The Safety and Efficacy of Pimecrolimus, 1%, Cream for the Treatment of Netherton Syndrome

Results From an Exploratory Study

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The Investigator Global Evaluation of Disease (IGED) was assessed at baseline and at each successive visit using the following scale:

0 = No signs of disease
1 = Almost clear of disease
2 = Mild disease (limited extent, mild lichenification, scaling, erythema)
3 = Moderate disease (moderate extent, moderate lichenification, scaling, erythema)
4 = Severe disease (extensive, severe lichenification, scaling, erythema)

The IGED was based on assessment of affected areas only, not entire body surface area. Areas assessed included the head and neck, trunk, upper extremities, and lower extremities. A composite score was generated combining the various body parts, with a maximum score of 16.

The Netherton Area Severity Assessment (NASA) represents a modification of the standard Eczema Area and Severity Index (EASI) and assesses the severity of dermatitis over 4 body areas. It assigns proportionate body surface areas to the head and neck (10%), trunk (30%), upper extremities (20%), and lower extremities (40%) for children 8 years or older. This is roughly consistent with the rule of 9. The numbers are modified when used with children aged 7 years or younger: head and neck (20%), trunk (30%), upper extremities (20%), and lower extremities (30%).

The area of involvement (affected by inflammation, not including dry skin) of each of the 4 body regions is represented by a 7-point numeric coded value (0-6) as shown in the following tabulation (the investigator is required to record the percentage of the area [0-100%], and it is suggested to record to the nearest 5%):

<table>
<thead>
<tr>
<th>Score</th>
<th>Area of Involvement, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No eruption</td>
</tr>
<tr>
<td>1</td>
<td>≤10</td>
</tr>
<tr>
<td>2</td>
<td>10-29</td>
</tr>
<tr>
<td>3</td>
<td>30-49</td>
</tr>
<tr>
<td>4</td>
<td>50-69</td>
</tr>
<tr>
<td>5</td>
<td>70-89</td>
</tr>
<tr>
<td>6</td>
<td>90-100</td>
</tr>
</tbody>
</table>

The head, trunk, upper limbs and lower limbs are assessed separately for erythema (E), infiltration/papulation (I), lichenification (L), and scaling (S). The average degree of severity of each sign in each of the 4 body parts is assigned a score of 0 to 3 indicating no involvement (0) or mild (1), moderate (2), or severe (3) expression of the clinical sign. Half steps are allowed. Further practical details to aid the assessment are as follows:

- The lower extremities region includes the buttocks.
- The trunk region includes the internal/medial axillae and groin.
- The head/neck region comprises the face and the anterior and posterior neck.
- The upper extremities region includes the hands and external axillae.

The definitions of the scoring signs of NASA are given in the eTable.
The NASA score for children 7 years or younger was then calculated according to the following formula, where the area is defined on the 7-point ordinal scale:

\[
\text{Location} \quad \text{(E + I + L + S)} \times \text{Area} \times 0.2
\]

- Head/Neck
- Trunk
- Upper limbs
- Lower limbs

NASA score equals: Sum of the above 4 body areas

For example, if there is no involvement of the head and neck, no involvement on the upper limbs, 55% involvement of the trunk (area score of 4) with the 4 signs all being mild (scores of 1), and 35% involvement on the lower limbs (area score of 3), with the 4 signs (E, I, L, and S), all equal a NASA score of 2 (moderate).

<table>
<thead>
<tr>
<th>Location</th>
<th>Head/Neck</th>
<th>Upper limbs</th>
<th>Trunk</th>
<th>Lower limbs</th>
<th>NASA score equals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>((1 + 1 + 1 + 1) \times 4 \times 0.3)</td>
<td>((2 + 2 + 2 + 2) \times 3 \times 0.3)</td>
<td>Sum of the above 4 body areas</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>4.8</td>
<td>7.2</td>
<td>12</td>
</tr>
</tbody>
</table>

This means that in this trial, the NASA score can theoretically vary from 0 to 72.

The calculation of NASA score for children 8 years or older is performed as follows (where the area is defined on the 7-point ordinal scale):

\[
\text{Location} \quad \text{(E + I + L + S)} \times \text{Area} \times 0.1
\]

- Head/Neck
- Trunk
- Upper limbs
- Lower limbs

NASA score equals: Sum of the above 4 body areas