Dermatological Clinical Endpoints and Trial Designs

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Efficacy Endpoints

- PASI
  1. PASI 75 at week 12.
  2. PASI 50, 75, and 90 at different time points.
  3. Median PASI change over time.
  4. Time to response
- sPGA
- TLPSS
- DLQI
- NAPSI
Severe psoriasis – oral therapy with a new retinoid.
Fredriksson T, Petersson U
Dermatologica 1978; 157:238-244

Psoriasis Area and Severity Score
PASI =

0.1 (Eh + Ih + Dh) Ah
[head]

+ 0.3 (Et + It + Dt) At
[trunk]

+ 0.2 (Eu + Iu + Du) Au
[upper extremities]

+ 0.4 (El + Il + Dl) Al
[lower extremities]
### Severity of Psoriatic Lesions

<table>
<thead>
<tr>
<th></th>
<th>Head</th>
<th>Trunk</th>
<th>Upper Extremities</th>
<th>Lower Extremities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infiltration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desquamation</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Severity of Psoriatic Lesions (0-4 scale): assessed based on three target symptoms: *erythema (E)*, *infiltration (I)*, and *desquamation (D)*

0 = no symptoms present
1 = slight symptoms
2 = moderate symptoms
3 = striking symptoms
4 = exceptionally striking symptoms
PASI =

0.1 (Eh + Ih + Dh) Ah

[head]

+ 0.3 (Et+ It + Dt) At

[trunk]

+ 0.2 (Eu+Iu+Du) Au

[upper extremities]

+ 0.4 (El+Il+Dl) Al

[lower extremities]
<table>
<thead>
<tr>
<th>Body Areas (corresponding to total body area)</th>
<th>Area of Involvement (numerical value 0-6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head (h) (10%)</td>
<td></td>
</tr>
<tr>
<td>Trunk (t) (30%)</td>
<td></td>
</tr>
<tr>
<td>Upper extremities (u) 20%</td>
<td></td>
</tr>
<tr>
<td>Lower extremities (l) 40%</td>
<td></td>
</tr>
</tbody>
</table>
Psoriatic Involvement (6 point scale)

0 = no involvement
1 = <10% involvement
2 = 10 to <30% involvement
3 = 30 to <50% involvement
4 = 50 to <70% involvement
5 = 70 to <90% involvement
6 = 90 to 100% involvement
PASI =

0.1 (Eh + Ih + Dh) Ah [head] + 0.3 (Et+ It + Dt) At [trunk]

+ 0.2 (Eu+Iu+Du) Au [upper extremities] + 0.4 (El+Il+Dl) Al [lower extremities]
PASI =

0.1 (Eh + Ih + Dh) Ah [head] + 0.3 (Et+ It + Dt) At [trunk]

+ 0.2 (Eu+Iu+Du) Au [upper extremities] + 0.4 (El+Il+Dl) Al [lower extremities]
## Severity of Psoriatic Lesions

<table>
<thead>
<tr>
<th></th>
<th>Head</th>
<th>Trunk</th>
<th>Upper Extremities</th>
<th>Lower Extremities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Erythema</strong></td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Infiltration</strong></td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Desquamation</strong></td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>
PASI =

0.1 (3+3+4) Ah [head] + 0.3 (3+3+4) At [trunk]

+ 0.2 (3+3+4) Au [upper extremities] + 0.4 (3+3+4) Al [lower extremities]
## 60% BSA

<table>
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<th>Body Areas (corresponding to total body area)</th>
<th>Area of Involvement (numerical value 0-6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head (h) (10%)</td>
<td>4</td>
</tr>
<tr>
<td>Trunk (t) (30%)</td>
<td>4</td>
</tr>
<tr>
<td>Upper extremities (u) 20%</td>
<td>4</td>
</tr>
<tr>
<td>Lower extremities (l) 40%</td>
<td>4</td>
</tr>
</tbody>
</table>
PASI = 40

\[
0.1 (3+3+4) 4 + 0.3 (3+3+4) 4 + 0.2 (3+3+4) 4 + 0.4 (3+3+4) 4
\]

[head] + [trunk] + [upper extremities] + [lower extremities]
Physician’s static global assessment of psoriasis
Induration

- 0 = no evidence of plaque elevation
- 1 = minimal plaque elevation $\approx 0.5\text{mm}$
- 2 = mild plaque elevation, $\approx 1\text{mm}$
- 3 = moderate plaque elevation, $\approx 1.5\text{mm}$
- 4 = marked plaque elevation, $\approx 2\text{mm}$
- 5 = severe plaque elevation, $\approx 2.5\text{mm}$ or more
Induration (2)

• 0 = no evidence of plaque elevation
• 1 = minimal plaque elevation $\approx 0.25\text{mm}$
• 2 = mild plaque elevation, $\approx 0.5\text{mm}$
• 3 = moderate plaque elevation, $\approx 0.75\text{mm}$
• 4 = marked plaque elevation, $\approx 1\text{mm}$
• 5 = severe plaque elevation, $\approx 1.25\text{mm}$ or more
Erythema

0 = no evidence of erythema, hypo- or hyperpigmentation may be present
1 = faint erythema
2 = light red coloration
3 = moderate red coloration
4 = bright red coloration
5 = dusky to deep red coloration
Scaling

0 = no evidence of scaling
1 = minimal: occasional fine scale over less than 5% of the lesion
2 = mild; fine scale predominates
3 = moderate; coarse scale predominates
4 = marked; thick, non-tenacious scale predominates
5 = severe; very thick tenacious scale predominates
Physician’s static global assessment of psoriasis (averaged over all lesions)

0=Clear, except for residual discoloration

1=Almost clear, majority of lesions have individual scores for induration\(^{(a)}\) erythema\(^{(b)}\) and scaling\(^{\copyright}\) (IES) that averages 1
• “Clear”: the average of IES must be zero (with standard rounding rules) and the score for “induration” must be zero.

• “Almost clear”:
  (1) The average of IES must be 1, and each of the individual components must be <3.
  (2) Pts with IES score of 1, 0, 0, will be considered as “almost clear”.
2=Mild, majority of lesions have individual scores for induration\(^{(a)}\) erythema\(^{(b)}\) and scaling\(^{(c)}\) (IES) that averages 2

3=Moderate, majority of lesions have individual scores for induration\(^{(a)}\) erythema\(^{(b)}\) and scaling\(^{(c)}\) (IES) that averages 3

4=Marked, majority of lesions have individual scores for induration\(^{(a)}\) erythema\(^{(b)}\) and scaling\(^{(c)}\) (IES) that averages 4

5=Severe, majority of lesions have individual scores for induration\(^{(a)}\) erythema\(^{(b)}\) and scaling\(^{(c)}\) (IES) that averages 5
Target Lesion Psoriasis Severity Score

TLPSS
Target Lesion Psoriasis Severity Score

TLPSS

Two-step process:

For each target lesion

Scaling (A), Erythema (B), and Elevation (C) are rated according to a 5-point scale

Calculate the TLPSS for each target lesion by adding Scaling, Erythema, and Elevation scores:

\[ TLPSS = A + B + C = \text{__________} \]
GROUND RULES:

- **CONSISTENT SCORING**
- **THE SAME PERSON SHOULD CONDUCT THE TLPSS AT EACH VISIT**
- **SCORE POST-INFLAMMATORY HYPO- OR HYPERPIGMENTATION AS ZERO**
Scaling, Erythema, Elevation grading

- Target lesions are individually graded for presence of scaling, erythema and elevation

<table>
<thead>
<tr>
<th>Score</th>
<th>Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Slight</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
</tr>
</tbody>
</table>
Scaling, Erythema, Elevation grading

<table>
<thead>
<tr>
<th>A - Scaling</th>
<th>B - Erythema</th>
<th>C – Plaque Elevation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - Clear</td>
<td>0 - No Erythema; Hyperpigmentation, diffused faint pink or red coloration</td>
<td>0 - No Plaque Elevation; No elevation above normal skin</td>
</tr>
<tr>
<td>No scale</td>
<td>1 - Slight; Up to moderate, up to definite red coloration</td>
<td>1 - Slight; Difficult to ascertain whether there is a slight elevation above normal skin</td>
</tr>
<tr>
<td>1 - Slight Scaling; Surface dryness with some white coloration</td>
<td>1 - Slight; Up to moderate, up to definite red coloration</td>
<td>2 - Mild; Slight, but definite elevation, typically edges are indistinct or sloped</td>
</tr>
<tr>
<td>2 - Mild Scaling; Fine scales partially or mostly covering lesions</td>
<td>2 - Mild; Up to moderate, up to definite red coloration</td>
<td>3 - Moderate; Moderate elevation with rough or sloped edges</td>
</tr>
<tr>
<td>3 - Moderate Scaling; Coarse scales, covering most or all the lesions</td>
<td>3 - Moderate; Moderate, definite red coloration</td>
<td>4 - Severe; Marked elevation typically with hard or sharp edges</td>
</tr>
<tr>
<td>4 - Severe Scaling; Coarse,-tenacious scale predominates covering most or all lesions</td>
<td>4 - Severe; Sever, very bright red coloration</td>
<td></td>
</tr>
</tbody>
</table>

TLPSS (Target Lesion Psoriasis Severity Score): A + B + C = __________
Assessment of Scale

0 = Clear (No scale)
1 = Slight Scaling (Surface dryness with some white coloration)
2 = Mild Scaling (Fine scales partially or mostly covering lesions)
3 = Moderate Scaling (Coarse scales, covering most or all the lesions)
4 = Severe Scaling (Coarse, tenacious scale predominates covering most or all of the lesions)
Assessment of Erythema

- 0 = No Erythema (Hyperpigmentation, pigmented macules, diffused faint pink or red coloration)
- 1 = Slight (Up to mild, reddish up to definite red coloration)
- 2 = Mild (Up to moderate, definite red coloration)
- 3 = Moderate (Moderate, definite bright red coloration)
- 4 = Severe (Severe, very bright red coloration)
<table>
<thead>
<tr>
<th>Height</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0mm</td>
<td>0</td>
<td>No plaque Elevation (no elevation above normal skin)</td>
</tr>
<tr>
<td>0.25mm</td>
<td>1</td>
<td>Slight (Possible but difficult to ascertain whether there is a slight elevation above normal skin)</td>
</tr>
<tr>
<td>0.5mm</td>
<td>2</td>
<td>Mild (Slight, but definite elevation, typically edges are indistinct or slopped)</td>
</tr>
<tr>
<td>1mm</td>
<td>3</td>
<td>Moderate (Moderate elevation with rough or slopped edges)</td>
</tr>
<tr>
<td>1.25mm</td>
<td>4</td>
<td>Severe (Marked elevation typically with hard or sharp edges)</td>
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Dermatology Life Quality Index (DLQI)

• 10 questions concerning patient’s perception of the impact of skin disease on different aspects of their QoL over the last week.

• 4-point Likert Score:
  0: Not at all/not relevant.
  1: A little
  2: A lot
  3: Very much

• Total score: sum of scores of individual items.
Dermatology Life Quality Index (DLQI)

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick □ one box for each question.

1. Over the last week, how itchy, sore, painful or stinging has your skin been?  
   - Very much □  
   - A lot □  
   - A little □  
   - Not at all □

2. Over the last week, how embarrassed or self conscious have you been because of your skin?  
   - Very much □  
   - A lot □  
   - A little □  
   - Not at all □

3. Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?  
   - Very much □  
   - A lot □  
   - A little □  
   - Not at all □  
   - Not relevant □
Fig 4. Dermatology Life Quality Index (DLQI) scoring distribution by body surface area in psoriasis patients. Higher DLQI scores indicate poorer functioning.