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 pp 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, 5%, 2mg

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


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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 RA pathogenesis has been established, while the role of baseline cytokine expression and JAK-STAT signaling has been not clear.

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 14 mg twice daily for three months. Levels of basal and cytokine-induced phosphorylated STATs and total STATs were measured by flow cytometry and mRNA expression of JAKs, STATs and suppressors of cytokine signaling (SOCS) was measured 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 (14 mg twice daily) led to a significant improvement in DAS28 from 4.4 to 2.6 (p < 0.001). Tocaitinib 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 phosphorylation.

Disclosure of Interests: K. Kuuliala, R. Peltomaa, A. Virtanen, A. Kuuliala, A. Kurttila, A. Kinnunen, M. Leirisalo-Repo, O. Silvennoinen, P. Isomäki, Tampere University, Faculty of Medicine and Life Sciences, Tampere, Finland; 2University of Helsinki, Department of Bacteriology and Immunology, Faculty of Medicine, Helsinki, Finland; 3University of Helsinki, Department of Pediatrics, Faculty of Medicine, Helsinki, Finland; 4Tampere University Hospital, Centre for Rheumatic Diseases, Tampere, Finland; 5Finnlab Laboratories, Pirkanmaa Hospital District, Tampere, Finland; 6University of Helsinki, Institute of Biotechnology, HiLIFE Helsinki Institute of Life Sciences, Helsinki, Finland

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