ORAL MOLECULE UPDATE: PSORIASIS (AND PSORIATIC ARTHRITIS)

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DISCLOSURES/POTENTIAL COI

SPEAKER/CONSULTANT/INVESTIGATOR

- ABBVIE, AMGEN, CELGENE
- LEO, LILLY, NOVARTIS, ORTHO-DERM, SIENNA, SUN PHARMA
COMBINATION THERAPY OF APREMILAST AND BIOLOGIC AGENT AS A SAFE OPTION OF PSORIATIC ARTHRITIS AND PSORIASIS

Metyas S, Messian R, Gettas T, Asfahani L, Quismorio A
Presented at: 2016 ACR/ARHP Annual Meeting

Poster Presentation
◆ Safety of apremilast in combination of biologic therapies in treatment of PsO & PsA

Methods
◆ Retrospective, open-label, single-center study of 22 patients with psoriasis and psoriatic arthritis who added apremilast to their current biologic therapy
APREMILAST AND NARROWBAND UVB COMBINATION THERAPY FOR TREATING MODERATE-TO-SEVERE PLACQUE PSORIASIS (CONT’D)

• 73% OF PATIENTS ACHIEVED PASI-75, OF WHICH 45% ACHIEVED PASI-90

• CONCLUSION: MORE PATIENTS ACHIEVED PASI-75 WITH APREMILAST AND NUVB COMBINATION THERAPY THAN PREVIOUSLY REPORTED WITH APREMILAST ALONE

Results

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild first-degree burn</td>
<td>12</td>
</tr>
<tr>
<td>Moderate first-degree burn</td>
<td>2</td>
</tr>
<tr>
<td>Nausea</td>
<td>2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2</td>
</tr>
<tr>
<td>Polymorphous light eruption</td>
<td>2</td>
</tr>
<tr>
<td>Second-degree nUVB burn</td>
<td>1</td>
</tr>
</tbody>
</table>

AEs Reported Over 12-Week Period

First-degree burns were the most commonly reported AE, suggesting an evaluation of this combination with respect to burns may be warranted

• CONCLUSION: MORE PATIENTS ACHIEVED PASI-75 WITH APREMILAST AND NUVB COMBINATION THERAPY THAN PREVIOUSLY REPORTED WITH APREMILAST ALONE
SYMPTOM RELAPSE FOLLOWING APREMILAST DISCONTINUATION IS RELATED TO LONGER DISEASE DURATION AT TREATMENT INITIATION IN PATIENTS WITH MODERATE TO SEVERE PSORIASIS

ABBY VAN VOORHEES, MD1; HOWARD SOFEN, MD2; JERRY WEAVER MS3;
JOSHUA CIRULLI, PHARMD3; YAO WANG, MD3; RICHARD B. WARREN, MD4

1EASTERN VIRGINIA MEDICAL SCHOOL, NORFOLK, VA; 2DERMATOLOGY RESEARCH ASSOCIATES, LOS ANGELES, CA;
3CELGENE CORPORATION, SUMMIT, NJ; 4THE UNIVERSITY OF MANCHESTER, MANCHESTER, UK

Presented at: the 2018 AAD Annual Meeting; February 16–20, 2018; San Diego, CA.
CONCLUSIONS

• THE PROPORTION OF PATIENTS WHO EXPERIENCED LOSS OF RESPONSE/RELAPSE AFTER APR DISCONTINUATION WAS GREATER AMONG PATIENTS WITH DISEASE DURATION ≥10 YEARS VS. PATIENTS WITH DISEASE DURATION <10 YEARS AT APR INITIATION.

• MOST PATIENTS REGAINED PASI-75/50 RESPONSE AFTER RE-INITIATION OF APR TREATMENT.

• FURTHER RESEARCH IS WARRANTED TO DETERMINE IF EARLIER INITIATION OF SYSTEMIC THERAPY MODIFIES THE COURSE OF DISEASE, AS WELL AS ADDITIONAL FACTORS THAT MAY CONTRIBUTE TO THE HIGHER FREQUENCY OF RELAPSE AMONG PATIENTS WITH LONGER DISEASE DURATION.

Safety and Efficacy of Apremilast Through 104 Weeks in Patients With Moderate to Severe Psoriasis Who Continued on Apremilast or Switched From Etanercept Treatment in the LIBERATE Study

Kristian Reich, MD\textsuperscript{1}; Mark Goodfield, MD\textsuperscript{2}; Lawrence Green, MD\textsuperscript{3}; Kristine Nograles, MD\textsuperscript{4}; Rongdean Chen, PhD\textsuperscript{4}; Eugenia Levi, PharmD\textsuperscript{4}; Richard G. B. Langley, MD\textsuperscript{5}

\textsuperscript{1}Dermatologikum Hamburg, Hamburg, Germany; \textsuperscript{2}Leeds General Infirmary, Leeds, UK; \textsuperscript{3}George Washington University School of Medicine, Washington, DC; \textsuperscript{4}Celgene Corporation, Summit, NJ; \textsuperscript{5}Dalhousie University, Halifax, NS, Canada

Presented at: the 75th Annual Meeting of the American Academy of Dermatology; March 3–7, 2017; Orlando FL.
This study was sponsored by Celgene Corporation.
The ≥75% reduction from baseline in PASI score (PASI-75) response achieved at Week 16 was sustained through Week 104 in patients continuing APR or switching from ETN to APR at Week 16.

*P < 0.0001 vs. PBO.

Response at Week 16 and Week 104 was determined using the LOCF methodology. The analysis for Week 16 includes all patients in the modified intent-to-treat (mITT) group, while the Week 104 analysis includes patients who entered the apremilast extension phase and were treated in the phase. The vertical lines indicate 2-sided 95% confidence intervals.
Among patients with baseline ScPGA ≥3 (moderate or greater), ScPGA response of 0 (clear) or 1 (almost clear) was achieved by significantly more patients receiving APR compared with patients receiving PBO at Week 16.

The ScPGA response achieved at Week 16 was sustained through Week 104 in APR/APR patients and ETN/APR patients. Responses at Week 104 among PBO/APR patients were generally similar to those in APR/APR patients.

ScPGA Response (mITT, LOCF)†

<table>
<thead>
<tr>
<th></th>
<th>PBO</th>
<th>PBO/APR</th>
<th>APR</th>
<th>APR/APR</th>
<th>ETN</th>
<th>ETN/APR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 16</td>
<td>25.9</td>
<td>50.0</td>
<td>44.4</td>
<td>59.2</td>
<td>50.0</td>
<td>56.6</td>
</tr>
<tr>
<td>Week 104</td>
<td>15/58</td>
<td>25/50</td>
<td>24/54</td>
<td>29/49</td>
<td>27/54</td>
<td>30/53</td>
</tr>
</tbody>
</table>

*P=0.0458 vs. PBO. §P=0.0083 vs. PBO. †Response at Week 16 and Week 104 was determined using the LOCF methodology. Week 104 analysis includes patients who entered the apremilast extension phase and were treated in the phase. The vertical lines indicate 2-sided 95% confidence intervals.
NAIL RESPONSE

- The proportions of patients with nail psoriasis at baseline (NAPSI ≥1) who achieved NAPSI-50 at Week 16 were higher with APR (25.0%) or ETN (48.0%) than PBO (10.9%; \( P=0.0701 \) vs. APR and \( P<0.0001 \) vs. ETN).
- At Week 104, NAPSI-50 response was 60.4% (APR/APR), 65.2% (ETN/APR), and 48.6% (PBO/APR).
- The mean percentage change from baseline in NAPSI score continued to improve in APR/APR patients and was sustained in ETN/APR patients through Week 104.

**Mean Percentage Change in NAPSI Score***

<table>
<thead>
<tr>
<th></th>
<th>Week 16</th>
<th>Week 104</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBO</td>
<td>42</td>
<td>33</td>
</tr>
<tr>
<td>Mean % Change</td>
<td>-10.1</td>
<td>-48.1</td>
</tr>
<tr>
<td>APR</td>
<td>50</td>
<td>48</td>
</tr>
<tr>
<td>Mean % Change</td>
<td>-18.7 ( $ )</td>
<td>-48.2</td>
</tr>
<tr>
<td>ETN</td>
<td>50</td>
<td>45</td>
</tr>
<tr>
<td>Mean % Change</td>
<td>-37.7 ( \dagger )</td>
<td>-51.1</td>
</tr>
</tbody>
</table>

*In patients with NAPSI score ≥1 at baseline. Includes all patients with a baseline value and a post-baseline value at the study week. Missing scores were imputed using the LOCF methodology. The mean NAPSI score at baseline was 4.14 (PBO), 4.18 (APR), and 4.30 (ETN). \( \$ P=0.4959 \) vs. PBO. \( \dagger P<0.0024 \) vs. PBO.
Efficacy and Safety of Apremilast in Systemic- and Biologic-Naive Patients With Moderate Plaque Psoriasis: 52-Week Results of UNVEIL

Linda Stein Gold, MD; Jerry Bagel, MD; Mark Lebwohl, MD; J. Mark Jackson, MD; Rongdean Chen, PhD; Joana Goncalves, MD; Eugenia Levi, PharmD; Kristina Callis Duffin, MD, MS

1Henry Ford Health System, West Bloomfield, MI; 2Psoriasis Treatment Center of Central New Jersey, East Windsor, NJ; 3Icahn School of Medicine at Mount Sinai, New York, NY; 4University of Louisville, Forefront Dermatology, Louisville, KY; 5Celgene Corporation, Summit, NJ; 6University of Utah, Salt Lake City, UT

PGAxBSA MEAN PERCENTAGE CHANGE FROM BASELINE AT WEEK 16 AND WEEK 52 (LOCF)

- At Week 16, significantly greater improvement in PGAxBSA occurred in patients receiving APR vs. PBO.
- At Week 52, improvement was maintained in the APR/APR group and emerged in the PBO/APR group after switching to APR.

Methotrexate: When Do I Use It?

- Medicare patients
- Lack of health insurance
- Psoriatic arthritis
- Prior to a biologic therapy (often mandated)
- Combined with a biologic therapy
Methotrexate

Adverse Effects – Hepatic

- Incidence varies from 0-25%
- MTX-induced fibrosis often nonaggressive and reversible
- Liver biopsy is a gold standard, but a poor test laden with risk and sampling error
- I no longer send patients for liver biopsy
- Future tests will be non-invasive and more accurate
XELJANZ/XELJANZ XR is indicated for the treatment of adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to methotrexate or other disease-modifying antirheumatic drugs (DMARDs). Limitations of Use: Use of XELJANZ/XELJANZ XR in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.¹
<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>Monitoring Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytes</td>
<td>Lymphocyte counts at baseline and every 3 months thereafter.</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Neutrophil counts at baseline and after 4-8 weeks of treatment and every 3 months thereafter.</td>
</tr>
<tr>
<td>Anemia</td>
<td>Hemoglobin at baseline and after 4-8 weeks of treatment and every 3 months thereafter.</td>
</tr>
<tr>
<td>Liver Enzymes</td>
<td>Routine liver tests and prompt investigation of the causes of liver enzyme elevations is recommended to identify potential cases of drug-induced liver injury.</td>
</tr>
<tr>
<td>Lipids</td>
<td>Lipid parameters approximately 4-8 weeks following initiation of Xeljanz/Xeljanz XR therapy.</td>
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T-cell–mediated immune response to pneumococcal conjugate vaccine (PCV-13) and tetanus toxoid vaccine in patients with moderate-to-severe psoriasis during tofacitinib treatment

Kevin L. Winthrop, MD, MPH, a Neil Korman, MD, b William Abramovits, MD, b Scott T. Rottinghaus, MD, c Huaming Tan, PhD, d Annie Gardner, MS, e Geoffrey Mukwaya, MD, e Mandeep Kaur, MD, e and Hernan Valdez, MD e
Portland, Oregon; Cleveland, Ohio; Dallas, Texas; Groton, Connecticut; Cambridge, Massachusetts; New York, New York; and Collegeville, Pennsylvania

Conclusion: Most psoriasis patients who receive tofacitinib can mount satisfactory T-cell–dependent immune responses to PCV-13 and tetanus vaccines. (J Am Acad Dermatol 2018;78:1149-55.)

Capsule Summary

- Tofacitinib is an oral Janus kinase inhibitor.
- Most patients with psoriasis who received tofacitinib mounted satisfactory T-cell–dependent immune responses to monovalent tetanus toxoid and 13-valent pneumococcal conjugate vaccines.
- PCV-13 and tetanus toxoid vaccine are likely to confer immunity for patients with psoriasis who receive tofacitinib.