Bimekizumab in Biologics-Refractory Psoriatic Arthritis: A Real-Life Analysis from a Combined Dermatology-Rheumatology Clinic

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Treatment of psoriatic arthritis (PsA) may pose some difficulties in clinical practice, with a relevant proportion of patients being refractory to at least two courses of biological treatment,1 thus leading to persistent inflammation/pain and diminished quality of life (sometimes regardless of objective signs of inflammation).2 Hence, there is a need to find alternative treatments in such a subset of biologics-refractory PsA patients.

In this analysis, we investigated the efficacy of bimekizumab (BKZ), an inhibitor of IL17A and IL17F, in biologics-refractory PsA (defined as the failure of at least two courses of biological treatment) in a real-life setting. Specifically, we considered psoriatic subjects from our combined dermatology-rheumatology clinic who also had active PsA and were candidates for BKZ therapy for skin disease. A comprehensive rheumatological examination including swollen joint count (SJC) in 66 joints, tender joint count (TJC) in 68 joints and Leeds Enthesitis Index (LEI), collection of PsA related Patient Reported Outcomes (PROs) and a sonographic assessment in 48 joints, 36 tendons and 12 enthesis were performed at baseline (w0), as well as week 12 (w12) and 24 (w24). The active sonographic site count score (ie, US active site count) was defined by a radiologist, blinded to the clinical evaluation as the sum of active synovitis,2 active tenosynovitis3 and active enthesitis4 in each patient. All data are expressed as mean values or percentages; statistical analysis was performed by using Mann–Whitney U-test with a p-value of 0.05 deemed as statistically significant.

In total, seven psoriatic patients (mean age 54.5 ± 15 years; 4/7 male; Psoriasis Area Severity Index (PASI): mean 8.5 ± 5.1) with active and biologics-refractory PsA (mean Disease Activity Index for Psoriatic Arthritis (DAPSA): 35.9 ± 20) were included in this analysis (Table 1). Among them, 5/7 (71.4%) were classified as difficult to treat (D2T) PsA patients (defined as failure of at least two mechanisms of action + persistent moderate disease activity).5 At w12, 5/7 patients (71.4%) experienced a significant joint improvement with achievement of DAPSA-low disease activity, whereas PASI100 was achieved in 5/7 patients (71.4%). Six out of seven patients (85.7%) reached the Minimum Clinically Important Difference (MCID) for both DAPSA and PASI.5–7 Interestingly, we observed an improvement even in three out of four patients who had previously failed other IL-17A inhibitors. In terms of mean values, we observed DAPSA and PASI amelioration, with figures of 13.8 ± 6.9 (△ DAPSA 22.1) and 3.2 ± 7.4 (△ PASI 5.3), respectively; at week 24, DAPSA-low disease activity and PASI100 rates were maintained (Figure 1). Notably, six out seven patients (85.7%) did not display significant joint inflammatory objective findings during baseline clinical and sonographic examinations (SJC mean 0.67 ± 0.81; US active site count mean 0.83 ± 0.75; CRP mean 0.21 ± 0.1 mg/dl) despite experiencing active disease according to TJC (mean 11.3 ± 15.8) and patient-reported outcomes (mean PtGA 6.33 ± 2.7; mean VAS pain 6.2 ± 2.5). Considering such a subset of patients, BKZ showed a 40% decrease in TJC (△ 4.5; p=0.26) and a significant reduction of Patient Global Assessment (PtGA) and Visual Analogue Scale (VAS) pain scores (p=0.025 and p=0.025, respectively).
respectively, at w12 and p=0.045 and p=0.037, respectively, at w24) (Figure 2). No adverse events were observed during the follow-up period.

In this real-life experience, BKZ emerges as a possible effective and safe treatment for active PsA refractory to at least two courses of biologic treatments, including TNF-inhibitors, anti-IL-17A and/or anti-IL-23. Moreover, this analysis underlines that BKZ may lead to joint low-disease activity also in those subjects lacking objective signs of inflammation, especially in terms of reduction of pain and improvement in patient’s disease perception. This might be due to a possible activity on pain control by dual IL-17A and IL-17F inhibition, yet a placebo effect cannot be ruled out. Limitations of this study include the small sample size and the lack of a long-term follow-up, thus future larger studies are needed to confirm our preliminary findings.

### Table 1 Baseline Characteristics of Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Sex</th>
<th>BMI</th>
<th>Smoke (yes/no)</th>
<th>csDMARDs (n°)</th>
<th>Previous bDMARDs (n°)</th>
<th>Mechanism of action failed</th>
<th>PASI (w0)</th>
<th>DAPSA (w0)</th>
<th>VAS pain (w0)</th>
<th>Main articular involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>57</td>
<td>Male</td>
<td>23</td>
<td>No</td>
<td>5</td>
<td>1</td>
<td>TNFi, PDE4i, JAKi</td>
<td>3</td>
<td>35,2</td>
<td>8</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Patient 2</td>
<td>28</td>
<td>Male</td>
<td>21</td>
<td>Yes</td>
<td>2</td>
<td>2</td>
<td>TNFi, IL17Ai, IL23i</td>
<td>7</td>
<td>39,5</td>
<td>8</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Patient 3</td>
<td>60</td>
<td>Female</td>
<td>44,6</td>
<td>No</td>
<td>2</td>
<td>3</td>
<td>TNFi, IL17Ai</td>
<td>6,2</td>
<td>22,5</td>
<td>8</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Patient 4</td>
<td>64</td>
<td>Male</td>
<td>27</td>
<td>No</td>
<td>3</td>
<td>2</td>
<td>TNFi, IL17Ai</td>
<td>2,5</td>
<td>62,5</td>
<td>7</td>
<td>Peripheral</td>
</tr>
<tr>
<td>Patient 5</td>
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<td>Female</td>
<td>19,5</td>
<td>Yes</td>
<td>2</td>
<td>3</td>
<td>TNFi, IL17Ai, IL23i</td>
<td>13,2</td>
<td>60,2</td>
<td>8</td>
<td>Axial</td>
</tr>
<tr>
<td>Patient 6</td>
<td>53</td>
<td>Female</td>
<td>21</td>
<td>Yes</td>
<td>3</td>
<td>4</td>
<td>TNFi, IL17Ai, IL23i</td>
<td>13</td>
<td>7,34</td>
<td>2</td>
<td>Peripheral</td>
</tr>
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<td>Patient 7</td>
<td>75</td>
<td>Male</td>
<td>27,7</td>
<td>No</td>
<td>4</td>
<td></td>
<td></td>
<td>15</td>
<td>24,2</td>
<td>7</td>
<td>Peripheral</td>
</tr>
</tbody>
</table>

**Abbreviations:** csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; bDMARDs, biologic disease-modifying antirheumatic drugs; PASI, Psoriasis Area Severity Index; DAPSA, Disease Activity Index for Psoriatic Arthritis; VAS pain, visual analogue scale; TNFi, tumor necrosis factor-alpha inhibitors; PDE4i, phosphodiesterase-4 inhibitor; IL17Ai, Interleukin 17A inhibitors; IL23i, Interleukin 23 inhibitors; JAKi, Janus kinase inhibitors.

Figure 1 Trend of DAPSA in the seven patients represented in the figure with different colors. DAPSA, Disease Activity Index for Psoriatic Arthritis.
Data Sharing Statement
All the data of the study are included in the present manuscript.

Compliance with Ethics Guidelines
The patients in this manuscript provided informed consent for the publication of case details, and institutional approval was not required, as the study was based on data retrospectively collected in a routine clinical setting. This study complies with the Declaration of Helsinki and no ethical approval was required as it results from clinical routine activity.

Author Contributions
All authors made a significant contribution to the work reported (ie, conception, study design, execution, acquisition of data, analysis, and interpretation); took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure
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References

Figure 2 Trend of PtGA and VAS pain of the six patients without the traditional objective signs of clinical and imaging inflammation during the follow-up. PtGA, Patient Global Assessment; VAS Pain, Visual Analogue Scale. *p = 0.025; **p = 0.025; †p = 0.045; ††p = 0.037.


