

Assessment of pain improvement in rheumatoid arthritis patients treated with baricitinib, who were inadequate responders to methotrexate and tumor necrosis factor inhibitors

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Background: During the development programme, baricitinib (BARI) demonstrated greater and faster pain relief relative to placebo (PBO) and active comparator in different RA populations. Here, we summarise the findings from two recent post hoc analyses focused on the effect of BARI on pain in two clinically relevant patient populations: methotrexate-inadequate responders (MTX-IR; RA-BEAM) and tumor necrosis factor inhibitor-inadequate responders (TNFi-IR; RA-BEACON).

Methods: In both clinical trials (RA-BEAM and RA-BEACON), pain was assessed with a visual analog scale (VAS, 0-100 mm) at each study visit. In RA-BEAM, 1,305 patients on stable background MTX were randomized 3:3:2 to PBO, BARI 4-mg, or adalimumab (ADA) 40-mg. The likelihood of achieving $\geq 30\%$, $\geq 50\%$, and $\geq 70\%$ pain VAS improvement through Week 24 and the median time when 50% of patients achieved these pain improvement thresholds was assessed with Cox proportional hazard models and the cumulative incidence estimate. Analyses were not adjusted for multiplicity. In RA-BEACON, 527 patients were randomised to placebo ($n = 176$), BARI 2-mg ($n = 174$), or 4-mg ($n = 177$) once daily for 24 weeks. Approximately 40% of patients had received >1 TNF inhibitor and a quarter of patients had received ≥ 3 bDMARDs, representing patients with highly refractory disease. The proportion of patients achieving $\geq 30\%$, $\geq 50\%$, and $\geq 70\%$ pain relief at Week-12 was compared between BARI 2-mg or 4-mg and PBO using logistic models. Missing pain values were imputed using modified last observation-carried-forward.

Results: In the MTX-IR population, BARI-treated patients were more likely to achieve at least 30%, 50%, and 70% pain improvement than PBO and ADA with HR of 1.7, 1.9 and 2.5, respectively ($p < 0.001$) compared to PBO, and 1.1 ($p = 0.145$), 1.2 ($p = 0.032$) and 1.3 ($p = 0.003$) compared to ADA. The median time for 50% of patients to achieve at least 30%, 50%, and 70% pain improvement, respectively, was 1.9, 4.0 and 12.4 weeks for BARI, 2.0, 7.9 and 20.0 weeks for ADA, and 4.6, 14.0 and >24 weeks for PBO. In the TNFi-IR population, at Week-12, significantly more patients achieved $\geq 30\%$, $\geq 50\%$, and $\geq 70\%$ pain relief with BARI 2-mg or 4-mg vs PBO ($p < 0.05$, for all comparisons). Consistent improvements were observed regardless of baseline pain. Regardless of treatment history, patients receiving BARI 2-mg or 4-mg were more likely to reach all pain relief thresholds than placebo.

Conclusion: In both MTX-IR and TNFi-IR populations, BARI demonstrated greater pain improvement than comparators at Weeks 24 and 12, respectively.