Identification of Biomarkers To Predict Therapeutic Response To Biologicals In Psoriasis

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INTRODUCTION & AIM

Primary non-response: etiology; yet not completely understood
Secondary non-response: ADA, resistance; yet no monitoring
Belgian costs: ≥ 27 million € in 2015 for adalimumab and etanercept
Need for stratification

MATERIALS & METHODS

- Patients recruited during consultations
- Dpt of Dermatology, Ghent University Hospital (BE) and Dpt of Dermatology, Amsterdam Medical Centre (NL)
- Whole blood (PAXgene Blood RNA Tubes) and serum
- Patients were started on either adalimumab or ustekinumab
- PASI assessed prior to treatment (baseline) and at 24 weeks to calculate ΔPASI
- Responder (R) to treatment if at least ΔPASI90, non-responder (NR) to treatment if ΔPASI175 or lower
- All patients provided written informed consent

RESULTS

<table>
<thead>
<tr>
<th>mRNA</th>
<th>Protein</th>
<th>Ustekinumab</th>
<th>Adalimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARD14</td>
<td>JAK3</td>
<td>Responder (n=9)</td>
<td>Non-responder (n=6)</td>
</tr>
<tr>
<td>CDKAL1</td>
<td>KL6</td>
<td>44.3 ±12.0 (19.0-55.0)</td>
<td>44.0 ±12.5 (26.0-62.0)</td>
</tr>
<tr>
<td>CTLA4</td>
<td>KYN</td>
<td>55.6%</td>
<td>100.0%</td>
</tr>
<tr>
<td>DDX58</td>
<td>LEPR</td>
<td>Baseline PASI</td>
<td>16.2 ±7.0 (10.4-27.6)</td>
</tr>
<tr>
<td>FBXL9</td>
<td>NF1</td>
<td>Disease duration (y)</td>
<td>17.0 ±10.3 (6.0-37.0)</td>
</tr>
<tr>
<td>FGZD28</td>
<td>IL13A</td>
<td>Prior smoking (yes)</td>
<td>44.40%</td>
</tr>
<tr>
<td>G0T1</td>
<td>TPTRC</td>
<td>BMI</td>
<td>27.2 ±6.6 (17.9-36.8)</td>
</tr>
<tr>
<td>G0T2</td>
<td>SC12A2B</td>
<td>IL-17A</td>
<td>42.7 ±13.4 (24.0-55.0)</td>
</tr>
<tr>
<td>D01</td>
<td>SPATS2L</td>
<td>IL-17C</td>
<td>75.0%</td>
</tr>
<tr>
<td>FNR2</td>
<td>ST1</td>
<td>Baseline PASI</td>
<td>16.7 ±8.8 (8.6-27.6)</td>
</tr>
<tr>
<td>FNB1</td>
<td>ST2</td>
<td>Disease duration (y)</td>
<td>16.0 ±2.3 (14.0-18.0)</td>
</tr>
<tr>
<td>L20</td>
<td>ST3</td>
<td>Prior smoking (yes)</td>
<td>50.0%</td>
</tr>
<tr>
<td>L2B</td>
<td>ST4</td>
<td>BMI</td>
<td>29.9 ±4.8 (24.6-34.8)</td>
</tr>
</tbody>
</table>

3. mRNA-based biomarkers

- No correlation between gene expression and ΔPASI
- Multivariate analysis (Table 2): significance was lost

4. Protein-based biomarkers

- Correlation with ΔPASI:
  - F7 in the ustekinumab group (p = 0.012)
  - Leptin and IL-6 in the adalimumab group (p = 0.024 and 0.012)
- Multivariate analysis (Table 2): significance was lost

5. Pooled data (responders)

- Significant difference between NR and R
- Leptin, adiponectin, VEGF and F7
- Correlation with APASI: Leptin and F7 (inverse, p < 0.01)
- Correlation with BMI: Leptin (p = 0.013)
- Correlation between leptin and adiponectin (p = 0.03)
- Possibility to create combination panels (multiple logistic regression)

DISCUSSION

- Small sample size
- Biased approach
- Interobserver-variation
- Heterogeneity

LIMITATIONS

- Technical feasibility: qPCR less optimal
- Reproducibility of prediction: not optimal
- VEGFa, adiponectin and leptin: promising
- Pilot confirms feasibility of serum proteins as response biomarkers to biologicals
- Unable to predict response between adalimumab and ustekinumab
- Need for unbiased approach

CONCLUSION

- No correlation between gene expression and ΔPASI
- Multivariate analysis (Table 2): significance was lost