IMPROVED RESPONSE TO ETANERCEPT IS ASSOCIATED WITH SERUM VITAMIN D LEVELS IN RHEUMATOID ARTHRITIS

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Background: Although treatment of rheumatoid arthritis (RA) has significantly improved during the past decades, many patients do not adequately respond or become resistant to current treatments. It is currently unknown why some patients respond well and others do not, and how the response rate could be improved. Vitamin D has strong immunomodulatory properties and it has been shown RA patients have a lower serum 25(OH)D level than healthy individuals. Moreover, vitamin D levels are correlated with disease severity.1,2 Interestingly, in vitro studies have shown that vitamin D augments the suppressive effects of etanercept in a simplified model for synovial inflammation.3 This suggests that vitamin D could improve the therapeutic response to etanercept in RA patients.

Objectives: To investigate if etanercept response is related to serum vitamin D (25(OH)D) levels in RA patients.

Methods: For this study, data were used from the IREACH trial, a multicenter stratified single blinded randomised clinical trial. RA patients, according to the 2010 classification criteria, who started with etanercept within the first 12 months of the study were included in the analysis. Serum vitamin D (25(OH)D) levels were determined at the start of treatment (Tstart) and 3 months later using the LIAISON 25 OH Vitamin D TOTAL assay. Correlation coefficients between vitamin D levels and the disease activity score (DAS) were calculated. Treatment response was determined with the EULAR response criteria, and difference in response rates was assessed using Chi-Square tests.

Results: 91 patients started etanercept in the first 12 months of the study, of which 24 did not have serum for 25(OH)D measurements at both start of treatment and three months later. Therefore, a total of 67 patients was included in this study, of which 82% was female. At baseline, 45 (87%) and 48 (73%) were positive for rheumatoid factor and anti-citrullinated protein antibodies, respectively. DAS after etanercept treatment was weakly inversely correlated with serum 25(OH)D after treatment (r=-0.29, p=0.02) and the change in 25(OH)D during treatment (r=-0.25, p=0.04). After correcting for DAS and serum 25(OH)D at the start of treatment the aforementioned correlations were still found. Importantly, EULAR response rate was significantly lower in patients who were vitamin D-deficient at the start of treatment (34.6% vs 59.4%) and in patients with decreasing 25(OH)D levels during treatment (39.2% vs 57.7%) (figure 1).

Conclusions: RA patients with a serum 25(OH)D level below 50 nmol/L at the start of etanercept treatment or a decreasing level during treatment have a lower EULAR response rate. Therefore, increasing serum 25(OH)D level in vitamin D-deficient patients may be important to achieve optimal effects of TNFα blocking therapy.

REFERENCES:

Impact of TNF inhibitors on need for joint replacement in patients with rheumatoid arthritis: A matched cohort analysis of UK Biobank Registry data

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Background: Previous ecological data from the UK and Denmark suggest a decline in the incidence of joint replacements for RA patients following the introduction of tumour necrosis factor inhibitors (TNFi). However, patient-level data on the comparative effectiveness of TNFi compared to conventional synthetic DMARD (csDMARD) use on the need for total hip (THR) or knee (TKR) replacement are lacking.

Objectives: To estimate the impact of TNFi use on subsequent need for THR or TKR (primary outcomes) or other joint replacement (OJR) (secondary outcome) in patients with RA.

Methods: A propensity score (PS) matched cohort was analysed using the British Society for Rheumatology Biologics Registry (2001–2016) for Rheumatoid Arthritis (BSRBR/RA) data. Exclusion criteria were: previous THR or TKR (all analyses) or OJR (secondary analysis), less than 6 months follow-up, prevalent biological DMARD use, or first biological DMARD use that was not a TNFi. Patients were followed from date of registration up to the earliest of date of outcome, death, loss-to-follow-up or change of TNFi exposure status (stopping, switching or starting).
SAFETY AND IMMUNE RESPONSE OF A LIVE ATTENUATED HERPES ZOSTER VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RANDOMISED PLACEBO-CONTROLLED TRIAL

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Objectives: To evaluate the safety and immune response of a live attenuated herpes zoster (HZ) vaccine in patients with systemic lupus erythematosus (SLE) in a randomised placebo-controlled trial.

Methods: Adult patients who fulfilled ≥4 ACR criteria for SLE and had a SLEDAI score ≤6 with stable immunosuppressive treatment for 6 months or more were recruited. Exclusion criteria were: active infection; lymphocyte <500/mm³; reduced serum IgG/A/M levels; serum creatinine >200 μmol/L; a history of cancer; and high-dose immunosuppressive treatment (prednisone >15 mg/day, azathioprine >100 mg/day, MMF >500 mg/day, cyclosporin >100 mg/day, tacrolimus >3 mg/day, CYC and biologics). Participants were randomly assigned to receive HZ vaccine (Zostavax) or placebo (same volume of normal saline) given subcutaneously. Anti-VZV IgG reactivity (baseline and 6 weeks post-vaccination) was measured by an ELISA coated with inactivated varicella-zoster viral antigen (Vidas VZV IgG, bioMerieux, France). Cell-mediated response to HZ was assessed by a specific VZV-stimulated IFN-γ enzyme linked immunospot (ELISPOT) assay. Disease activity of SLE was assessed by the SLEDAI and PGA. Adverse events (AEs) and immune responses to HZ of the two groups were compared.

Results: 90 SLE patients were recruited (age 45.6±14.1 years; 93% women); 45 assigned to HZ vaccine and 45 to placebo. All participants had a history of HZ.

chickenpox infection. The baseline clinical profile of the two groups of patients was similar. Only 3 patients in the vaccine and 1 patient in the placebo group had mild SLE activity (ACR criteria >50% improvement). Baseline SLEDAI and PGA scores of the two groups were not significantly different (1.58±1.8 vs 1.64±1.77; p=0.86 and 0.21±0.18 vs 0.27±0.25; p=0.18, respectively). The proportion of patients receiving various immunosuppressive agents, lymphocyte count, serum creatinine, IgG/A/M levels were also similar in the two groups. The mean baseline VZV IgG index value was 3.28±1.19 and 3.45±1.07 in the vaccine and control group of patients, respectively (p=0.48). The paired VZV IgG titer at week 6 was significantly higher in the vaccine than in control group, even after adjustment for baseline value (4.16±1.26 vs 3.32±1.01; p=0.001), lymphocyte count, Ig levels, SLEDAI, and other clinical variables. The increase in VZV IgG antibody was significantly higher in the vaccinated than control patients (+5.89% vs –2.1%; p<0.01), indicating an effect of vaccine. 21 and 6 AEs were reported in the vaccinated and control patients, respectively, but none were serious. Significantly more vaccinated patients reported pain and erythema at the injection site than controls (31% vs 7%; p<0.01) (mild in all and subsided in a few days). Other AEs more commonly reported with vaccination included dizziness (2%), arthralgia (2%) and subjective fever (4%). Two vaccinated patients (4.4%) had mild flare of skin/joint disease, and one control patients (2.2%) had mild increase in proteinuria between week 0 and 6. None of the patients had clinical HZ infection post-vaccination.

Conclusions: Our findings suggest TNI vaccine may reduce the need for TH in older and more severe RA patients, although no evidence was found for a reduction in younger or less severe patients or in rates of TH or OJ. Further work is needed to confirm these results.

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SLE, Sjögren’s and APS- new criteria, novel diagnostic tools and co-morbidities

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SAFETY AND IMMUNE RESPONSE OF A LIVE ATTENUATED HERPES ZOSTER VACCINE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RANDOMISED PLACEBO-CONTROLLED TRIAL

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Background: Individuals with systemic lupus erythematosus (SLE) are at increased risk of cardiovascular disease, which is possibly related to metabolic syndrome (MetS). Previous studies suggest that inflammation may be an important underlying mechanism in MetS development, but include patients with prevalent MetS only. In order to assess whether the development of incident MetS could be predicted, we examined the association between the onset of MetS and disease activity, therapeutic exposure, and biomarkers of inflammation overtime in patients with SLE.

Objectives: 1) To identify the clinical characteristics of patients with recently diagnosed SLE who develop incident MetS during first two years of follow-up; 2) To determine whether metabolic and inflammatory biomarkers improve the ability to predict incident MetS during follow-up.

Methods: We studied 1687 recently diagnosed SLE patients (<15 months) enrolled into the SLICC Inception Cohort from 11 countries. Clinical, therapeutic and laboratory data were recorded at baseline and annually at follow-up visits. Serum concentrations of adiponectin, B-lymphocyte stimulator, high sensitivity C-reactive protein, interleukin (IL)-6, IL-18, IL-18 binding protein, insulin, leptin and tumour necrosis factor alpha were measured, if samples were available. A complete-case analysis was performed. Only patients with both MetS status available at baseline, year 1 and year 2 visits were analysed. Logistic regression was performed to analyse which factors were predictive of the development of incident MetS in the first 2 years of follow-up. Patients who developed incident MetS were compared with those who were free of MetS throughout follow-up.

Results: Overall, 436 (26%) patients were included in this complete-case analysis. Of these, 243 (56%) were free of MetS throughout the follow-up period, 87 (20%) had persistent MetS at each visit, and 106 (24%) developed incident MetS during follow-up. In a multivariable logistic regression model that excluded bio-markers, clinical factors associated with future onset of MetS included increased age, Hispanic ethnicity, active renal disease, higher disease activity and current corticosteroid use. This model performed ‘fairly’ well when identifying patients likely to develop incident MetS (Area Under Receiver Operating Characteristic Curve (AUC ROC)=0.77). In a multivariable model that included the inflammatory and