BARICITINIB PROVIDES GREATER IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES ACROSS ALL DISEASE ACTIVITY LEVELS COMPARED TO PlaceBO AND ADALIMUMAB IN RHEUMATOID ARTHRITIS


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Background: Baricitinib (BARI) is a JAK1/JAK2 inhibitor which provides improvements to clinical signs, symptoms, and patient-reported outcomes (PROs) in patients with rheumatoid arthritis [1, 2].

Objectives: The effect of BARI on the relationship between disease activity and pain has been explored previously [3]. The purpose of this post hoc analysis was to determine the association between additional PROs (physical function, fatigue, and duration of morning joint stiffness) and disease activity status after 12 weeks of treatment and to evaluate whether patients with an inadequate response to methotrexate treated with BARI 4 mg experienced greater PRO improvement than patients treated with either placebo (PBO) or adalimumab (ADA) across all levels of disease activity.

Methods: Data for these analyses were derived from the Phase 3 study RA-BEAM (N=1305; NCT01710358). Pain was evaluated using a 0-100 mm visual analog scale, physical function was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI), fatigue was measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale, and duration of morning joint stiffness (MJS, minutes) was measured by the patient. Disease activity was measured using the Clinical Disease Activity Index (CDAI) and categorized as remission (REM, ≤2.8), low disease activity (LDA, >2.8 to ≤10), moderate disease activity (MDA, >10 to ≤22), or high disease activity (HDA, >22). Linear regression was used to model the relationship between change in PROs at Week 12 (response) and CDAI values at Week 12 (primary explanatory variable) to evaluate the extent of improvement in PROs with BARI relative to PBO and ADA across a spectrum of disease activity levels. Last observation carried forward was used to impute missing values.

Results: At baseline, 91% of patients were classified as having HDA and 9% as having MDA by CDAI across all treatment groups. After 12 weeks of treatment, 2%, 7%, and 9% of patients achieved REM; 16%, 27%, and 33% of patients achieved LDA; and 33%, 40%, and 38% of patients achieved MDA with PBO, ADA, and BARI, respectively [3].

At Week 12, the estimated changes in measures of pain and physical function, as well as duration of MJS, for BARI 4 mg were greater than both PBO and ADA at all disease activity level threshold values of CDAI (Table 1). The estimated change in fatigue for BARI 4 mg was similar to that of ADA, and greater than PBO, at all disease activity level threshold values (Table 1).

Table 1. Estimate of PRO Improvement by Disease Activity Threshold Level (CDAI) at Week 12

<table>
<thead>
<tr>
<th>PRO</th>
<th>CDAI=2.8</th>
<th>CDAI=10</th>
<th>CDAI=22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain VAS&lt;sup&gt;a&lt;/sup&gt; (mm)</td>
<td>-28.4</td>
<td>-37.9</td>
<td>-40.5</td>
</tr>
<tr>
<td>HAQ-DI&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-0.6</td>
<td>-0.7</td>
<td>-0.9</td>
</tr>
<tr>
<td>FACIT-F&lt;sup&gt;c&lt;/sup&gt;</td>
<td>9.8</td>
<td>11.8</td>
<td>11.1</td>
</tr>
<tr>
<td>Duration of MJS (min)</td>
<td>-6.9</td>
<td>-37.8</td>
<td>-64.9</td>
</tr>
</tbody>
</table>

<sup>a</sup>Pain VAS scores range from 0 (no pain) to 100 (worst pain).
<sup>b</sup>HAQ-DI scores range from 0 (no disability) to 3 (completely disabled).
<sup>c</sup>FACIT-F scores range from 0 (worst fatigue) to 52 (no fatigue).

Abbreviations: ADA, adalimumab; BARI, baricitinib; CDAI, Clinical Disease Activity Index; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MJS, morning joint stiffness; PBO, placebo; PRO, patient-reported outcomes; VAS, visual analog scale.

Conclusion: Estimates of treatment differences suggest that patients treated with BARI 4 mg may experience greater improvements in pain, physical function, and MJS duration than patients treated with PBO or ADA regardless of their disease activity status reached after 12 weeks of treatment. Using this approach, improvements in fatigue with BARI 4 mg may be greater than with PBO and similar to ADA after 12 weeks.

REFERENCES:

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POS0650

PREDICTORS OF DURABLE CLINICAL RESPONSE TO TOFACITINIB 11 MG ONCE DAILY WITH OR WITHOUT METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: POST HOC ANALYSIS OF DATA FROM A PHASE 3a/4 METHOTREXATE WITHDRAWAL STUDY


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Background: The objective of this post hoc analysis was to identify predictors of durable clinical response to tofacitinib 11 mg once daily with or without methotrexate (MTX) in patients with rheumatoid arthritis (RA) enrolled in the Phase 3a/4 withdrawal study.[1,2]

Methods: Data from two post hoc analyses were derived from the Phase 3 study RA-TOF (N=1305; NCT01710358). One analysis assessed predictors of clinical response (≥20% reduction in the American College of Rheumatology improvement criteria [ACR20]) at Week 12 with or without MTX. The other analysis assessed predictors of clinical response (≥60% reduction in the (ACR50)) at Week 12 with or without MTX. Both analyses included 11 mg tofacitinib once daily (OD) with or without MTX. The primary endpoint was change from baseline in disease activity index (DAS28-ESR) at Week 12. Secondary endpoints included the proportion of patients achieving ACR20 and ACR50 at Week 12. Multivariate logistic regression was used to identify predictors of clinical response at Week 12.

Results: At Week 12, 19.2% of patients achieved ACR20 and 11.3% achieved ACR50 with or without MTX. The multivariate logistic regression model identified several predictors of clinical response at Week 12, with or without MTX. These predictors included baseline disease activity, baseline ACR20 status, and duration of MTX use. The model also identified several predictors of clinical response at Week 12 with MTX, including baseline ACR20 status, baseline DAS28-ESR, and duration of MTX use.

Conclusion: The results of this post hoc analysis suggest that several demographic, clinical, and treatment-related factors may predict durable clinical response to tofacitinib 11 mg OD with or without MTX in patients with RA. Further research is needed to validate these findings and explore the potential clinical implications of these predictors.