**AB0249**

**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 market 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=64y; mean RA duration 12y). Bari dose regimen was as follows: 4mg, 60mg, 2mg, 27%, 4mg→2mg, 5mg, 2mg→4mg, 5%, and others, 2%. Concomitant use of MTX and/or biologic dmard (bDMARD) was in 45% 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, 24 wks. AE and SAE were recognized in 887 (26%) and 122 pts (4%), respectively. 6 pts died of pneumonia, aspiration pneumonia, bacterial pneumonia, miliary tuberculosis, and colorectal cancer. Major AEs were as follows: herpes zoster=3%, liver dysfunction=3%, severe infection=1%, anemia=1%, hyperlipidemia=1%, malignancy=0.3%, interstitial pulmonary oedema=0.2%, MACE=0.1%, and VTE=0.015%.

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


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**AB0250**

**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). Several cytokines involved in RA pathogenesis act through Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway. The effects of JAK-inhibitor tofacitinib on cytokine signaling in vitro and ex vivo has been established, whereas the evidence in patients is scarce. We aimed to expand our baseline knowledge of the activity of tofacitinib in patients with RA.

**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 for twice daily for three months. Baseline samples of peripheral blood mononuclear cells (PBMCs) were stimulated with JAK-si- 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 resulted in statistically significant changes between baseline and week 12 in 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


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