Patient-reported outcomes from a phase 3 study of baricitinib versus placebo or adalimumab in rheumatoid arthritis: secondary analyses from the RA-BEAM study

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ABSTRACT

Background To assess the effect of baricitinib on patient-reported outcomes (PROs) in patients with active rheumatoid arthritis and an inadequate response to methotrexate (MTX).

Methods In this double-blind phase 3 study, patients were randomised 3:3:2 to placebo (n=488), baricitinib 4 mg once daily (n=487), or adalimumab 40 mg biweekly (n=330) with background MTX. PROs included the SF-36, EuroQol 5-D (EQ-5D) index scores and visual analogue scale, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Health Assessment Questionnaire-Disability Index (HAQ-DI), Patient’s Global Assessment of Disease Activity (PtGA), patient’s assessment of pain and Work Productivity and Activity Impairment Questionnaire-Rheumatoid Arthritis (WPAI-RA), and measures collected in electronic patient daily diaries: duration and severity of morning joint stiffness (MJS), Worst Tiredness and Worst Joint Pain. The primary study endpoint was at week 12. Treatment comparisons were assessed with logistic regression for categorical measures or analysis of covariance for continuous variables.

Results Compared with placebo and adalimumab, baricitinib showed statistically significant improvements (p≤0.05) in HAQ-DI, PtGA, pain, FACIT-F, SF-36 physical component score, EQ-5D index scores and WPAI-RA daily activity at week 12. Improvements were maintained for measures assessed to week 52. Statistically significant improvement in patient diary measures (MJS duration and severity), worst tiredness and worst joint pain were observed for baricitinib versus placebo and adalimumab at week 12 (p≤0.05).

Conclusions Baricitinib provided significantly greater improvement in most PROs compared with placebo and adalimumab, including physical function MJS, pain, fatigue and quality of life. Improvement was maintained to the end of the study (week 52). Trial registration NCT01710358.

INTRODUCTION

Rheumatoid arthritis (RA) is characterised by inflammatory activity and joint damage that often result in disability, pain, limitations in physical function and other impairments important to patients. Outcomes can be improved with effective therapy.1–3 Decreases in physical function may be a consequence of both disease activity and irreversible, progressive joint damage.1–6

Patient-reported outcome (PRO) measures include health-related quality of life (HRQOL), physical function, disability, fatigue, sleep, mental health status, work productivity and work activity impairment.7 These are standardised measures, and minimum clinically important differences (MCIDs) have been determined for many. Because these PRO measures are obtained directly from the patients, they may more accurately reflect how the patient feels and functions in relation to RA and to therapy.8 9 The PRO measures also may facilitate doctor–patient communication and shared decision making to improve the quality of patient care.10–12

Baricitinib is a selective inhibitor of Janus kinase (JAK)1/JAK2 that interrupts signalling in pathways believed to be important in RA pathogenesis. The efficacy of baricitinib has been demonstrated in clinical studies in patients with RA.13–17 In the phase 3 RA-BEAM clinical trial (NCT01710358), baricitinib 4 mg once daily (QD) was associated with clinical improvement and inhibition of progression of radiographic joint damage compared with both placebo and adalimumab in patients with RA and an inadequate response to methotrexate (MTX). Specifically, 70% of patients treated with baricitinib achieved the American College of Rheumatology 20% response rate compared with 40% of placebo-treated patients and 61% of adalimumab-treated patients. This manuscript describes the PRO data collected in the RA-BEAM clinical trial of baricitinib.18

METHODS

Patients and study design

RA-BEAM was a randomised, double-blind, double-dummy, placebo-controlled and active-controlled, parallel-arm, 52-week study conducted at 281 centres in 26 countries. Detailed methods of the RA-BEAM study have been published previously.18 Briefly, patients were ≥18 years old with active RA (≥6/68 tender and ≥6/66 swollen joints; serum
high-sensitivity C reactive protein ≥6 mg/L). Patients had inad- equate response to MTX. At baseline, patients were required to have either ≥3 joint erosions (based on radiographs) or >1 joint erosion with seropositivity for rheumatoid factor or anticitrulli- nated peptide antibodies.

Patients were randomised 3:3:2 to receive placebo, baricitinib 4 mg once daily, or biweekly subcutaneous adalimumab 40 mg, in addition to their existing background therapy (including MTX). The primary analysis time point for the study was at week 12. At week 24, patients receiving placebo switched to baricitinib. At week 16, patients whose tender and swollen joint counts improved from baseline by <20% at both weeks 14 and 16 were assigned rescue treatment (baricitinib 4 mg). After week 16, patients could be rescued at investigators’ discretion based on joint counts. The study was conducted in accordance with ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines and was approved by each centre’s institutional review board or ethics committee. All patients provided written informed consent.

Study endpoints and assessments

PROs were prespecified as secondary objectives of the study. Physical function was measured using the Health Assessment Questionnaire-Disability Index (HAQ-DI). Scores range from 0 to 3, with lower scores reflecting better physical function and, thus, less disability. The HAQ-DI score changes were assessed in the context of an MCID of 0.22, and the percentage of patients who reported scores that met or exceeded the population normative value (<0.5) was also assessed. Disease activity and arthritis pain were measured using the Patient’s Global Assessment of Disease Activity (PtGA) and the patient’s assessment of pain, statistically significant improve- ments of regular activities, as measured during the past 7 days. Scores are calculated as impairment percentages with higher percentages indicating greater impairment and less productivity.

Non-diary PROs were assessed at baseline and at weeks 1, 2, 4 and every 4 weeks thereafter to week 32 and after week 32, they were assessed at weeks 40 and 52. There were, however, some exceptions to the schedule before week 4. The FACIT-F, SF-36 and the EQ-5D were assessed at baseline and week 4, and the WPAI-RA was assessed at baseline, week 2 and week 4. These measures followed the same schedules as the other PROs after Week 4.

Statistical analyses

Randomised patients treated with ≥1 dose of placebo, barici- tinib or adalimumab were included in the efficacy analyses on the basis of a modified intention-to-treat principle (analysis set). Least squares mean (LSM) change from baseline for treatment comparisons of continuous efficacy variables were obtained using analysis of covariance with treatment, geographical region, baseline joint erosion status and baseline value in the model. For diary PRO data, analyses were based on the average of scores collected in the 7 days prior to the study visit, without baseline adjustment, until the week 12 visit date; daily scores from the day of randomisation (day 1) up to day 28 were also assessed. For the daily score analysis, mixed models for repeated measures were applied, with duration of MJS analysed by non-parametric methods.

As per the predefined analysis plan, patients who were rescued or discontinued from study or study treatment were thereafter defined as non-responders (non-responder imputation) for analysis of all categorical efficacy measures. For continuous efficacy measures, modified last observation carried forward was used, where the last observation before rescue or discontinuation was used for all subsequent time points. The WPAI-RA measures were censored after rescue or discontinuation without imputation applied.

All analyses are based on a significance level of 0.05 (two sided). p Values were not adjusted for multiple comparisons.

RESULTS

Patient disposition and baseline characteristics

A total of 1307 patients were randomised (488 placebo, 487 baricitinib 4 mg and 330 adalimumab) and 1305 patients received treatment. Patient disposition has been previously reported. Baseline patient characteristics and disease activity were similar among groups (online supplementary file 1). Most patients (>99%) were receiving background MTX. The majority of patients had received ≥2 prior conventional synthetic disease modifying antirheumatic drugs (csDMARDs). Baseline PROs indicated a significant disease burden, consistent with the baseline clinical disease activity (online supplementary file 1).

Patient-reported outcomes

HAQ-DI, PtGA and pain

As reported in Taylor, et al., for HAQ-DI, PtGA, and the patient’s assessment of pain, statistically significant improve- ments in the baricitinib group versus placebo were evident as early as week 1, the first assessment. Significant improvements in physical function and reductions in PtGA and pain were main- tained at week 12 and through week 52, the end of the study (table 1). When compared with adalimumab, statistically signifi- cant improvements in HAQ-DI were seen as early as week 4 and
at week 2 for PtGA and pain, respectively; these improvements were maintained at week 12 and week 52.

The percentages of patients who reported improvements that met or exceeded the HAQ-DI MCID of ≥0.22 at week 12 for placebo, baricitinib and adalimumab, respectively, were 58%, 75%, and 71% (p≤0.001 for baricitinib vs placebo and adalimumab vs placebo; p=0.302 for baricitinib vs adalimumab) and were 68% and 58% at week 52 for baricitinib vs adalimumab (p<0.001). The percentage of patients who reported scores that met or exceeded the population normative value of <0.5 at week 12 or those who met or exceeded at week 52 ranged from 24% to 32% for baricitinib and adalimumab (online supplementary file 2). The percentages for baricitinib and adalimumab were statistically different (p<0.001) than placebo at week 12.

MJS duration, MJS severity, worst tiredness and worst joint pain
Baricitinib treatment resulted in significant improvement versus placebo and adalimumab for all four measures at the primary time point of the study, week 12 (table 2). Improvements versus placebo were significant from week 1 for severity of MJS, Worst Tiredness and Worst Joint Pain and from week 2 for the duration of MJS. Improvements of baricitinib versus adalimumab were observed from as early as week 2 for Worst Joint Pain, week 4 for severity of MJS and week 8 for Worst Tiredness; for duration of MJS, improvements were statistically different at weeks 1 and 12, as reported by Taylor et al.18

Consistent with the weekly averaged data, the daily diary scores showed significant improvement in patients receiving baricitinib compared with both placebo and adalimumab. Improvements relative to placebo were observed as early as day three for the severity of MJS, Worst Tiredness, and Worst Joint Pain and by day five for the duration of MJS (figure 1). Improvements relative to adalimumab were observed as early as day 19 for the severity of MJS, day 21 for Worst Tiredness and day 17 for Worst Joint Pain. No significant differences were observed in the first 28 days between baricitinib and adalimumab for the duration of MJS.

FACIT-F
Treatment with baricitinib or adalimumab was associated with significant improvements in FACIT-F at the first assessment of the measure at week 4 (p≤0.001 for baricitinib versus placebo). Improvements versus placebo were observed as early as day three for each measure at weeks 12 and 52 (figure 2). Improvements versus adalimumab were observed as early as day 19 for FACIT-F at week 12, as reported by Taylor et al.18

Table 1  Least squares mean change from baseline at 12 and 52 weeks for PRO

<table>
<thead>
<tr>
<th>PRO measures</th>
<th>Week 12</th>
<th>Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n=488)</td>
<td>Baricitinib (n=487)</td>
</tr>
<tr>
<td>Physical function (HAQ-DI)</td>
<td>-0.34 (-0.39, -0.29)</td>
<td>-0.66*** †† (-0.71, -0.61)</td>
</tr>
<tr>
<td>Patient’s Global Assessment of Disease Activity (PGA)</td>
<td>-16.7 (-18.9, -14.6)</td>
<td>-31.2*** †† (-33.3, -29.1)</td>
</tr>
<tr>
<td>Patient’s Assessment of Pain</td>
<td>-17.1 (-19.4, -14.9)</td>
<td>-31.5*** †† (-33.7, -29.3)</td>
</tr>
<tr>
<td>VAS</td>
<td>7.7 (5.6, 9.8)</td>
<td>14.8*** †† (12.8, 16.9)</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, ***p<0.001 versus placebo. †p<0.05, ††p<0.01, †††p<0.001 versus adalimumab.

HAQ-DI, Health Assessment Questionnaire-Disability Index; PRO, patient-reported outcomes; VAS, visual analogue scale.

Table 2  Day 1, week 1 and week 12 data from patient daily diaries

<table>
<thead>
<tr>
<th>PRO measures</th>
<th>Day 1 median (IQR)</th>
<th>Week 1 median (IQR)</th>
<th>Week 12 median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n=488)</td>
<td>Baricitinib (n=487)</td>
<td>Adalimumab (n=330)</td>
</tr>
<tr>
<td>Duration of morning joint stiffness, minutes, median (IQR)</td>
<td>60.0 (30.0, 180.0)</td>
<td>60.0 (30.0, 180.0)</td>
<td>60.0 (20.0, 180.0)</td>
</tr>
<tr>
<td>Severity of morning joint stiffness</td>
<td>5.5 (2.2)</td>
<td>5.4 (2.2)</td>
<td>5.3 (2.3)</td>
</tr>
<tr>
<td>Worst Tiredness</td>
<td>5.6 (2.2)</td>
<td>5.6 (2.2)</td>
<td>5.5 (2.2)</td>
</tr>
<tr>
<td>Worst Joint Pain</td>
<td>5.9 (2.1)</td>
<td>5.9 (2.1)</td>
<td>5.7 (2.2)</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, ***p<0.001 versus placebo. †p<0.05, ††p<0.01, †††p<0.001 versus adalimumab.

LSM, least squares mean; PRO, patient-reported outcome.
Clinical and epidemiological research

The improvements in the FACIT-F score were sustained to week 24 for both baricitinib and adalimumab versus placebo (p≤0.001) and were significant at weeks 20, 28 and 52 for baricitinib versus adalimumab (p≤0.05; figure 2).

For the FACIT-F, the percentage of patients who reported improvements that met or exceeded the MCID (≥3.56) was 59%, 66% and 68% for placebo, baricitinib and adalimumab, respectively (p≤0.05 for baricitinib vs placebo; p≤0.01 for adalimumab vs placebo), at week 12 and were 60% and 54% at week 52 for baricitinib and adalimumab, respectively (p=0.084; figure 2). The percentage of patients who reported scores that met or exceeded the population normative value of ≥40.1 ranged from 41% to 46% for baricitinib and adalimumab at weeks 12 and 52 (online supplementary file 2).

Figure 1 Change from baseline over time for the patient-reported outcomes collected by the daily patient electronic diaries (data and either SD or 95% CIs are presented in online supplementary file 5). (A) Duration of Morning Joint Stiffness: data are mean duration of morning joint stiffness in minutes, based on daily diary entries. Daily question: ‘Please indicate how long your morning joint stiffness lasted today’. Indications of statistical significance based on analysis of median difference. (B) Severity of Morning Joint Stiffness: data are LS mean scores for severity of morning joint stiffness, based on daily diary entries. Higher values indicate greater severity with numeric rating scale anchors (0–10). Daily question: ‘Please rate the overall level of morning joint stiffness you had from the time you woke up today’. (C) Worst Tiredness: data are LS mean scores for Worst Tiredness, based on daily diary entries. Higher values indicate greater tiredness with numeric rating scale anchors (0–10). Daily question: ‘Please rate your tiredness by selecting the one number that describes your tiredness at its worst in the last 24 hours’. (D) Worst Joint Pain: data are LS mean scores for Worst Joint Pain, based on daily diary entries. Higher values indicate greater pain with numeric rating scale anchors (0–10). Daily question: ‘Please rate your joint pain by selecting the one number that describes your joint pain at its worst in the last 24 hours’. LS, least squares; NRS, numeric rating scale.

vs placebo; p≤0.01 for adalimumab vs placebo; figure 2).

Health-related quality of life

SF-36

Patients treated with baricitinib or adalimumab showed statistically significantly improved differences compared with placebo in most of the eight SF-36 domains at week 12 except for the mental health domain (both baricitinib and adalimumab) and role-emotional domain (adalimumab), which improved but did not achieve statistical significance (table 3). Compared with adalimumab, patients treated with baricitinib showed statistically significant improvement in most of the domains at week 52, except for the mental health domain (table 3).

Compared with placebo, SF-36 PCS was statistically significantly improved for patients treated with baricitinib and adalimumb (figure 3A) from the first postbaseline assessment at week 4 and was maintained through weeks 12 and 52. At week 12, the percentage of patients who met or exceeded the MCID (≥5) for
placebo, baricitinib and adalimumab, respectively, was 40%, 65% and 56% at week 12 (for both groups vs placebo, p≤0.001 and baricitinib vs adalimumab, p≤0.05) and was 60% and 52% at week 52 for baricitinib versus adalimumab (p≤0.05). For the SF-36 MCS measure, numeric, but not statistically significant differences in the change from baseline were found for both baricitinib and adalimumab versus placebo at all time points, except for baricitinib versus placebo at week 24 (p≤0.01). The

**Figure 2** Change from baseline over time for the FACIT-F. Higher scores indicate less fatigue. Range=0–52. FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; MCID, minimum clinically important differences. p Value versus placebo: *p≤0.05; **p≤0.01; ***p≤0.001. p Value versus adalimumab: +p≤0.05; ++p≤0.01; +++p≤0.001.

### Table 3 Baseline values and least squares mean changes from baseline at weeks 12 and 52 for SF-36 domain scores.

<table>
<thead>
<tr>
<th>SF-36 domain scores</th>
<th>Baseline mean (SD)</th>
<th>Week 12 LSM</th>
<th>Week 52 LSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baricitinib (n=487)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n=488)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab (n=330)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>32.4 (10.4)</td>
<td>32.3 (10.2)</td>
<td>31.6 (10.7)</td>
</tr>
<tr>
<td>Role physical</td>
<td>36.3 (10.3)</td>
<td>35.5 (10.3)</td>
<td>34.5 (10.5)</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>34.9 (7.7)</td>
<td>34.6 (7.5)</td>
<td>34.5 (8.5)</td>
</tr>
<tr>
<td>General health</td>
<td>36.6 (8.6)</td>
<td>37.3 (8.1)</td>
<td>36.3 (8.7)</td>
</tr>
<tr>
<td>Vitality</td>
<td>43.9 (10.1)</td>
<td>43.8 (9.5)</td>
<td>43.2 (10.5)</td>
</tr>
<tr>
<td>Social functioning</td>
<td>41.3 (11.3)</td>
<td>40.9 (11.6)</td>
<td>40.0 (12.2)</td>
</tr>
<tr>
<td>Role emotional</td>
<td>41.4 (12.5)</td>
<td>41.4 (12.5)</td>
<td>40.3 (12.9)</td>
</tr>
<tr>
<td>Mental health</td>
<td>42.9 (11.3)</td>
<td>43.3 (11.1)</td>
<td>42.5 (11.5)</td>
</tr>
</tbody>
</table>

*p≤0.05, **p≤0.01, ***p≤0.001 versus placebo. t*p≤0.05, t+t*p≤0.01, t+t+t*p≤0.001 versus adalimumab.

LSM, least squares mean; SF-36, Short-Form-36.
Figure 3  Change from baseline for the physical and mental component score for the SF-36. (A) Physical component score: data in table are % patients who met or exceeded the minimum clinically important difference in SF-36 PCS (≥5 points). Higher scores indicate improvement. (B) Mental component score: data in table are % patients who met or exceeded the minimum clinically important difference in SF-36 MCS (≥5 points). Higher scores indicate improvement. p Value versus placebo: *p≤0.05; **p≤0.01; ***p≤0.001. p Value versus adalimumab: +p≤0.05; ++p≤0.01; +++p≤0.001.
In this analysis and in the results presented by Taylor et al.,
treatment with baricitinib resulted in a rapid improvement in
PROs; patients showed statistically significant improvements
as early as week 1 in HAQ-DI, PtGA and the patient’s assessment
of pain, and these results were maintained until the end of the trial at
week 52. Compared with placebo, a significantly greater propor-
tion of patients treated with baricitinib or adalimumab reported
improvements that met or exceeded the MCID and the population
normative values for HAQ-DI and FACIT-F at week 12.

Similar results were seen for duration and severity of MJS,
Worst Tiredness and Worst Joint Pain as assessed using the
patient daily diaries and improvement continued to week 12.
The rapid onset of action, with improvement in relevant signs
and symptoms (such as pain and tiredness) as early as 3 days after
the start of treatment, is a useful complement to the efficacy
observed at the later time points.

Consistent with these results, patients treated with baricit-
inib reported improvements in HRQOL, as measured by
the EQ-5D and SF-36 PCS compared with placebo and adali-
umab. For the SF-36, improvements across most of the
SF-36 domains were observed for baricitinib and adalim-
umab compared with placebo at week 12 and for baricitinib
compared with adalimumab at week 52. Furthermore, when
a five-point change was used for the MCID, it was found
that 65% of the baricitinib-treated patients met or exceeded
the MCID for the SF-36 PCS (figure 3A). In contrast with
the PCS, no statistically significant differences were observed
between baricitinib-treated and adalimumab-treated patients
compared with placebo-treated patients with the SF-36 MCS. Acrosstreatment groups at baseline, the SF-36 MCS values
ranged from 46 to 47, which are close to the population
normative data of 50. This suggests only modest impair-
ment for the MCS at baseline such that a marked improve-
ment with therapy would not be expected. This SF-36 MCS
result aligns with previous results from other trials.

Compared with placebo, patients treated with baricitinib
showed statistically significant improvement across all scores
of the work productivity assessment at week 12. When
compared with adalimumab, the baricitinib-treated patients
showed statistically significant improvement in work produc-
tivity loss and impairment of regular activity at week 12;
these improvements continued through week 52 but were not
statistically significantly different.

The results from this analysis are similar to those observed in
other phase 3, randomised clinical trials of baricitinib in different
patient populations. The limitations of this analysis include the use of carrying
forward the last observations before rescue or discontinua-
tion. This method assumes that the PRO values do not change
over time. Also, as in most double-blind comparator trials,
the inclusion and exclusion criteria restrict patient participa-
tion such that these results may not be fully generalisable to
the population seen in clinical practice.

This study used well-established PRO measures that can
holistically evaluate the burden of RA and the treatment
effects across many health domains. Some of the PRO
measures are incorporated into the patient ratings in the
ACR core set, while others, such as the EQ-5D and SF-36,
are established HRQOL instruments that may more broadly
measure the effects of RA and treatment on patients. The
use of diary records allowed patients to report the impact
of symptoms of importance to them as they arose, therefore
permitting a more complete evaluation than by means of
periodic recording of recollected symptoms. Furthermore,

EQ-5D
A statistically significant improvement in the EQ-5D index scores
(both US and UK) were observed at the first postbaseline assess-
ment, week 4 (data not shown), for both baricitinib and adalimu-
numab versus placebo and was maintained to week 12 (table 1).
By week 52, statistically significant improvements in EQ-5D
index scores were observed for baricitinib versus adalimumab
(table 1). For the EQ-5D VAS at 4 weeks, baricitinib-treated
and adalimumab-treated patients showed statistically significant
improvement compared with placebo-treated patients (data not
shown). By week 12, however, statistically significant improve-
ment in EQ-5D VAS was observed for only baricitinib-treated
patients (p≤0.001 vs placebo; p≤0.01 versus adalimumab); this
was maintained through week 52 for baricitinib versus adalimu-
umab (p≤0.001; table 1).

Work Productivity and Activity Impairment
At baseline, 41%–43% of the patients were employed. Patients
with baricitinib reported statistically significantly
improved daily activity compared with placebo and adalimumab
at week 12 (p≤0.001 for both groups vs placebo; p≤0.01 for
baricitinib vs adalimumab); improvements compared with adali-
umab, however, were not statistically significant at week 52
(on supplementary file 4). Among those patients who were
employed at baseline and those who maintained employment at
week 12, statistically significant improvements in absenteeism
(p≤0.05), presenteeism (p≤0.001) and work productivity loss
(p≤0.001) were seen with baricitinib compared with placebo;
improvements compared with adalimumab, however, were not
statistically significant at week 52. Only work productivity loss
was statistically significantly improved with baricitinib versus
adalimumab at week 12 (p≤0.05; on supplementary file 3).

DISCUSSION
The RA-BEAM study evaluated baricitinib 4 mg once daily in
patients with an inadequate response to MTX who were naive
to biological DMARDs using placebo and adalimumab 40 mg
biweekly as comparators. Patients continued to take stable
background csDMARDs (including MTX) during the study. This
paper evaluates whether the clinical efficacy data for baricitinib
were complemented by corresponding changes in PROs.
Baseline PROs describe substantial duration (≥60 min)
and severity of MJS, severe impairment of physical function and high
levels of pain and fatigue (including tiredness) among patients
enrolled in the study. Baricitinib treatment produced significantly
greater improvements compared with placebo and adalimumab
in most of the prespecified PROs, including physical function,
 pain, fatigue, duration and severity of MJS and HRQOL at week
12. Furthermore, baricitinib produced rapid improvements in
the diary PROs compared with placebo and adalimumab, with
significant differences vs placebo appearing within days of initi-
ating treatment. Improvements were maintained to week 52
compared with adalimumab in physical function, pain, fatigue
and HRQOL (eg, SF-36 PCS and EQ-5D).

This study used well-established PRO measures that can
holistically evaluate the burden of RA and the treatment
effects across many health domains. Some of the PRO
measures are incorporated into the patient ratings in the
ACR core set, while others, such as the EQ-5D and SF-36,
are established HRQOL instruments that may more broadly
measure the effects of RA and treatment on patients. The
use of diary records allowed patients to report the impact
of symptoms of importance to them as they arose, therefore
permitting a more complete evaluation than by means of
periodic recording of recollected symptoms. Furthermore,
these PRO measures may help facilitate discussions between patients and their healthcare providers; they may help address patient concerns such as how long it will take to feel improvement (onset of action), how long to try the new treatment before determining that it is not effective (efficacy plateau) and how long the treatment will be effective (sustainability or the risk of relapse). In addition to facilitating the physician–patient dynamic, PRO measures are being increasingly used in randomised clinical trials and allow for epidemiological assessments across different patient populations and disease states. PRO assessments such as the work productivity measure also provide an insight into the broader, societal impact of RA.

The use of a variety of PRO measures also allows for an assessment of the clinical importance of the present study’s results. Similar trends were observed between comparisons of baricitinib with both placebo and adalimumab in most of the PROs. Additionally, some PRO measures were assessed with established and validated MCID values. Statistically significant differences in MCIDs between treatment groups implies clinical significance on a group level. Collectively, the results of the present study demonstrate treatment benefits for baricitinib that appear clinically relevant.

The RA-BEAM study demonstrated that patients treated with baricitinib experienced a greater improvement compared with patients treated with placebo or adalimumab in most PROs across different domains of RA, including physical function, MJIS, fatigue, pain and HRQOL. These improvements tended to occur within the first weeks of treatment and were maintained throughout the 52-week trial.

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