cases occurred both early and lately during treatment courses, suggesting LTBI screening failures, treatment non-adherence or re-exposure. Current application and content of the protocol for screening and treatment of LTBI needs to be reviewed.

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Molecular characterization of the serum profile associated to the increased cardiovascular risk in rheumatoid arthritis patients. Effects of biological drugs.

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Background: Objectives: 1- To characterize the serum molecular profile associated to the increased cardiovascular risk in rheumatoid arthritis patients. 2- To evaluate the in vivo and in vitro effects of biological drugs on the reestablishment of this altered molecular profile.

Methods: Serum samples of 280 RA patients and 100 healthy donors (HD) were studied. miRNomes were identified using next-generation sequencing miRNA assay (HTG EdgeSeq technology). The inflammatory profile, Netosis-derived products, and circulating biomolecules related to atherosclerosis marker. The in vivo effects of biologic drugs such as Infliximab (IFX), Tocilizumab (TCZ) and Rituximab (RTX) were evaluated before and after 6 months of therapy in 45, 20 and 25 RA patients, respectively. Serum from RA patients with high and low CV risk scores - either before and after IFX, TCZ and RTX therapies-, were further added with HUVECs, monocytes, and neutrophils purified from HD, and activity profiles were evaluated.

Results: The mRNA whole transcriptome assay identified 104 circulating miRNAs altered in RA patients. Functional classification (IPA) established their involvement in inflammatory response, as well as in immunological and hematological diseases. Circulating biomolecules related to inflammation -interleukins, chemokines, adhesion molecules-, Netosis -cell-free nucleosomes, elastase and DNA- and oxidative stress -lipperoxides, nitrated proteins, and total antioxidant capacity- were also found coordinately altered in the serum of RA patients. Multivariant analyses showed that levels of a number of those altered biomolecules and circulating microRNAs were predictors of a high Cardiovascular Risk SCORE and the presence of a pathologic CIMT in RA patients.

The in vivo treatments with IFX, TCZ and RTX for six months reduced disease activity and induced the re-establishment of normal levels in those altered biomolecules, reducing the CV risk in RA patients.

Conclusion: Biologic drugs such as IFX, TCZ and RTX, restore the normal levels of these altered biomolecules, reducing the CV risk in RA patients.

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Scientific Abstracts

SAT0124

LONG-TERM SAFETY WITH SARILUMAB PLUS CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS AND SARILUMAB MONOTHERAPY IN RHEUMATOID ARTHRITIS: AN INTEGRATED ANALYSIS WITH 9,000 PATIENT-YEARS OF FOLLOW-UP

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Background: Sarilumab, a human IL-6R blocker approved for the treatment of RA, has shown efficacy as monotherapy and in combination with csDMARDs in Phase 3 trials.

Objectives: We assessed long-term safety from the sarilumab clinical development program in adult patients with RA who received subcutaneous (SC) sarilumab in eight clinical trials and their open-label extensions: MOBILITY (NCT01061736), TARGET (NCT0179578), ASCERTAIN (NCT01768572), EASY (NCT02057520), COMPARE (NCT01764997), ACT11575 (NCT01217814), MONARCH (NCT02392500), ONE (NCT02121210), and the open-label extension EXTEND (NCT01146652).

Methods: Data (cut-off Jan 15, 2018) were pooled from patients on sarilumab-csDMARD (N=2867) or sarilumab monotherapy (N=4417). Patients had received sarilumab 200 mg or 150 mg qw SC, except for 151 patients from MOBILITY Part A who received 100 mg qw, 150 mg qw, or 100 mg qw. Treatment-emergent (TE) adverse events (AEs), AEs of special interest (AESIs), and discontinuations were assessed.
A PHASE 2 STUDY OF E6011, AN ANTI-FRACTALKINE MONOClonal AntibOdy, IN PATIENTS WITH RHEUMATOID ARTHRITIS INADEQUATELY RESPONDING TO BIOLOGICS

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Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. We have conducted clinical trials of E6011, a novel humanized anti-FKN monoclonal antibody, for patients with rheumatoid arthritis (RA) in Japan1. This is the first report of a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study of E6011 in RA patients inadequately responding to biologics (NCT02906490).

Objectives: To evaluate efficacy and safety of E6011 compared with placebo.

Methods: During the 24-week double-blind period, patients with moderately to severely active RA of inadequate response to biologics were randomly assigned to E6011 400 mg or placebo groups at a 1:1 ratio within the initially assigned group. Patients received either E6011 400 mg or placebo at Weeks 0, 1, and every 2 weeks subsequently until Week 10 and then E6011 200 mg or 400 mg every 2 weeks between Weeks 12 and 22 in a double-blind manner. This abstract reports the results from the first 12-week placebo-controlled period.

Results: A total of 64 subjects (33 in the placebo group and 31 in the E6011 400 mg group) received study drug. Of the 64 subjects, 55 completed and 9 discontinued study treatment prematurely during the 12-week placebo-controlled double-blind period. The ACR20 response rate on Week 12 (non-responder imputation), the primary endpoint, was 27.3% (9/33 subjects) in the placebo group and 22.6% (7/31 subjects) in the E6011 group. ACR50 and ACR70 response rate at Week 12 were 3.0%, 0% in the placebo group and 9.7%, 3.2% in the E6011 group, respectively. Numerically greater improvement from baseline was found for some parameters of the ACR components in the E6011 group, however, no statistically significant differences were found in any of the ACR components between the placebo and E6011 groups. From the exploratory PK exposure analysis, there was a tendency that the effect of E6011 became clearer in the subjects who achieved higher serum trough E6011 concentration. Adverse events that occurred in at least 2 subjects in each group were nasopharyngitis, upper respiratory tract infection, and injection site reaction.

Conclusion: The long-term safety profile of sarilumab, either as monotherapy (observed for >3.5 years) or with bDMARDs (observed for >7 years), remains stable and consistent with the anticipated profile of an IL-6R blocker.