PGA x BSA as a PASI Surrogate

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DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY

Current Consulting/Advisory Board Agreements/or Speakers Bureau:


Research/Educational Grants:

Janssen, Incyte
Why quantitate severity of disease and treatment response in clinical practice?

• Treat to target strategies require outcome measures useful and feasible in clinical practice

• Payers want treatment decisions based upon quantifiable outcome measures in clinical practice, similar to HbA1C for diabetes or blood pressure measurements for hypertension*

• Pay for performance initiatives make use of large databases which currently lack useful dermatology-specific outcome measures
  
  o In the absence of outcome measures, payers are tiering physicians mostly on their costs vs those of their “peers” without knowing the physician’s average case-mix is and whether he/she actually clear patients and improves patient quality of life

• Facilitates real world clinical research

• Helpful in communicating clinical response with patients

What is wrong with PASI?

• Too complicated and time consuming for clinical practice

• Not responsive to change at low BSAs

• Not understood well by practitioners or patients

• Local areas not measured, e.g., palmar plantar, genital, nail psoriasis

• No patient reported outcomes
PGA x BSA

• PGA x BSA = composite tool to measure:
  o severity and extent of psoriasis
  o sensitive to change
  o correlates with PASI
  o highly feasible measure
  o potential for use in both trials and clinical practice settings
  o Weakness: PGA is not standardized
Correlation with PASI


- Spearman correlation coefficient with PASI of $r=0.87$ ($p<0.001$)
Kristina Duffin MD MS, Kim A. Papp MD PhD, Jerry Bagel MD, Eugenia Levi PharmD BCPS, Rongdean Chen PhD, and Alice B. Gottlieb MD PhD.


In ESTEEM 1 and 2, PGA x BSA and PASI exhibited significant positive correlations for measuring disease severity at baseline ($r \geq 0.757$) and Week 16 ($r \geq 0.807$). At Week 16, $\geq 79\%$ concordance was observed between PGA x BSA and PASI for 75% and 90% improvement from baseline; greater concordance ($>88.0\%$) was observed using 50% improvement from baseline. Cohen’s effect sizes $>0.8$, indicating sensitivity to therapeutic change, were observed. At Week 16, PGAxBSA and PASI were moderately correlated with DLQI.
PGA x BSA: An Outcome Measure for Treat to Target Strategies

National Psoriasis Foundation Urges Dermatologists to Treat to Target in Psoriasis

April W. Armstrong, MD, MPH, Michael P. Siegel, PhD, Jerry Bagel, MD Erin E. Boh, MD, PhD, Megan Buell, Kevin D. Cooper, MD, Kristina Callis Duffin, MD, MS, Lawrence F. Eichenfield, MD, Amit Garg, MD, Joel M. Gelfand, MD, MSCE, Alice B. Gottlieb, MD, PhD, John Y. M. Koo, MD, Neil J. Korman, MD, PhD, Gerald G. Krueger, MD, Mark G. Lebwohl, MD, Craig L. Leonardi, MD, Arthur M. Mandelin, MD, PhD, M. Alan Menter, MD, Joseph F. Merola, MD, MMSC, David M. Pariser, MD, Ronald B. Prussick, MD, FRCP, Caitriona Ryan, MD, p Kara N. Shah, MD, Jeffrey M. Weinberg, MD, Mary Jane O. U. Williams, MD, Jashin J. Wu, MD, Paul S. Yamauchi, MD, PhD, and Abby S. Van Voorhees, MD From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. ( J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.10.017.)
Assessing Clinical Response and MDA with the PGAxBSA Tool: An Analysis of Apremilast Phase 3 Esteem Data Continued*

• Mod-severe plaque psoriasis
  o PASI>=12, BSA >=10%, sPGA >=3
  o Week 16 primary endpoints, maintenance to week 32; (wk 32-52 randomized w/d phase)
    – 5 point PGA, DLQI, PASI, BSA
  o PGAxBSA score range 0-400

Examples of Scoring

<table>
<thead>
<tr>
<th>Severity</th>
<th>Mild to Moderate</th>
<th>Moderate to Severe</th>
<th>Severe</th>
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</thead>
<tbody>
<tr>
<td>PGA</td>
<td>4</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>BSA (%)</td>
<td>4</td>
<td>18</td>
<td>32</td>
</tr>
<tr>
<td>PGA x BSA</td>
<td>16</td>
<td>54</td>
<td>128</td>
</tr>
</tbody>
</table>
Figure 3. Proposed IQR-Based PGAxBSA Score Bands

Proposed “MDA” criterion

Data as observed.
Figure 4. Patients Achieving Response at Week 16, by PASI, PASI+DLQI, and PGxBSA Criteria in ESTEEM 1 (A) and ESTEEM 2 (B)

Data as observed.

n=n=number of patients achieving response/total number of patients with evaluable data.

Patients (%) Achieving Response at Week 16, by PASI or PGAxBSA Criteria in ESTEEM1 and ESTEEM2

Study Conclusions

• PGAxBSA is sensitive to change in disease severity in apremilast treated patients with moderate to severe psoriasis

• PGAxBSA bands can aid measurement and interpretation of meaningful clinical response, including MDA, in patients with psoriasis

• Suggested MDA of $\leq 1.5$ for PGA x BSA (0-400) range in patients presenting with moderate to severe plaque psoriasis

• Limitation: Validation in only moderate to severe psoriasis patients

Investigator Initiated, Collaborative, Retrospective, pooled post hoc analysis of Phase III clinical trials that included patients with moderate to severe psoriasis randomized to secukinumab 150/300 mg and placebo (ERASURE, FIXTURE, FEATURE, and JUNCTURE) or etanercept (FIXTURE)\(^1\)\(^-\)\(^3\)
Conclusions

• PGAxBSA is sensitive to change in disease severity in apremilast and secukinumab treated patients with moderate to severe psoriasis

• PGAxBSA correlates with PASI

• PGAxBSA bands can aid measurement and interpretation of meaningful clinical response, including MDA, in patients with psoriasis

• MDA values which correspond to PASI $> 90$ and DLQI 0.1 have been defined for two treatments of moderate to severe psoriasis

• Limitations
  o Validation in only moderate to severe psoriasis patients
  o PGAs not standardized among clinical trials
  o Localized areas not measured: nails, genital
  o No patient reported outcomes