Quality of Life Worsens out of Proportion to Worsening in the Objective Signs of Disease

At Week 52; mean PASI scores were lower (improved); yet mean DLQI scores were higher (worse) than they had been early in treatment (Week 4).

Mean PASI and DLQI scores

<table>
<thead>
<tr>
<th></th>
<th>PASI</th>
<th>DLQI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>19.5</td>
<td>11.6</td>
</tr>
<tr>
<td>Week 4</td>
<td>8.0</td>
<td>4.3</td>
</tr>
<tr>
<td>Week 33</td>
<td>1.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Week 52</td>
<td>6.7</td>
<td>5.3</td>
</tr>
</tbody>
</table>

Quality of Life Worsens Out of Proportion to Worsening in the Objective Signs of Disease

The same PASI score predicted a higher DLQI score for patients at Week 52 than at Week 4.

Psoriasis patients who are effectively treated may display a “reset” of what disease level is tolerated.

Treatment discontinuation after initial success may result in a rebound dissatisfaction with returning disease.

Dose reduction after initial treatment success may result in a similar phenomenon.

Skin Symptom Location Can Significantly Affect Quality of Life in Patients with Psoriasis (REVEAL study)

*All departures from the reference (contribution to BSA) were statistically significant. Skin lesion severity on the head and upper extremities had disproportionately large impacts on DLQI compared with BSA, particularly for younger women and men.

Kimball AB; et al. AAD. 2012.
Question to Audience

Do you feel we need additional assessment tools to help us better understand patient needs?

1. **No** – What we already have is adequate.

2. **Yes** – We cannot fully understand our patients and their needs with what is available.
Psoriasis-Specific PROs May Reflect Patient Status Better than DLQI

- Dermatology Life Quality Index (DLQI) does not adequately provide coverage for psoriasis-specific symptom measurement
- The use of a PRO that adequately captures symptoms associated with psoriasis is important in assessing treatment efficacy
- For example; the Psoriasis Symptom Inventory (PSI) was developed as a psoriasis-specific patient reported eight-item measure of symptom severity and has demonstrated good reliability and validity in patients with psoriasis

Psoriasis-Specific PROs
Should Meet Four Criteria

- Assess patient experiences most relevant to psoriasis
- Ask questions about experiences in a manner patients can understand
- Avoid unreasonable burden on patients’ recollection of events
- Easy to complete in approximately five minutes

## PROs Provide Information on Patient Perception of Psoriasis

<table>
<thead>
<tr>
<th>Disease factors assessed</th>
<th>Recall period</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatology Life Quality Index (DLQI)(^1)</td>
<td>Symptoms, Psychosocial impact, Physical impairment, Treatment</td>
<td>1 week</td>
</tr>
<tr>
<td>Psoriasis Symptom Assessment (PSA) Scale(^2)</td>
<td>Symptom frequency and burden</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Psoriasis Symptom Inventory (PSI)(^3)</td>
<td>Symptom frequency and severity</td>
<td>1 day or 1 week</td>
</tr>
<tr>
<td>Psoriasis Symptom Diary (PSD)(^4,5)</td>
<td>Symptom frequency; burden; and severity, Psychosocial impact, Physical impairment</td>
<td>1 day</td>
</tr>
</tbody>
</table>

**Longer recall periods and failure to assess symptoms relevant to psoriasis may limit utility of some PROs**

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**American Academy of Dermatology**
Psoriasis Symptom Diary: Higher Levels of Skin Clearance Can Have a Meaningful Impact on Key Symptoms

Likelihood of a response at week 12
Phase III ERASURE and FIXTURE studies of secukinumab
Gottlieb AB; et al. AAD. 2015.
Psoriasis Symptom Inventory: 8-Item Measure of Psoriasis Symptom Severity¹-²

For the following group of questions; the “last 24 hours” means from right now - back to yesterday at this time.

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Overall; during the last 24 hours; how severe was the <strong>itch</strong> from your psoriasis?</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2) Overall; during the last 24 hours; how severe was the <strong>redness</strong> of your skin lesions?</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) Overall; during the last 24 hours; how severe was the <strong>scaling</strong> of your skin lesions?</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>4) Overall; during the last 24 hours; how severe was the <strong>burning</strong> of your skin lesions?</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>5) Overall; during the last 24 hours; how severe was the <strong>stinging</strong> of your skin lesions?</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>6) Overall; during the last 24 hours; how severe was the <strong>cracking</strong> of your skin lesions?</td>
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<tr>
<td>7) Overall; during the last 24 hours; how severe was the <strong>flaking</strong> of your skin lesions?</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8) Overall; during the last 24 hours; how severe was the <strong>pain</strong> of your skin lesions?</td>
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</tr>
</tbody>
</table>

- **Symptoms:** itch; redness; scaling; burning; stinging; cracking; flaking; pain
- Each symptom is scored from 0 (not at all severe) to 4 (very severe)
- Total Score ranges from 0 (best) to 32 (worst)

Psoriasis Symptom Inventory: Higher Levels of Skin Clearance Can Have a Meaningful Impact on Key Symptoms

Feldman SR; et al. AAD. 2015.

Mean Total and Item PSI Scores in Patients with sPGA 0 vs 1

- **sPGA 0, n = 79**
- **sPGA 1, n = 151**

P < 0.001 for total and each item PSI score

Patients received ustekinumab; adalimumab; infliximab; or etanercept

sPGA 0 = complete skin clearance; sPGA 1 = almost clear skin
Summary

• Patients may view psoriasis differently versus dermatologists
  – Priorities when considering treatment options
  – Expectations of treatment outcomes

• Higher levels of skin clearance can improve QoL; and may be associated with a meaningful impact on key patient reported symptoms
  – Discontinuation of therapy can have negative effects in patients; including a loss of objective response and a disproportionately large negative impact on HRQoL

• Obtaining feedback from patients is an important part of clinical practice
  – PROs help patients better “weigh in” and validate PASI score reduction

HRQoL = health-related quality of life
Thank you

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