

Generalization of the Effectiveness of Baricitinib 4mg among bDMARD-IR Rheumatoid Arthritis Patients from a RCT to a Real-world Population in China

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BACKGROUND

■ Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation and joint destruction associated with pain, progressive disability, systemic comorbidities and early death¹.

■ Baricitinib is an oral selective Janus kinase (JAK) inhibitor (JAK1/JAK2)² approved for the treatment of patients with moderate to severe active RA in China.

■ Baricitinib 4mg was approved in China for 1) TNFi-IR RA patients or 2) cDMARDs-IR RA patients with inadequate response to baricitinib 2mg for at least 3 months.

■ Although randomized controlled trials (RCT) have demonstrated the efficacy of baricitinib 4mg, the generalizability of trial results to Chinese RA patients may be questioned since RCTs lack “external validity”.

■ The rationale of the current study is to generate weights and generalize the efficacy results from the RA-BEACON³ (phase III RCT) of baricitinib 4mg in bDMARDs-IR RA patients to a local Chinese RA population (CREDIT)⁴ using reweighting approach.

OBJECTIVES

■ To generalize the effectiveness of baricitinib 4mg once daily in Chinese bDMARD-IR RA patients from the phase III RCT to a “real-world” population using the reweighting approach.

- Weights at baseline for RA-BEACON IPD and CREDIT data
- Generalized effectiveness of baricitinib 4mg versus placebo by ACR20, ACR50 and ACR70 at Week 12
- Generalized effectiveness of baricitinib 4mg versus placebo by change from baseline to Week 12 in HAQ-DI, DAS28-hsCRP, DAS28-ESR, CDAI and SDAI scores.

METHODS

Study Design

■ This study was a post hoc retrospective analysis using individual patient data (IPD) from the RA-BEACON trial and aggregated data from the CREDIT registry to explore the generalizability of RA-BEACON results to moderate-to-severe RA patients in China

Key Inclusion Criteria

- RA-BEACON
 - Age≥18 with moderate to severely active RA
 - Insufficient response or intolerance to previous TNFi treatment
- CREDIT
 - Registered from 1 January 2016 to 1 July 2021
 - Age≥18 with active RA
 - Insufficient response to ≥1 bDMARDs

Statistical Analysis

■ Weights were calculated using IPD from the RA-BEACON trial (phase III RCT, bDMARD-IR patients) and Aggregated Real-world data (AGR) from CREDIT registry in China by generalized method of moments

– Generalized method of moments is an optimization algorithm subject to the constraints of the first moment equality between selected covariates from both populations

- Match IPD to AGR with respect to covariates including gender, age, RF/ACPA, ESR, CDAI and CRP
- Balance achieved after reweighting so as to generalize the effectiveness of baricitinib 4mg versus placebo to the real-world population

■ Weighted Logistic regression was used to evaluate binary effectiveness indicators including ACR20, ACR50 and ACR70

■ Weighted covariance analysis was used to evaluate continuous effectiveness indicators including CDAI, SDAI, DAS28-ESR, DAS28-CRP and HAQ-DI scores

■ Sandwich estimators were utilized for evaluating p-values and 95% CIs of odds ratio and LSM from weighted analyses.

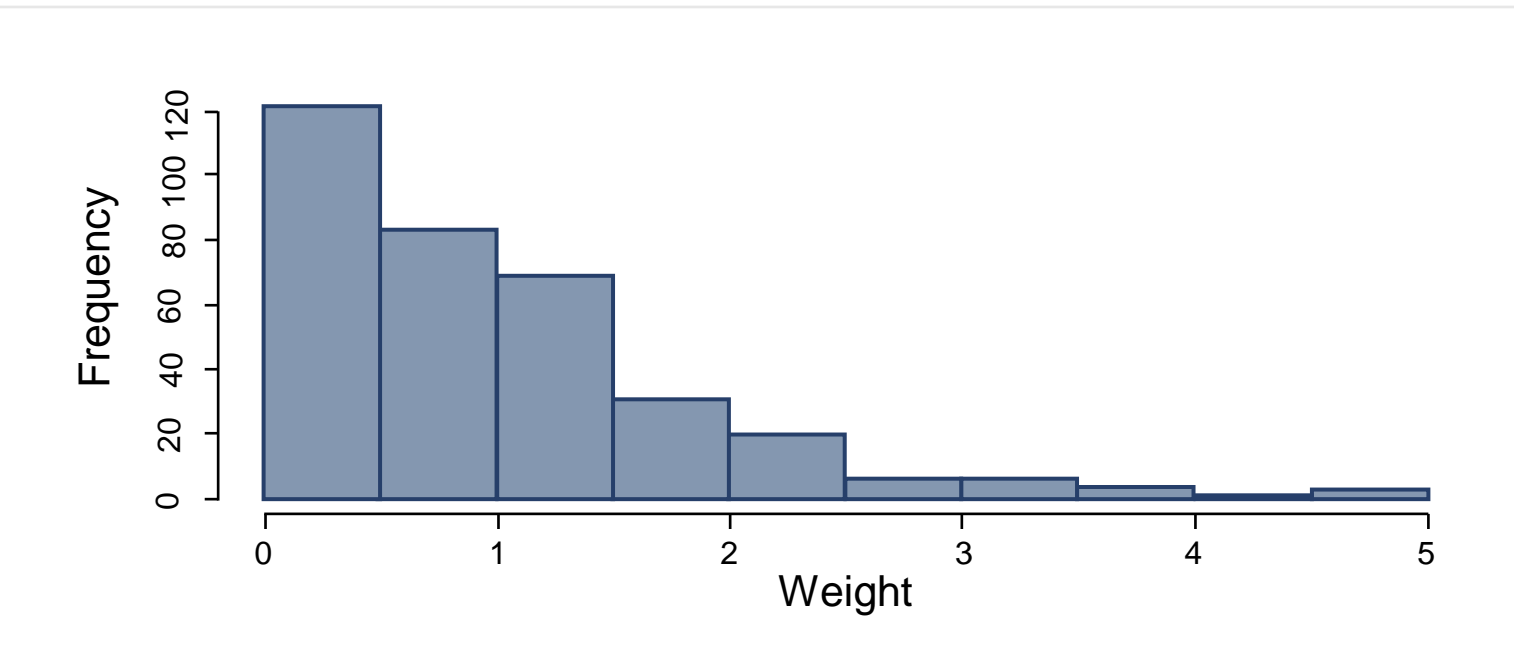
RESULTS

■ Baseline characteristics matched for reweighting. Non-missing IPD of 343 patients from RA-BEACON were matched to a corresponding CREDIT population of 1006. Balance was achieved after reweighting with respect to covariates including gender, age, RF/ACPA, ESR, CDAI and CRP.

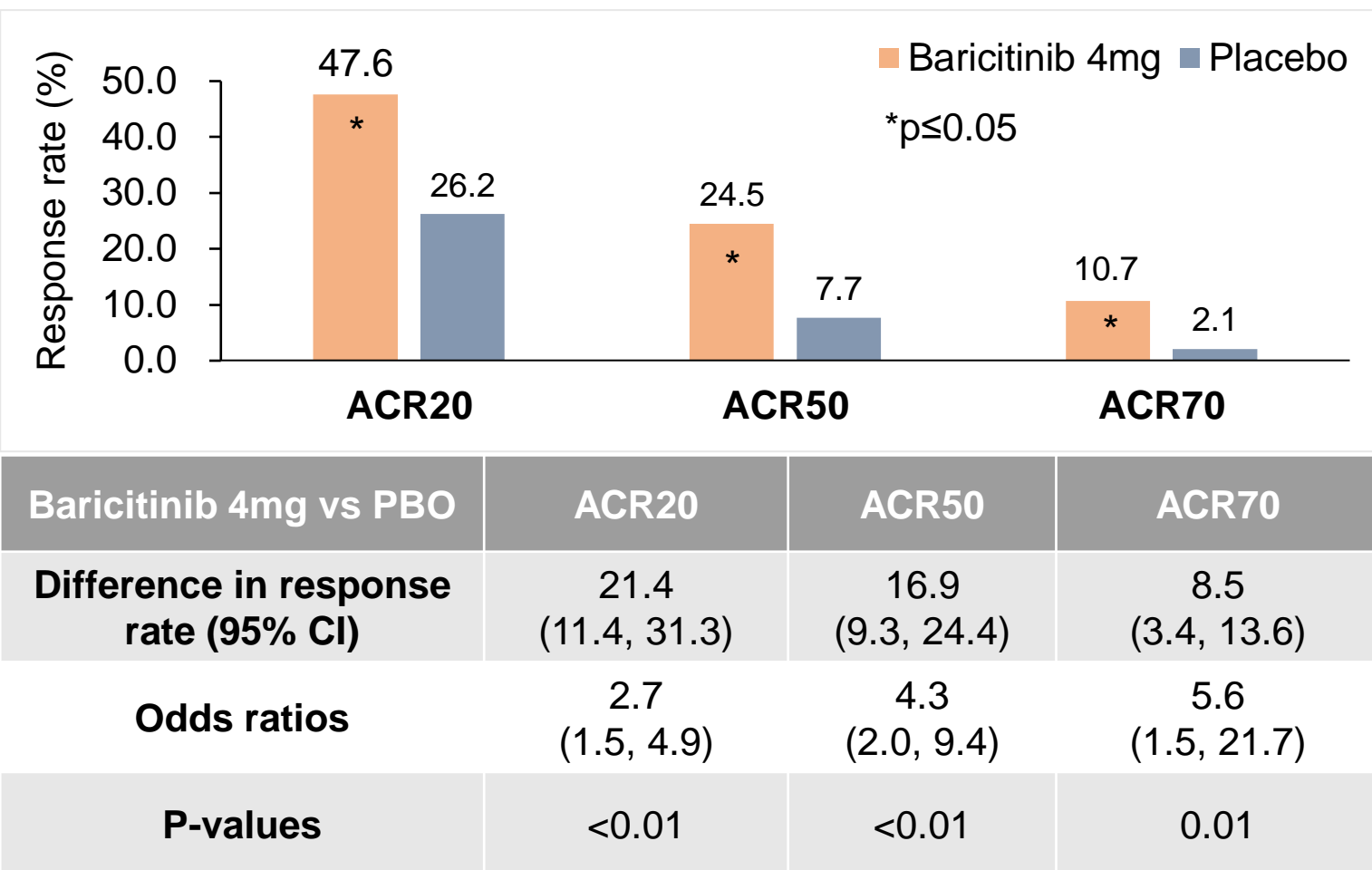
Baseline covariates matched on			
Covariate	RA-BEACON / Pre-Match/(N=343)	RA-BEACON / Post-Match/(N=193.8*)	CREDIT (N=1006)
Gender (Female)	83.1% (285)	80.5% (156)	80.5% (809)
Age	56.2±10.9	52.5±11.8	52.5±12.5
RF/ACPA Positive [Y]§	79.0% (271)	97.3% (189)	97.3% (979)
ESR	47.6±25.0	48.0±25.5	48.0±51.0
CDAI	40.5±13.2	33.6±12.0	33.6±16.0
CRP	20.1±24.8	17.4±19.1	17.4±40.7

*The Post-Match population (N=193.8) is the effective sample size (ESS), indicating number of patients actually contributing to the analysis based on the size of weights.
§The covariate “RF/ACPA Positive” turns to Y(yes) if the patient has positive RF/positive ACPA/both positive.

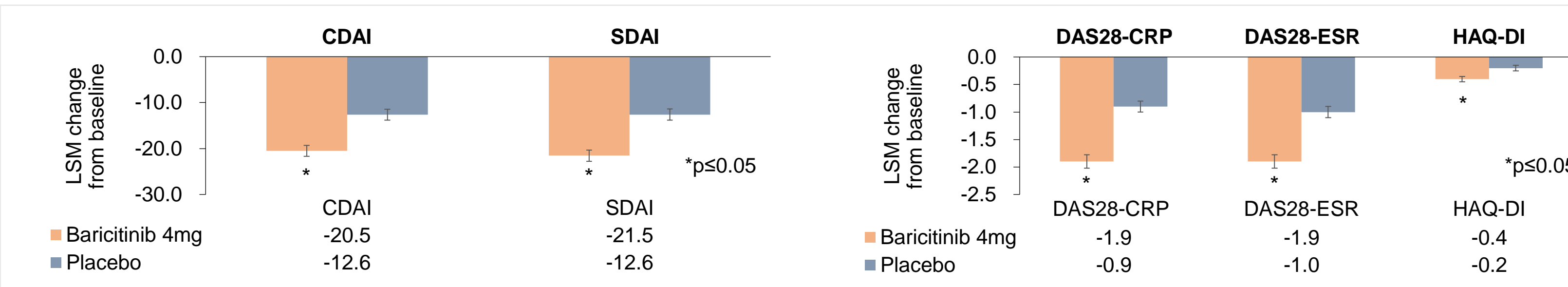
■ Weight distribution. Obtained by generalized method of moments that matches IPD to AGR, weights are smoothly distributed without extreme values.



■ Higher response rates were observed in weighted ACR20 (47.6% vs 26.2%), ACR50 (24.5% vs 7.7%) and ACR70 (10.7% vs 2.1%) scores in patients from the baricitinib 4mg arm compared to the placebo arm at Week 12 (p≤0.05 for all outcomes). Difference in response rate and odds ratios between arms was evaluated.



■ From analysis of covariance with weights (ANCOVA), statistically significant improvements in continuous endpoints(CDAI, SDAI, DAS28-CRP, DAS28-ESR and HAQ-DI) were also observed in patients from the baricitinib 4mg arm compared to the placebo arm (p≤0.05 for all outcomes) at Week 12.



CONCLUSIONS

- Comparable outcomes were observed between the original and reweighted population, indicating the generalizability of efficacy results from the RA-BEACON trial population to the real-world Chinese RA population.
- This study provided evidence for the effectiveness of baricitinib 4mg for the treatment of Chinese bDMARD-IR RA patients.

DISCLOSURES

■ Jiang N, Li M, Wang Y, Zhao J, Tian X, Zeng X have been investigators of this study; Zhu H, Li J, Xu J, Zhang Y are employees Eli Lilly and Company.

■ This study was sponsored by Eli Lilly and Company.

ABBREVIATION

■ **ACR**: American College of Rheumatology; **ACPA**: Anti-cyclic Citrullinated Peptides Antibodies; **AGR**: Aggregated Real-world data; **bDMARD**: Biologic Disease-modifying Antirheumatic Drug; **bDMARD-IR**: Biologic Disease-modifying Antirheumatic Drug:Inadequate Response; **CDAI**: Clinical Disease Activity Index; **CI**: Confidence interval; **CREDIT**: Chinese Registry of Rheumatoid Arthritis; **CRP**: C-reactive Protein; **cDMARDs**: Conventional Disease-Modifying Antirheumatic Drugs; **DAS28**: Disease Activity Score with 28-Joint; **ESR**: Erythrocyte Sedimentation Rate; **HAQ-DI**: Health Assessment Questionnaire-disability Index; **IPD**: Individual Patient Data; **JAK**: Janus kinase; **LSM**: Least Square Mean; **PBO**: Placebo; **RA**: rheumatoid arthritis; **RCT**: Randomized Controlled Trials; **RF**: Rheumatoid Factor; **SDAI**: Simplified Disease Activity Index; **TNFi**: Tumor Necrosis Factor Inhibitor

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