and spleen of arthritis model mice, detailed analysis of MDSCs in inflammatory joints is limited.

**Objectives:** The purpose of this study is to characterize the MDSCs in the joints of autoimmune arthritis.

**Methods:** We isolated CD11b\(^+\)Gr1\(^+\) cells as MDSCs from joints (Jo-MDSCs), bone marrow (BM-MDSCs) and spleen (Sp-MDSCs) of arthritis-induced SKG mice, and investigated differential expressed genes (DEGs) among MDSCs from three tissues by microarray expression analysis. Furthermore, we analyzed the suppressive function of each MDSCs by investigating the effect of them on T cell proliferation and the osteoclast differentiation of each MDSCs stimulated by M-CSF and RANKL.

**Results:** Microarray analysis revealed that Jo-MDSCs highly expressed immunosuppressive DEGs (Pdil, Arg1, Egr2 and Egr3) compared to BM MDSCs or Sp MDSCs. In addition, Jo-MDSCs highly expressed NF-κB non-canonical pathway DEGs (Nfkβ2 and Relb), which are related to osteoclast differentiation. BM-MDSCs differentiated into osteoclasts but didn't suppress T cell-proliferation and Sp-MDSCs suppressed T cell-proliferation but didn't differentiate into osteoclasts. On the other hand, Jo-MDSCs was found to have both functions: T cell suppression and osteoclast differentiation potential.

**Conclusion:** Jo-MDSCs have a strong inhibitory effect on T cell proliferation and have the ability osteoclast differentiation potential.

**REFERENCES:**
We have further shown that BSSL is secreted from activated granulocytes, binds to monocytes and stimulates their migration in vitro. With that knowledge, we developed a humanized anti-BSSL antibody (SOL-116) that blocks BSSL from binding to monocytes and we are now evaluating SOL-116 as candidate drug for treatment of chronic inflammatory joint diseases, including RA, PsA and JIA in man.

Objectives: The aim of the present study was to characterize SOL-116’s biological activity in vitro and verify the therapeutic efficacy in the pristane induced arthritis (PIA) rat model.

Methods: The affinity of SOL-116 to human, mouse and rat BSSL was measured by surface plasmon resonance biosensor technology. The epitope on human BSSL was mapped by hydrogen deuterium exchange mass spectrometry (HDX-MS) and confirmed by crystallization of SOL-116 Fab-fragments with human BSSL. For efficacy evaluation, arthritis was induced in DA rats by administration of pristane. SOL-116 at three different doses (10, 30 and 90 mg/kg) or vehicle control were administered subcutaneously on day 5, 10 and 15 after disease induction. Disease activity was evaluated daily from day 7 in a blinded fashion using a macroscopic scoring system of the four limbs. To gain knowledge about the mechanism of action, the effect of SOL-116 on BSSL induced cell migration was evaluated using a transwell migration assay.

Results: SOL-116 binds to human, mouse, and rat BSSL, although a single amino acid deviation in the BSSL epitope results in approximately 80-fold lower affinity to rat BSSL. A decrease in disease severity was also seen with SOL-116 at 30 mg/kg and 10 mg/kg, indicating a dose response, albeit not statistically significant. The plasma concentration of SOL-116 at day 19 correlated significantly to the arthritis score (Figure 1B). Mechanistic studies show that BSSL stimulates migration of CD14+ monocytes and that SOL-116 is a promising biologic drug candidate for novel treatment of chronic inflammatory joint diseases.

Conclusion: The present study verifies that BSSL plays an important role in inflammation and that SOL-116 is a promising biologic drug candidate for novel treatment of chronic inflammatory joint diseases.


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POS0435 IMPACT OF COMBINATION THERAPY WITH csDMARDs ON THE EFFECTIVENESS OF BIOLOGIC OR TARGETED SYNTHETIC DMARDs IN A REAL-LIFE SETTING: RESULTS FROM THE SWISS RHEUMATOID ARTHRITIS REGISTRY (SCQM-RA)

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Background: Management guidelines of RA suggest to administer biologic or targeted synthetic DMARD (b/tsDMARD) in combination with conventional synthetic DMARD (csDMARD). Limited data exists about the impact of such csDMARD combination therapy (co-therapy) in real life settings, in particular for baricitinib use compared to other types of b/tsDMARD.

Objectives: To assess the impact of concomitant csDMARD prescription on b/tsDMARD maintenance, in a real-world setting.

Methods: This is a nested cohort study within the Swiss registry of RA patients (Swiss Clinical Quality Management (SCQM-RA)), of treatment courses with bDMARDs or baricitinib (BARI) initiated between 2017-09-01 and 2020-06-01, with at least one follow-up visit. We compared the time-to-drug-discontinuation (drug maintenance), as a measure of drug effectiveness of b/tsDMARDs, with or without csDMARD co-therapy. Our exposure of interest was the impact of csDMARD co-therapy compared to monotherapy in 3 categories of b/tsDMARDs: baricitinib (BARI), TNFI inhibitors (TNFI) and other modes of action bDMARDs (OMA). Co-therapy was defined as receiving at least one csDMARD during at least 40% of the b/tsDMARD treatment courses (TC) duration. Baseline characteristics were compared using t-tests or χ². Survival Kaplan-Meier curves, with Log-rank test, were used to assess time-to-discontinuation. Cox models were applied to obtain adjusted hazard ratios (HR) using age, BMI, corticosteroid treatment, CDAD score, disease duration, smoking, line of therapy, seropositivity, gender as covariates. Missing baseline CDAI values were imputed using linear model with quadratic regression time.

Results: 1065 TC were included (273 BARI, 319 OMA, 473 TNFI), about half of which were initiated with csDMARD co-therapy (Table 1). In the co-therapy groups, csDMARD were taken on average 88% of the TC duration. Method-wise the most prescribed csDMARD (Table 1). Even after adjustment, we found no difference in drug maintenance with and without concomitant csDMARD in the BARI group (crude p = 0.67; HR co-therapy 2.17, 95% CI [0.61;7.77], p = 0.16) and in the TNFI group (crude p = 0.13; HR co-therapy 1.24, 95% CI [0.56;2.74], p = 0.60). Adjusted drug maintenance with or without csDMARD was also similar in the OMA group, despite non-adjusted p-value in favor of monotherapy (Figure 1) (crude p = 0.007; HR co-therapy 0.66, 95% CI [0.25;1.80], p = 0.39).

Conclusion: Our data suggest that drug maintenance of BARI, OMA and TNFI, were not significantly modified by concomitant csDMARD therapy.

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