Efficacy of baricitinib in patients with moderate-to-severe rheumatoid arthritis with 3 years of treatment: Results from a long-term study

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Background: Baricitinib (Bari) is an oral, selective and reversible Janus kinase 1 and 2 inhibitor approved for the treatment of adults with active RA. In addition to long-term safety which has been disclosed previously with data up to 7 years [1], an important clinical consideration is whether treatment efficacy can be maintained over the long term.

Objective: To evaluate the long-term efficacy of once-daily Bari 4 mg in patients with active rheumatoid arthritis (RA) who were either naïve to or who had inadequate response (IR) to methotrexate (MTX).

Methods: Post hoc analyses of data from two phase 3 studies, RA-BEGIN (MTX-naïve) and RA-BEAM (MTX-IR) for 52 weeks, and one long-term extension (LTE) study (RA-BEYOND) for an additional 96 weeks were conducted (148 weeks in total). At week 52, MTX-naïve patients initially treated with MTX monotherapy, Bari 4 mg monotherapy, or Bari 4 mg +MTX in RA-BEGIN were switched to open-label Bari 4 mg monotherapy for treatment in the LTE. Similarly, at week 52, MTX-IR patients initially treated with Bari 4 mg [+ background MTX noted as (+MTX) for RA-BEAM] or adalimumab (ADA) (+MTX) in RA-BEAM were switched to open-label Bari 4 mg (+MTX) for treatment in the LTE. Patients who received placebo...
(+MTX) were switched to open-label Bari 4 mg (+MTX) at week 24. The analyses of efficacy (SDAI) and physical function (HAQ-DI) were conducted on all patients who were randomized into the RA-BEGIN and RA-BEAM studies and had received ≥1 dose of study drug after randomization (mITT population). The proportion of patients who reached low disease activity (LDA), as measured by SDAI ≤11, was evaluated along with change from baseline in HAQ-DI. The non-responder imputation (NRI) method was used for the categorical analysis.

**Results:** By week 24 in RA-BEGIN (N=584), 62% of patients treated with Bari 4 mg monotherapy or Bari 4 mg +MTX achieved SDAI LDA in comparison to 40% of pts in the MTX monotherapy group; response rates seen at week 24 in the Bari treatment groups were maintained through week 148 (Fig 1A). Similarly, by week 24 in RA-BEAM (N=1,305), 52% of patients treated with Bari 4 mg (+MTX) and 50% of patients treated with ADA (+MTX) achieved a SDAI LDA in comparison to 26% of patients from the PBO (+MTX) group. The response rate seen at week 24 with Bari 4 mg and ADA were maintained through week 148, even after patients switched from ADA to Bari 4 mg at week 52 (Fig 1B). Similar improvement and maintenance patterns in physical function measured by HAQ-DI were demonstrated. The overall discontinuation rate across treatment groups from RA-BEGIN (19.5%) and RA-BEAM (14.2%) have been published. In the LTE, the discontinuation rate from Bari treatment was 13.7% for patients originating from RA-BEGIN (1.1% due to lack of efficacy, 6.4% due to safety) and 12.6% for patients originating from RA-BEAM (1.8% due to lack of efficacy, 5.9% due to safety).

**Conclusions:** Long-term treatment with Bari 4 mg demonstrated the maintenance of clinically-relevant outcomes for up to 3 years. Low discontinuation rates during the LTE indicated that Bari 4 mg treatment was well-tolerated.
Reference: [1] Genovese et al. *Annals of the Rheumatic Diseases*. 2019;78:308-309.

**Figure Legend:**
†In RA-BEGIN, rescue to Bari 4 mg + MTX was offered at week 24.
‡In RA-BEAM, rescue to Bari 4 mg (+ MTX) was offered at week 16. At week 24, all PBO + MTX patients were switched to Bari 4 mg + MTX.
§Upon entering RA-BEYOND at week 52, MTX and ADA patients were switched to Bari 4 mg.

**Figure 1. Proportion of patients achieving SDAI ≤11 in the NRI analysis**