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.

References:

- [1] Koopman FA, et al. (2016) Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis. *Proc Natl Acad Sci* 2016; 113: 8284–9.

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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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Background: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease potentially leading to disability, impaired functioning, and premature death. Most treatment strategies include the early use of disease-modifying antirheumatic drugs (DMARDs) such as methotrexate (MTX) which is considered as an established 'anchor' therapy. Since it takes some weeks until MTX shows clinical efficacy, glucocorticoids (GC) are widely used for bridging.

Objectives: The aim of the study "Comparison of the efficacy and safety of two starting dosages of prednisolone in early active RA" (CORRA) is to compare the efficacy and safety of two standard GC bridging schedules vs. placebo in addition to MTX, following a treat-to-target regimen, in early RA.

Methods: CORRA is an investigator-initiated, randomised, multi-center, double-blind, placebo-controlled trial. Adult RA patients who were eligible for inclusion in the trial if they had a disease duration of less than 3 years and moderate or high disease activity were recruited in one hospital and 18 rheumatology practices in Germany. Patients were randomised (1:1:1) to receive 60mg or 10mg prednisolone (Pred) orally once daily (tapered down to 5mg Pred within 8 weeks) or placebo. The duration of the intervention was 12 weeks, followed by an open observational phase for another 40 weeks. All patients were also treated with MTX (usually starting with 15mg/week followed by a treat-to-target scheme). The primary efficacy endpoint was the progression of the radiographic joint damage after one year compared to baseline as determined by the van der Heijde modification of the Sharp score (SHS). Patients, physicians and readers of radiographs were unaware of the treatment assignments. For the comparison of the two GC groups, a non-inferiority margin of 1.3 points of the SHS was set. This trial was registered at ClinicalTrials.gov, number NCT02000336.

Results: Between February 2014 and February 2017, 395 patients were included in the trial, 381 of which had sufficient data also of follow-up visits. A total of 129 patients were assigned to the 60mg Pred group, 124 to 10mg Pred and 128 to the placebo group. At baseline, mean age was 58 years, 58% were female, 55% were rheumatoid factor and 52% ACPA positive. The mean number of swollen joints was 12.8 out of 28, mean ESR was 33.6mm/h, mean CRP 2.2mg/dL, mean DAS 28 6.0. Radiographic damage was 4.9 as measured by the SHS. In the 60mg, 10mg Pred group and in the placebo group, the DAS 28 was 2.6, 3.1, 4.5 at week 4 ($p<0.001$), 3.1, 2.8, 3.6 at week 12 ($p<0.001$), and 2.7, 2.6, 2.8 at week 52 ($p=0.411$), respectively. After 12 months the radiographic progression could be determined in 375 patients. In the 60mg, 10mg Pred group, and in the placebo group, the mean progression after 1 year was 1.0, 1.0, 1.1 for the total SHS and 0.5, 0.6, 0.7 for the erosion score of the SHS, respectively. Statistical analysis showed non-inferiority of the 10mg Pred and of the placebo group in comparison to the 60mg Pred group. Regarding safety issues, there were 10, 5, 6 serious adverse events and 31, 16, 20 adverse events in the MedDRA system organ class "infections and infestations" for the 60mg Pred, 10mg Pred, and the placebo group, respectively.

Conclusion: The bridging schedule starting with 60mg Pred reduced disease activity better than the 10mg schedule or placebo only for a short time. The primary outcome structural damage was non-inferior in the 10mg Pred and the placebo group in comparison to the 60mg Pred group. Initial advantages of the higher dose may have been compromised by the long follow-up with the possible escalation of therapy due to the treat-to-target regimen.

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SAT0136

RELATIVE EFFICACY AND SAFETY OF TOFACITINIB, BARICITINIB, UPADACITINIB, AND FILGOTINIB, IN COMPARISON WITH ADALIMUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Methotrexate (MTX), an effective disease-modifying antirheumatic drug (DMARD) [2], is the most widely used DMARD for the treatment of rheumatoid arthritis (RA). However, not all patients are responsive to the drug; 30% of the patients discontinue therapy within 1 year of commencing the treatment, usually because of the lack of efficacy or undesirable adverse effects. Small-molecule Janus kinase inhibitors are clinically developed for the treatment of RA.

Objectives: The aim of this study is to investigate the relative efficacy and safety of tofacitinib, baricitinib, upadacitinib, and filgotinib in comparison with adalimumab in patients with active RA and having inadequate responses to MTX.

Methods: We performed a Bayesian network meta-analysis to combine direct and indirect evidence from randomized controlled trials (RCTs) to examine the efficacy and safety of tofacitinib, baricitinib, upadacitinib, filgotinib, and adalimumab in RA patients having inadequate responses to MTX.

Results: Four RCTs, comprising 5,451 patients, met the inclusion criteria. The baricitinib 4mg+MTX and upadacitinib 15mg+MTX group showed a significantly higher American College of Rheumatology 20% (ACR20) response rate than the adalimumab 40mg+MTX group. The ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that baricitinib 4mg+MTX had the highest probability of being the best treatment for achieving the ACR20 response rate, followed by upadacitinib 15mg+MTX, tofacitinib 5mg+MTX, filgotinib 200mg+MTX, filgotinib 100mg+MTX, adalimumab 40mg+MTX, and placebo+MTX. The upadacitinib 15mg+MTX and baricitinib 4mg+MTX groups showed significantly higher ACR50 and ACR70 response rates than adalimumab 40mg+MTX. In terms of Herpes zoster infection, the ranking probability based on the SUCRA indicated that placebo+MTX were likely to be the safest treatments, followed by filgotinib 200mg+MTX, filgotinib 100mg+MTX, adalimumab 40mg+MTX, tofacitinib 5mg+MTX, upadacitinib 15mg+MTX, and baricitinib 4mg+MTX. Regarding safety analysis, no statistically significant differences were found between the respective intervention groups.

Conclusion: In RA patients with an inadequate response to MTX, baricitinib 4mg+MTX and upadacitinib 15mg+MTX showed the highest ACR response rates, suggesting a difference in efficacy among the different JAK inhibitors.

References:

- [1] Fleischmann R, Mysler E, Hall S, Kivitz AJ, Moots RJ, Luo Z, DeMasi R, Soma K, Zhang R, Takiya LJTL (2017) Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomised controlled trial. 390:457-468
- [2] Taylor PC, Keystone EC, van der Heijde D et al (2017) Baricitinib versus Placebo or Adalimumab in Rheumatoid Arthritis. N Engl J Med 376:652-662
- [3] Fleischmann R, Pangan AL, Mysler E, Bessette L, Peterfy C, Durez P, Ostor A, Li Y, Zhou Y, Othman AA (2018) A phase 3, randomized, double-blind study comparing upadacitinib to placebo and to adalimumab, in patients with active rheumatoid arthritis with inadequate response to methotrexate. ARTHRITIS & RHEUMATOLOGY. WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA, pp
- [4] Combe B, Kivitz A, Tanaka Y, van der Heijde D, Matzkies F, Bartok B, Ye L, Guo Y, Tasset C, Sundy J (2019) LB0001 EFFICACY AND SAFETY OF FILGOTINIB FOR PATIENTS WITH RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE: FINCH1 PRIMARY OUTCOME RESULTS. BMJ Publishing Group Ltd, pp

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SAT0137

METHOTREXATE ASSOCIATED ADVERSE EVENTS AND THEIR PREDICTORS IN METHOTREXATE-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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Background: The adverse events (AEs) associated with methotrexate (MTX) treatment for rheumatoid arthritis (RA) have been studied extensively, but precise estimates of the incidence and prevalence of AEs are lacking. There is also limited published data on the predictors of AEs.

Objectives: To summarise and pool incidence and prevalence rates of AEs in patients treated with MTX for RA, and to identify treatment, clinical and disease related predictors of AEs.