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

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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.

References:

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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)

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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,