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SAFETY OF BARICITINIB IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS (RA): THE 2020 INTERIM REPORT FROM ALL-CASE POST MARKETING SURVEILLANCE IN CLINICAL PRACTICE

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Background: An all-case post marketing surveillance (PMS) of baricitinib (Bari), that started in Sep 2017, collects safety and effectiveness for the first 24 wks of treatment and continues to collect serious adverse events (SAEs) for 3 yrs.

Objectives: To evaluate Bari safety in RA patients (pt) in clinical practice.

Methods: We report pt baseline demographics and adverse events (AEs) up to 24 wks for pts whose case report files for 24-wk data were completed as of Jun 2020.

Results: Data from 3445 pts were analyzed (females=80%, mean age=64yr, mean RA duration 12yr). Bari dose regimen was as follows: 4mg, 60%, 2mg, 27%, 4mg→2mg, 5%, 2mg→4mg, 5%, and others, 2%. Concomitant use of MTX and glucocorticoid was 65% and 48%, respectively. 74% continued treatment for 24 wks. AE and SAE were recognized in 887 (26%) and 122 pts (4%), respectively. 6 pts died of pneumonia, aspiration pneumonia, bacterial pneumonia, cerebral infarction/ILD/aspiration pneumonia, adenocarcinoma, and colorectal cancer. Major AEs were as follows: herpes zoster=3%, liver dysfunction=3%, serious infection=1%, anemia=1%, hyperlipidemia=1%, malignancy=0.3%, interstitial pneumonia=0.2%, MACE=0.1%, and VTE=0.1%.

Conclusion: Data do not show new safety concerns and encourage guideline-compliant use of Bari.

Disclosure of Interests: Takao Fujii Speakers bureau: Chugai Pharmaceutical Co. Ltd.; Eisai Co. Ltd.; Eli Lilly Japan K.K.; Janssen Pharmaceutical K.K.; Ono Pharmaceutical Co. Ltd., Consultant of: Asahikasei Pharma Corp, Grant/research support from: Asahikasei Pharma Corp; AbbVie Japan GK; Chugai Pharmaceutical Co. Ltd.; Eisai Co. Ltd.; Eli Lilly Japan K.K.; Mitsubishi-Tanabe Pharma Co.; Ono Pharmaceutical Co., Ltd.; Tatsuya Atsumi Speakers bureau: AbbVie Japan GK; Astellas Pharma Inc.; Bristol-Myers Squibb Co. Ltd.; Chugai Pharmaceutical Co. Ltd.; Daiichi Sankyo Co. Ltd.; Eisai Co. Ltd.; Eli Lilly Japan K.K.; Mitsubishi Tanabe Pharma Co.; Pfizer Japan Inc.; Takeda Pharmaceutical Co. Ltd., UCB Japan Co. Ltd., Consultant of: AbbVie Japan GK; AstraZeneca plc.; Boehringer Ingelheim Co. Ltd.; Medical & Biological Laboratories Co. Ltd.; Novartis Pharma K.K.; Ono Pharmaceutical Co. Ltd.; Pfizer Japan Inc., Grant/research support from: Astellas Pharma Inc., Alexion Inc.; Chugai Pharmaceutical Co. Ltd., Daiichi Sankyo Co. Ltd., Mitsubishi Tanabe Pharma Co., Otsuka Pharmaceutical Co., Ltd. Pfizer Japan Inc.; Takeda Pharmaceutical Co. Ltd., Nami Okamoto Speakers bureau: AbbVie Japan GK; Asahikasei Pharma Co.; AYUMI Pharmaceutical Co. Eisai Co. Ltd.; Bristol-Myers Squibb Co. Ltd.; Eli Lilly Japan K.K.; Mitsubishi-Tanabe Pharma Co.; Pfizer Japan Inc. Sanofi K.K.; Chugai Pharmaceutical Co. Ltd.; Novartis Pharma Co.; Teijin Pharma Ltd.; Torii Pharmaceutical Co., Ltd., Nobunori Takahashi Speakers bureau: AbbVie Japan GK; Eisai Co. Ltd.; Mitsubishi Tanabe Pharma Co.; Pfizer Japan Inc.; Chugai

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TOFACITINIB SUPPRESSES SEVERAL JAK-STAT PATHWAYS IN RHEUMATOID ARTHRITIS AND BASELINE SIGNALING PROFILE ASSOCIATES WITH TREATMENT RESPONSE

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Background: Cytokines are important mediators of inflammation and tissue destruction in rheumatoid arthritis (RA) ¹. Several cytokines involved in RA pathogenesis act through Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway ². The effects of JAK-inhibitor tofacitinib on cytokine signaling *in vitro* are well established, while *in vivo* evidence in patients remains scarce.

Objectives: To investigate *in vivo* in rheumatoid arthritis patients i) which JAK-STAT pathways are inhibited by tofacitinib and ii) if baseline signaling profile is associated with the treatment response.

Methods: Sixteen patients with active RA, despite treatment with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), received tofacitinib 5mg twice daily for three months. Levels of basal and cytokine-induced phosphorylated STATs and total STAT1 and STAT3 in peripheral blood monocytes, T cells and B cells were measured by flow cytometry. mRNA expression of JAKs, STATs and suppressors of cytokine signaling (SOCS) were measured from peripheral blood mononuclear cells (PBMCs) by quantitative PCR. Association of baseline signaling profile with treatment response (the change from baseline in disease activity score (DAS28)) was studied by calculating correlation coefficients.

Results: Treatment with tofacitinib and csDMARDs decreased median DAS28 from 4.4 to 2.6 ($p < 0.001$). Tofacitinib significantly decreased cytokine-induced phosphorylation of all JAK-STAT pathways studied. Basal STAT1, STAT3, STAT4 and STAT5 phosphorylation in monocytes and/or T cells was downregulated by tofacitinib. No changes were observed in STAT1 and STAT3 protein