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SAT0152

EFFICACY OF BARICITINIB IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS WITH 3 YEARS OF TREATMENT: RESULTS FROM A LONG-TERM STUDY

J. S. Smolen¹, L. Xie², B. Jia², P. C. Taylor³, G. R. Burmester⁴, Y. Tanaka⁵, A. Elias², A. Cardoso², R. Ortmann², C. Walls², M. Dougados⁶. ¹Medical University of Vienna, Division of Rheumatology, Vienna, Austria; ²Eli Lilly and Company, Indianapolis, United States of America; ³University of Oxford, Oxford, United Kingdom; ⁴Charité - University Medicine Berlin, Berlin, Germany; ⁵University of Occupational and Environmental Health, Japan, Kitakyushu, Japan; ⁶Hospital Cochin Paris, Paris, France

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.

Objectives: 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).

Figure 1. Proportion of patients achieving SDAI ≤11 in the NRI analysis¹In RA-BEGIN, rescue to Bari 4 mg + MTX was offered at week 24.¹In 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.²Upon entering RA-BEYOND at week 52, MTX and ADA patients were switched to Bari 4 mg.

Conclusion: 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.

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SAT0153

GENDER DOES NOT INFLUENCE CLINICAL RESPONSE TO JAK INHIBITORS IN RHEUMATOID ARTHRITIS: AN ITALIAN MULTICENTRE ANALYSIS

F. R. Spinelli¹, M. S. Chimenti², M. Vadacca³, C. Iannuccelli¹, P. Conigliaro², S. L. Bosello⁴, F. Ceccarelli¹, C. Garufi¹, G. Raffone², P. Di Noi³, D. Bruno⁵, A. Afeltra³, R. Perricone², F. Conti⁶, E. Gremese^{4,5} on behalf of FRS, MSC, PC, MV, CI, SLB and EG on behalf of ReDo - Reumatologhe Donne - association of Italian female rheumatologists.. ¹Sapienza Università di Roma, Rheumatology Unit, 00161, Italy; ²University of Rome Tor Vergata, Rheumatology, Allergy and Clinical Immunology, Rome, Italy; ³Campus Biomedico University of Rome, Rheumatology, Allergy and Clinical Immunology, Rome, Italy; ⁴Fondazione Policlinico Universitario A. Gemelli IRCCS, Rheumatology Division, Rome, Italy; ⁵Università Cattolica del Sacro Cuore, Rheumatology Division, Rome, Italy; ⁶Sapienza Università di Roma, Rheumatology Unit, Rome, Italy

Background: Gender medicine aims at describing how diseases differ between men and women in terms of epidemiology, clinical feature, therapeutic approach, treatment response and prognosis, psychological and social impact. Rheumatoid Arthritis (RA) affects women 2-3 times more than men. Female gender seems to be independently associated to a more refractory disease and a worst response to conventional synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs) and biological DMARDs. Male patients achieve remission more often than females probably due to the higher number of tender joints reported by the latter.

Objectives: In the light of the effect of Janus kinases inhibitors (JAKi) on pain, the objective of the study was to investigate whether gender might affect the achievement of remission or low disease activity in RA patients treated with baricitinib and tofacitinib.

Methods: We performed a multicentric, prospective study on consecutive patients starting one of the two available JAKi: baricitinib and tofacitinib. Demographic and clinical data were recorded in a dedicated database and included: gender, age, disease duration, serological status (Rheumatoid Factor – RF; anti-citrullinated peptide antibodies, ACPA) number of previous csDMARDs and bDMARDs, number of tender joints (TJ) and swollen joints (SJ), C reactive protein (CRP); patient global assessment (PGA) and pain were recorded on a 0-100 mm visual-analogue scale (VAS). Disease activity score (DAS) 28 was calculated at baseline and at two follow-up visits (after 3-4 months and after 6-8 months). Data were expressed as mean ± standard deviation or median (interquartile range) according to variables' distribution. Continuous variables were compared by Mann Whitney test while dichotomous ones by Chi-squared test; p value < 0.05 were considered statistically significant.

Results: We enrolled 182 RA patients (149 F:33M) with similar age (F 58±12 vs M 60±10) and disease duration (F 143±101 vs M 147±105 months). Females and males were previously treated with the same number of csDMARDs [2(2)] but female have previously received numerically more bDMARDs [2(3) vs 1(2)]. At the 3 timepoints females and males showed similar number of TJ, SJ, similar values of CRP, PGA and pain. We did not observe any difference in percentage

of males and females achieving remission or low disease activity according to gender (figure 1A) nor in terms of reduction of TJ, SJ and PGA; only pain decreased significantly more in male than in female patients at both timepoints (figure 1B).

Conclusion: In RA patients treated with JAK inhibitors, even if the effect of JAKi on pain seems to be more relevant in male than in female, gender seems not to influence the overall clinical response, allowing men and women the same probability of reaching the therapeutic target

References:

Figure 1. remission and low disease activity (A) and pain (B) in male and female patients

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SAT0154

EXAMINATION OF CYP3A5 GENOTYPE IS USEFUL FOR INTRODUCTION OF TACROLIMUS TREATMENT IN OUTPATIENTS WITH RHEUMATIC DISEASES

S. Takahashi^{1,2}, S. Horibata^{2,3}, S. Hatachi¹, M. Takahashi², M. Katayama¹, S. Mukohara¹, N. Amano¹, K. Yoshida¹, K. Yorifuji^{2,3}, S. Kumagai^{1,2}. ¹Center for Rheumatic Disease, Shinko Hospital, Kobe, Japan; ²Shinko Institute for Medical Research, Kobe, Japan; ³Department of Pharmacy, Shinko Hospital, Kobe, Japan

Background: Though several studies showed the efficacy of tacrolimus (TAC) in patients with rheumatoid arthritis (RA) in a dose-dependent manner [1], the relationship between efficacy and concentration of TAC remained unclear. Genetic polymorphisms of cytochrome P450 (CYP) 3A5 were reported not only to play an important role in pharmacokinetics of TAC but also to have an influence on clinical outcomes in patients of rheumatic diseases. Several reports showed that the blood concentration of TAC in patients with a CYP3A5 *1 allele (EX, expressor) was lower than that of patients with a CYP3A5 *3/*3 (NEX, non-expressor) [2].

Objectives: To assess the relationship between efficacy and concentration of TAC in patients with RA, and to examine the usefulness of CYP3A5 genotype screening to detect outpatients suitable for TAC treatment.

Methods: We examined the relationship between disease activity score (DAS) 28-CRP and concentration of TAC in patients with RA. TAC was taken after the evening meal and blood samples were taken 12±4h after TAC administration. Next we investigated the relationship between genotype frequencies of CYP3A5 and concentration of TAC in patients with rheumatic disease without having renal dysfunction (eGFR<60) and also investigated the influence of concomitant drugs, such as strong inhibitors of CYP3A4/5 or metabolized by CYP3A4/5, to C/D value in each NEX and EX group. The blood concentration of TAC normalized to the corresponding dose per body weight (C/D, ng/ml per mg/kg) was analyzed according to genetic variation in CYP3A5. Furthermore we investigated the relationship between genotype frequencies of CYP3A5 and concentration of TAC in patients with rheumatic disease at first visit and second visit after starting TAC administration to assess the possibility for making rapid attainment of enough concentrations of TAC in early stage of treatment.

Results: The concentration of TAC tended to be negatively correlated with the disease activity of RA. The C/D value in the NEX group (n=16) was 124.7±62.1, which was significantly higher than that in the EX group (n=23; 67.7±29.8; $P<0.001$). When comparing patients using concomitant drugs which are strong inhibitors of CYP3A4/5 or metabolized by CYP3A4/5 with patients not using those drugs, the each C/D value of NEX group was

122.9±52.3 (n=9) and 126.9±77.3 (n=7), and that of EX group was 71.3±32.2 (n=12) and 63.8±28.0 (n=11). There were no significant differences between these groups. In NEX group, when comparing concentration of TAC at first visit and second visit after starting TAC administration, the each concentration of TAC was 3.14±2.06 ng/ml and 3.80±2.20 ng/ml in NEX group (n=10), and that of TAC was 1.82±0.82 ng/ml and 2.69±1.52 ng/ml (n=11) in EX group (Figure).

Conclusion: TAC showed efficacy in patients with RA in a concentration-dependent manner. EX patients may be impossible to achieve enough concentration of TAC even though using TAC of 3mg/day, approved dose for patients with RA in Japan, and NEX patients could make rapid attainment of enough concentrations of TAC in early stage of treatment, suggesting that we should consider induction of TAC only in NEX outpatients. Furthermore, drugs only slightly affected concentration of TAC in this study, suggesting that we can use TAC without any special attention to concomitant drugs.

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NEX patients rapidly gain higher TAC concentration than EX patients in early stage of treatment

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SAT0155

WHOLE BLOOD TRANSCRIPTIONAL CHANGES FOLLOWING SELECTIVE INHIBITION OF JANUS KINASE 1 (JAK1) BY FILGOTINIB IN MTX-NAÏVE ADULTS WITH MODERATELY-TO-SEVERELY ACTIVE RHEUMATOID ARTHRITIS (RA) (FINCH3)

P. C. Taylor¹, B. Downie², E. Elboudwarej², S. Kim², A. Hertz², A. M. Mirza², J. Siegel², R. E. Hawtin², J. Liu². ¹University of Oxford, Botnar Research Centre, Nuffield Dept Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom; ²Gilead Sciences Inc., Foster City, United States of America

Background: Filgotinib (FIL), an oral selective JAK1 inhibitor, has shown efficacy and safety in multiple phase 3 studies in adults with moderately-to-severely active rheumatoid arthritis (RA). We have previously described the molecular response to FIL in large-scale RNA sequencing studies of gene expression in other RA populations¹⁻³ and conducted a similar study in methotrexate (MTX)-naïve RA patients (pts) (FINCH3).

Objectives: Identify gene transcripts and biological pathways associated with RA and those altered in response to FIL treatment.

Methods: MTX-naïve RA pts who were enrolled in FINCH3 (ClinicalTrials.gov NCT02886728) received a stable dose of MTX with placebo (PBO+MTX), FIL 200mg alone (FIL 200mg monotherapy), or one of two doses of FIL once daily (QD) together with MTX (FIL 100mg+MTX, FIL 200mg+MTX). Whole blood samples were collected from pts using PAXgene tubes at baseline, week 4,