ASSOCIATION BETWEEN BASELINE HAEMOGLOBIN LEVELS AND RADIOGRAPHIC JOINT DAMAGE PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB OR STANDARD OF CARE

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Background: In patients with active rheumatoid arthritis (RA), haemoglobin (Hb) levels have been inversely associated with radiographic progression of structural joint damage.[1-3]. In two randomized 52-week (wk) studies, baricitinib (BARI), a selective JAK1/JAK2 inhibitor, reduced radiographic progression in patients with moderate to severe active RA who had received no/minimal prior methotrexate (MTX; RA- BEGIN)[4] or had inadequate response to MTX (RA-BEAM).[5]

Objectives: To assess the association between baseline Hb levels and structural damage progression and to study the effect of BARI 4-mg once daily on structural damage progression at 52 wks based on baseline Hb levels.

Methods: Data from the modified intention-to-treat (mITT) populations of RA-BEGIN (MTX=210; BARI 4-mg=159; BARI 4-mg + MTX=215 patients) and RA-BEAM (placebo [PBO]=488, adalimumab [ADA]=328, BARI 4mg=487 patients) were included for analysis. Structural damage progression was defined as change from baseline (CFB) greater than the smallest detectable change (SDC) in the modified total Sharp score (mTSS) at wk 52. In RA-BEGIN SDC was 1.4 and in RA-BEAM SDC was 1.5. Missing mTSS data at wk 52 were imputed using linear extrapolation based on baseline data and the most recent radiographic data prior to the missed radiograph. Observed proportions of patients with CFB in mTSS >SDC at wk 52 were calculated for low (males:<13.0g/dL, females:<12.0g/dL) or normal baseline Hb for each treatment arm from both studies. Multivariate logistic regression (MLR) was used to study the association of baseline Hb with structural joint damage at 52 wks. The MLR included treatment, baseline Hb (g/dL), baseline hsCRP (Normal $\leq$3mg/L; Elevated >3mg/L), baseline CDAI, baseline HAQ-DI, BMI, smoking status (Yes/No), geographical area and joint erosion status at baseline (Yes/No in RA-BEGIN; $\geq$3/1 or 2 + seropositivity in RA-BEAM). Thirty-nine patients from RA-BEGIN (MTX=18; BARI 4-mg=5; BARI 4-mg + MTX=16) and 68 patients from RA-BEAM (PBO=36; ADA=18; BARI 4mg=14) with missing baseline/post-baseline radiographic data were excluded from MLR analyses; in addition, 7 and 19 patients from RABEGIN and RA-BEAM with missing data for the covariates of the MLR were excluded. All analyses were post-hoc.

Results: Overall, RA-BEGIN and RA-BEAM patients with higher baseline Hb were less likely to show CFB in mTSS >SDC (RA-BEGIN: adjusted odds ratio [OR]=0.72, p=0.001; RA-BEAM: adjusted OR=0.76, p<0.001) at 52 wks, independent of other factors included in the MLR model. In RABEGIN (Figure A), CFB in mTSS >SDC was less frequent in patients with low baseline Hb who received BARI alone or BARI + MTX versus those on MTX alone; in patients with normal baseline Hb, the difference between treatments was less pronounced. In RA-BEAM (Figure B), CFB in mTSS >SDC was less frequent in patients with both low or normal baseline Hb for patients receiving BARI or ADA versus PBO.
Conclusion: In patients with RA, lower baseline Hb levels were associated with increased structural damage progression. Treatment with BARI 4-mg reduced structural progression, irrespective of patient baseline Hb status; structural progression at 52 wks was more pronounced in patients with low baseline Hb receiving MTX alone (RA-BEGIN) or PBO and background MTX (RA-BEAM).

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Figure. Observed proportions of patients with change from baseline in mTSS >SDC at week 52 based on baseline haemoglobin levels. ADA, adalimumab; BARI, baricitinib; CFB, change from baseline; Hb, haemoglobin; IR, inadequate response; mTSS, modified total Sharp score; MTX, methotrexate; PBO, placebo; SDC, smallest detectable change.

Figure A. RA-BEGIN (no/minimal previous MTX; N=545)

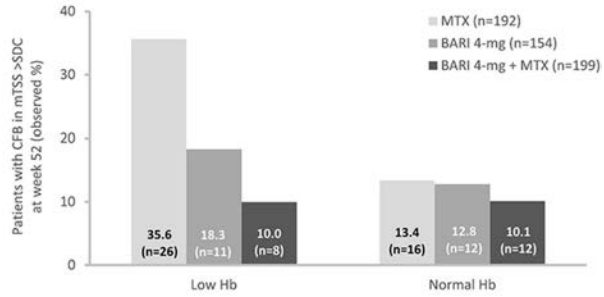

Figure B. RA-BEAM (MTX IR, on background MTX; N=1235)