SAT0132

DOES JANUS KINASE INHIBITION INDUCED HYPERLIPIDAEMIA ASSOCIATE WITH AN INCREASE OF AORTIC STIFFNESS IN PATIENTS WITH ARTHRITIS? PRELIMINARY RESULTS OF A PROSPECTIVE PILOT STUDY ON CARDIOVASCULAR RISK

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Background: Treatment with Janus Kinase inhibitors (JAK-i) (Tofacitinib, Baricitinib) can cause an increase of serum lipids such as total cholesterol, low-(LDL) and high-(HDL) density lipoproteins in patients with arthritis (1). On the other hand, JAK-i can reduce systemic inflammation and have therefore a beneficial effect on the cardiovascular system of treated patients. However, the effects of JAK-i on the CV system have not been adequately examined. In particular, we are not aware of any "real world" data concerning CV risk of patients receiving JAK-i treatment.

Stiffness of the aortic vasculature is a modifiable, valid and independent surrogate predictor of CV risk and can be measured by carotid femoral pulse wave velocity (cfPWV). Its predicted value has been shown in a series of epidemiological studies and cfPWV is characterized as the gold standard marker for the assessment of aortic stiffness (2)

Objectives: Aim of this study was to evaluate for the first time changes of cfPWV, lipid profile and traditional CV risk factors in patients receiving JAK-i therapy.

Methods: Measurements of cfPWV, total cholesterol, LDL, HDL and inflammation markers were performed directly before and 5-12 months (median 6.5 months; 5-7, IQR) after initiation of JAK-i therapy. Additionally, traditional CV risk factors such as nicotine, obesity (Body-Mass-Index), diabetes and arterial hypertension were documented for both time points next to clinical activity markers, such as the Disease Activity Score 28 (DAS28). Differences in lipids, DAS28 and inflammation markers between the two time points were examined by paired t-Test. Given the fact that cfPWV can be confounded by mean arterial pressure (MAP), a mixed linear model, with MAP as a covariate, was used in order to test for differences in adjusted cfPWV values between two measurements.

Results: 29 patients with rheumatoid arthritis (RA) (72.4%, female) with a median age of 61.5 (51-75, IQR) years and a median DAS28-CRP of 5.27 (3.62-6.21, IQR) were recruited before (planned) initiation of JAK-i therapy. 30.7% of the patients were smokers, 38.5% had arterial hypertension and 0.4% diabetes. Median BMI was 24 kg/m² (22-29, IQR).

Mean total cholesterol and LDL values increased significantly under treatment with JAK-i (196.76±38.70 vs. 220.28±40.41 mg/dl; $p=0.010$ and 119.12±31.88 vs. 138.72±37.43 mg/dl; $p=0.032$, respectively). Moreover, MAP increased significantly during the same time period (105±9.82 vs. 109.91±11.22 mmHg; $p=0.005$). On the other hand, C-reactive protein (CRP) had decreased significantly between the two measurements [15.27 (3.82-38.9, IQR) vs. 3.82 (1.4-15.9) mg/dl; $p=0.05$]. No statistical significant difference of cfPWV values could be observed under JAK-i treatment [-0.035 95% CI (-0.615 - 0.545); $p=0.903$].

Conclusion: Our results reveal that JAK-i induced hyperlipidaemia did not associate with an increase of a surrogate marker of CV risk, such as aortic stiffness. More data are needed to conclude whether JAK-i could have a (positive or negative) effect on the CV system.

An additional examination of the current patients in 12-18 months from treatment initiation and the recruitment of new RA and psoriatic arthritis patients are currently taking place.

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- [2] Laurent S, et al (2006) Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Hear J* 27:2588–2605.

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SAT0133

PILOT CLINICAL STUDY OF A NON-INVASIVE AURICULAR VAGUS NERVE STIMULATION DEVICE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Despite the clinical benefit of current pharmacological treatments for rheumatoid arthritis (RA), there remains an unmet need for alternative treatment approaches. Vagus nerve stimulation (VNS) via an implanted device has been shown to attenuate RA disease severity in patients resistant to therapy,¹ as evidenced by a reduction in the DAS28-CRP score following a month of daily stimulation.

Objectives: This pilot study investigated the safety and efficacy of a wearable (non-invasive) device that attaches to the outer ear to treat RA via electrical stimulation of the auricular branch of the vagus nerve.

Methods: Patients with active RA (≥ 4 tender/swollen joints based on a 28-joint count, Disease Activity Score-28 with C-reactive protein (DAS28-CRP) >3.8 , active synovitis detected on ultrasound and MRI) and inadequate response to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), or csDMARD and biologic DMARDs (bDMARDs), were enrolled in this open-label study. Patients used the device for up to 30 minutes daily over the course of the 12-week study. The primary endpoint was the change in DAS28-CRP score at Week 12. Secondary endpoints included a safety analysis, proportion of patients achieving ACR20/50/70, the mean change in HAQ-DI and the proportion of patients achieving a HAQ-DI MCID of at least 0.22 over 12 weeks. Additionally, sleep scores were assessed using a visual analogue scale (0-100) at baseline and 12 weeks.

Results: Thirty patients with active RA were enrolled, of which 27 patients completed the 12-week protocol. Three patients dropped out of the study: two patients decided to seek other treatment and one patient moved out of the country. Data for three additional patients was not included in this dataset as it was still being collected. Of the 24 patients with complete 12-week datasets, 88% were female, the average age was 54.9 years, mean disease duration was 7.3 years, and four patients had an inadequate response to one or two bDMARDs.

The mean change in DAS28-CRP from baseline to Week 12 was -1.43 ($p<0.05$; Figure 1) and ACR20/50/70 response rates were 58.3%, 37.5%, and 16.7%, respectively (Figure 2). HAQ-DI change from baseline was -0.50 ($p<0.05$) at 12 weeks, and 15 out of 24 patients achieved an overall HAQ-DI reduction of 0.22 (62.5%). VAS sleep scores were significantly improved over the 12-week study. Scores for trouble falling asleep, awakened by pain at night, and awakened by pain in morning decreased by 64%, 70%, and 60%, respectively ($p<0.05$, $n=23$). Three study adverse events (AEs) were reported: two device related AEs due skin irritation at the earpiece insertion site and one AE due to mucous accumulation in the throat.

Figure 1

Percentage of subjects meeting ACR20/50/70 at 12 weeks.

Figure 2 Average DAS28-CRP is shown for each study visit. Error bars indicate standard error of mean. Percentage of subjects meeting ACR20/50/70 at 12 weeks.

Conclusion: In this pilot study, auricular stimulation was well tolerated and daily use over 12 weeks attenuated RA disease severity. Further evaluation in larger controlled studies are needed to confirm whether a non-invasive wearable device might offer an alternative approach for the treatment of RA.

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SAT0134

COMPARATIVE RISK OF CANCER ASSOCIATED WITH FIRST-LINE DMARDS USE IN RHEUMATOID ARTHRITIS: REAL WORLD EVIDENCE FROM THE OHDSI NETWORK

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Background: Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) are recommended as first line treatment for rheumatoid arthritis (RA) patients, but limited information exists on the comparative risk of cancer associated with their use.

Objectives: To compare the risk of incident overall (excluding non-melanoma skin) and site-specific cancers (colorectal, lung, lymphoma, leukaemia) associated with first-line use of csDMARDs in patients with RA.

Methods: We conducted a multinational cohort study informed by data from 7 healthcare databases including claims and electronic medical records from 4 countries (SIDIAP-Spain, MDCR-US Optum-US, CCAE-US, IQVIA AMBEMR-US, IQVIA-Germany, THIN-UK) part of the Observational Health Data Sciences and Informatics (OHDSI) network. All patients aged ≥18 years who initiated methotrexate (MTX), hydroxychloroquine (HCQ), sulphasalazine (SSZ), or leflunomide (LEF)

as first-line monotherapy after a diagnosis of RA between 2005 to 2018 were eligible. Individuals with a prior diagnosis of another inflammatory arthropathy or cancer, or <1 year of follow-up were excluded. Patients were followed from 1-year after treatment initiation to the earliest of incident cancer, loss to follow-up, or 5-years. Cox proportional-hazard models for MTX against each other csDMARD were performed after propensity score stratification. A large set of negative control outcomes were analysed to calibrate hazard ratios (cHRs). Estimates were pooled where homogeneity across sources was adequate ($I^2 < 0.4$).

Results: Across the databases, 127,547 RA patients initiating csDMARD therapy were included in the analyses (MTX: 73,996, HCL: 36,381 SSZ: 9,383 LEF: 7,787). The pooled incidence rate of overall cancer for MTX was 22.8 per 1,000 person years. The pooled summary and source-specific estimated cHRs for overall cancer are shown below in Figure 1. While little difference was seen for HCQ and SSZ compared to MTX, LEF was consistently associated with a reduced cancer risk: pooled cHR (95% CI) 0.67 (0.59 to 0.76) and cHRs ranged from 0.53 (0.36 to 0.80) in CCAE-US to 0.84 (0.58 to 1.22) in SIDIAP-Spain. There were insufficient cases to look site-specific cancers within data sources, although pooled results suggest little risk difference in leukemia, lymphoma, colorectal, or lung cancers.

Figure 1. Calibrated hazard ratios (cHRs) of overall cancer risk with their respective confidence intervals (95%CI) by study database. Database estimates not reported where adequate covariate balance not attained. Meta-analysis results not reported where $I^2 > 0.4$.

Conclusion: Compared to MTX users, patients treated with LEF had a lower risk of overall cancer. Risk of four specific cancers did not differ by first line csDMARD exposure.

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SAT0135

COMPARISON OF THE EFFICACY AND SAFETY OF TWO BRIDGING SCHEDULES OF PREDNISOLONE IN EARLY ACTIVE RHEUMATOID ARTHRITIS (CORRA): A DOUBLE-BLIND, RANDOMISED, PLACEBO-CONTROLLED TRIAL

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