Rheumatoid arthritis - comorbidity and clinical aspects

POS0579

ABSENCE OF ASSOCIATION BETWEEN ABATACEPT EXPOSURE LEVELS AND INITIAL INFECTION IN PATIENTS WITH RA: A POST HOC ANALYSIS OF THE RANDOMIZED, PLACEBO-CONTROLLED AVERT-2 STUDY

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Background: Infections are the most commonly reported AE observed in patients with RA treated with immunosuppressive therapies and can be clinically significant. A recent review reported differences in the risk of infection for some biologics such as tocilizumab and TNF inhibitors.[1] Abatacept selectively modulates T-cell co-stimulation and is approved for the treatment of RA. In patients with polyarticular-course juvenile idiopathic arthritis, no association was found between higher serum abatacept exposure and the incidence of infection.[2] This has not been evaluated for adult patients with RA.

Objectives: To determine if higher serum abatacept exposure during treatment with SC abatacept was associated with increased risk of infection in adult patients with RA.

Methods: AVERT-2 (Assessing Very Early Rheumatoid arthritis Treatment-2) was a randomized, placebo-controlled study of SC abatacept + MTX vs abatacept placebo + MTX in MTX-naive, anti-citrullinated protein antibody–positive patients with early, active RA.[3] A post hoc population pharmacokinetic (PK) analysis was performed using PK-evaluable patient data from the induction period (year 1) of AVERT-2. Association between steady-state abatacept exposure (min plasma concentration [C_{min}], max plasma concentration [C_{max}], and average plasma concentration [C_{avg}]) and first infection was evaluated using Kaplan–Meier plots of probability vs time on treatment by abatacept exposure quartiles and Cox proportional-hazards models.

Results: PK of SC abatacept was defined as a linear 2-compartment model with first-order absorption and first-order elimination. The findings of the updated PK analysis were consistent with those reported in prior population analyses of abatacept PK in adults with RA. The final model included effects of baseline body weight, estimated glomerular filtration rate, sex, age, albumin, MTX use, NSAID use, SJC, and race on abatacept clearance. The only covariate with a clinically relevant effect was higher body weight, which caused an increase in clearance and volume. Infections occurred in a total of 330/693 (47.6%; serious, 1.6%) patients treated with abatacept, and 134/301 (44.5%; serious, 1.3%) with placebo during the first year of AVERT-2. In patients taking abatacept, the mean (SD) study exposure to abatacept was 376 (60) days, while mean (SD) prednisone equivalent dose was 6.7 (3.8) mg/day and mean (SD) MTX dose was 9.6 (3.0) mg/week. No exposure–response relationship was observed between the probability of first infection and steady-state abatacept exposure quartiles (C_{avg}, C_{min}, and C_{max}), or compared with placebo (Figure 1A–C). Kaplan–Meier assessment also showed no increase in risk of infection with concomitant use of MTX and glucocorticoids.

Conclusion: No association was found between initial infection and steady-state abatacept exposure (C_{avg}, C_{min}, C_{max}) or MTX and glucocorticoid use in patients with RA treated with SC abatacept.

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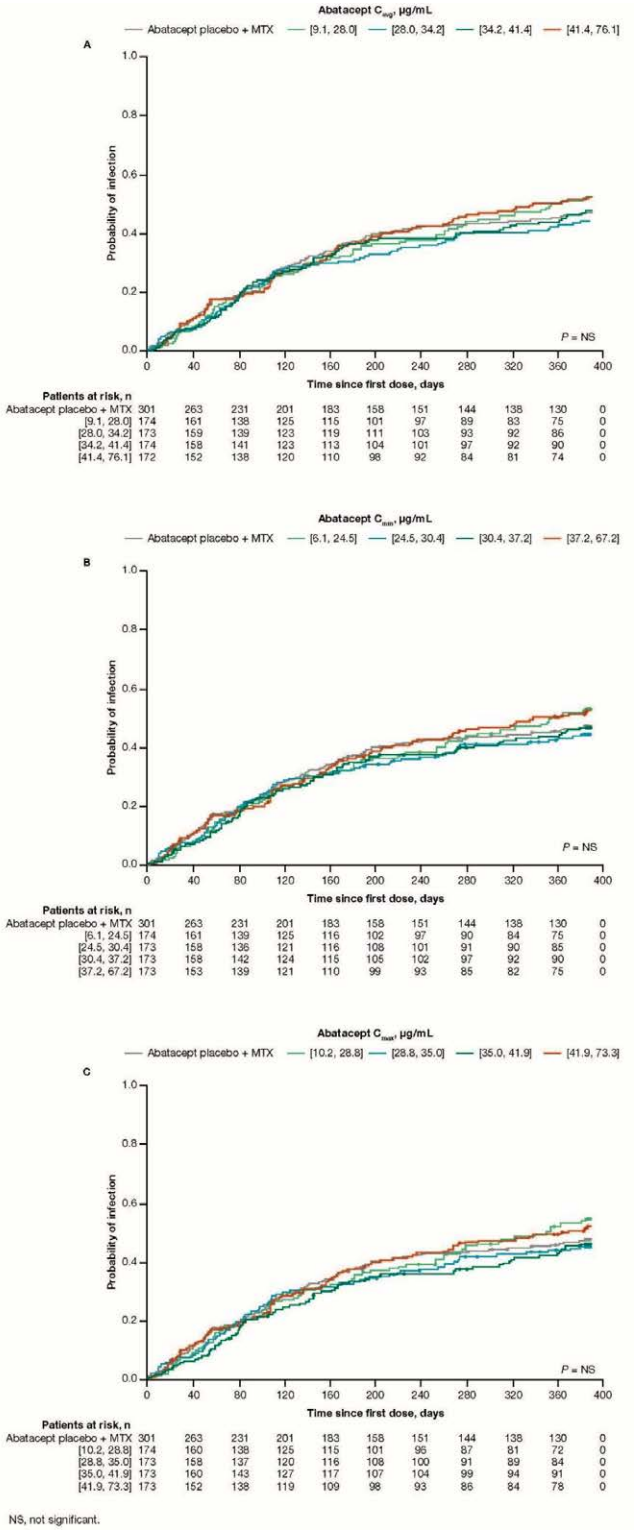

NS, not significant.

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POS0580 TRENDS IN THE OCCURRENCE OF ISCHEMIC HEART DISEASE OVER TIME IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY FROM NORWAY OF 1821 PATIENTS FROM 1972 TO 2014

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Background: Previous studies have shown that rheumatoid arthritis is associated with a 1.5 to 2.0 times increased risk of acute myocardial infarction (AMI) and ischemic heart disease (IHD) compared with the general population [1,2]. RA treatment has improved vastly over the last two decades, due to the focus on early and aggressive treatment and the use of synthetic and biologic DMARDs. Several studies have documented higher rates of remission and better long-term outcomes in patients with early introduction of DMARDs [3]. This "window of opportunity" may also be a critical phase for intervention against the development of atherosclerosis in RA. There is little information about the occurrence of AMI and IHD in RA patients diagnosed after the introduction of modern RA treatment.
Objectives: To evaluate trends of AMI and IHD in RA patients compared with the general population over time.
Methods: We performed a retrospective cohort study of 1821 RA patients diagnosed from 1972 to 2013. The total population of Hordaland, Norway was used as a comparison cohort. Information on AMI and IHD events was obtained from hospital patient administrative systems or cardiovascular registries during 1972-2014. Aggregated counts of AMI, IHD and population counts of the comparison cohort were used to calculate expected counts of AMI and IHD in the RA cohort per 5-year age group, sex and calendar year. We then used Poisson regression with expected counts as an offset to estimate standardized event ratios (SER) as a measure of excess events.
Results: The difference in events (excess events) in RA patients compared with the general population declined on average 1.3% per year for AMI and 2.3% for IHD from 1972 to 2014. There was no significant excess AMI (SER 1.05, 95% CI 0.82–1.35) and IHD events (SER 1.02, 95% CI, 0.89–1.16) for RA patients diagnosed after 1998 compared with the general population.
Conclusion: RA patients have historically had an excess risk of IHD compared with the general population. Our study did not find excess AMI or IHD events in RA patients diagnosed after 1998. Our findings may reflect improved management of RA, CVD prevention or changes in the case-mix of RA patients over time.

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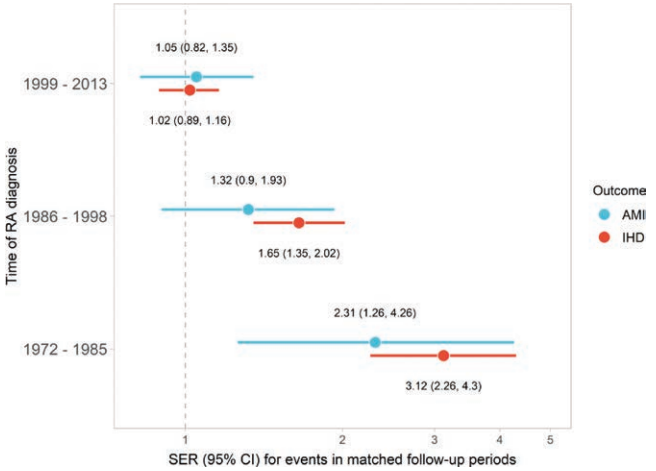

Figure 1. Excess AMI and IHD events in RA patients compared with the general population. RA patients are divided into three groups by the time of RA diagnosis. End of follow-up was set to 1 year after the end of each diagnostic period (1986, -99 and 2014 respectively) to allow for equal RA duration between groups. Point estimates are standardized event ratios comparing the number of events in the RA cohort to the expected number of events calculated from reference rates in the general population and standardized for age, sex and year of the event. All estimates are given with robust 95% confidence intervals (CI). Both the RA and general population were obtained from Hordaland, Western Norway. AMI, acute myocardial infarction; IHD, ischemic heart disease.

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POS0581 HIGHER SKIN AUTOFLUORESCENCE IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS: RESULTS FROM A LARGE POPULATION BASED COHORT

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Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease which is associated with increased mortality, mostly because of a higher incidence of cardiovascular disease (CVD), which cannot be explained by traditional risk factors alone. (1,2) Also studies showed that the cardiovascular events can already occur at a higher than expected rate shortly after the first symptoms of RA. (3)This raises the question if individuals with clinical suspect arthralgia (CSA) but not yet diagnosed with RA, already have an increased risk for developing cardiovascular disease compared to healthy controls and if this is also true for ACPA positive individuals without symptoms of clinical suspect arthralgia. In our study we used skin autofluorescence (SAF), measured with the AGE reader, as an early non-invasive tool to identify subjects who are at increased risk for developing cardiovascular disease. (4) SAF measures the accumulation of AGEs in the skin and thereby offers a simple alternative to invasive measurement of AGE accumulation. (5)
Objectives: To investigate skin autofluorescence (SAF) levels, as an early indicator for cardiovascular disease, in relation to the presence of anticitrullinated