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OVERALL INFECTION RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING ABATACEPT, RITUXIMAB AND TOCILIZUMAB. AN OBSERVATIONAL COHORT STUDY

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Background: Most infections in patients with rheumatoid arthritis (RA) are treated in primary care with a prescription of antibiotics. Only a small fraction requires hospitalization. Existing studies of infection risk in patients with RA, who receive non-tumor-necrosis-factor-inhibitor biologic (non-TNFi) therapy, however, have focused primarily on hospitalized infections.⁽¹⁾

Objectives: In Danish RA patients treated in routine care with the three non-TNFi abatacept, rituximab and tocilizumab 1) to compare adjusted incidence rates (IR) of infections overall, and 2) to estimate the relative risk (RR) of infections across the drugs during the first year of non-TNFi treatment.

Methods: We conducted an observational cohort study including all RA patients in DANBIO who started a non-TNFi treatment between January 2010 and December 2017. Clinical characteristics at baseline were described. We defined infections as either a prescription of antibiotics or a hospitalization due to infection. Baseline comorbidities, antibiotic prescriptions and hospitalized infections were identified through linkage to national registries. We calculated IRs of infections per 100 person-years (age and gender adjusted) and rate ratios (as estimates of RRs, adjusted for additional covariates) during the first year of treatment (Poisson regression).

Results: We identified 3,696 treatment series of non-TNFi (abatacept 1,115/rituximab 1,017/tocilizumab 1,564). Patients receiving rituximab tended to be older, had longer disease duration and more previous malignancies. During the first year of treatment, 1,747 infections were identified. Age and gender adjusted IRs per 100 person years were (abatacept/rituximab/tocilizumab): 76.1(69.3; 83.6)/87.3(79.3; 96.1)/77.4(71.4; 83.9). Adjusted RRs (Table) were 0.88(0.76; 1.02) for abatacept and 0.87 (0.75; 1.00) for tocilizumab compared to rituximab. For abatacept vs. tocilizumab it was 1.02 (0.89; 1.16).

Table. Baseline characteristics, one-year IRs and RRs of infections in RA patients starting non-TNFi treatment stratified by drug.

Variable	Abatacept, N=1115	Rituximab, N=1017	Tocilizumab, N=1564
Female gender, %	78 %	78 %	78 %
Age, years	59 (50-68)	62 (53-70)	59 (50-67)
Disease duration, years	8 (3-16)	11 (5-19)	9 (3-16)
DAS28	4.7 (3.9-5.4)	4.8 (4.0-5.9)	4.9 (4.1-5.7)
CRP, mg/L	8 (3-20)	10 (4-22)	12 (4-30)
HAQ	1.4 (0.9-1.9)	1.5 (1.0-2.0)	1.4 (1.0-2.0)
Previous cancer, %	1 %	9 %	2 %
Previous infection*, %	24 %	28 %	24 %
Incidence rates (IR) of infections, 0-12 months			
Person years	631	520	888
Infections, n	512	500	735
IR/100 PY (95%CI)*	76.1 (69.3; 83.6)	87.3 (79.3; 96.1)	77.4 (71.4; 83.9)
Risk ratios (RR) for infections, 0-12 months			
	ABA vs TCZ (ref)	ABA vs RTX (ref)	TCZ vs RTX (ref)
Adjusted RR (95%CI)**	1.02 (0.89; 1.16)	0.88 (0.76; 1.02)	0.87 (0.75; 1.00)

Numbers are medians [IQR] unless otherwise stated. *previous hospitalized infection **adjusted for age and sex. ** Adjusted for age, sex, DAS28, smoking, disease duration, HAQ, glucocorticoids use at baseline, previous hospitalized infection, previous cancer, previous chronic obstructive pulmonary disease. Abbreviations: CI: confidence interval; DAS28: disease activity score of 28 joints, HAQ: health assessment questionnaire, PY: person years

Conclusion: In patients with RA receiving treatment with abatacept, rituximab or tocilizumab in routine care, rituximab had the highest risk of infection during first year of treatment. However, this finding should be interpreted with caution due to differences in baseline characteristics across drugs and potential residual confounding.

REFERENCES:

- [1] Grøn KL, Arkema EV, Glintborg B, Mehnert F, et al. Risk of serious infections in patients with rheumatoid arthritis treated in routine care with abatacept, rituximab and tocilizumab in Denmark and Sweden. *Annals of the rheumatic diseases*. 2019.

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THE ASSOCIATION BETWEEN ANTI-CCP TITRE LEVEL AND DISEASEACTIVITY AND DISABILITY OVER ONE YEAR FOLLOWING THE INITIATION OF METHOTREXATE OR BIOLOGIC THERAPY FOR ANTI-CCP+ RHEUMATOID ARTHRITIS

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Background: Whilst anti-cyclic citrullinated peptide antibody (anti-CCP) positivity is associated with poor outcomes in patients with rheumatoid arthritis (RA), it is unclear whether titre level over time is associated with outcome.

Objectives: Whilst anti-cyclic citrullinated peptide antibody (anti-CCP) positivity in associated with poor outcomes in patients with rheumatoid arthritis (RA), it is unclear whether titre level over time is associated with outcome.

Methods: Patients were recruited to one of two, UK-based, multi-centre prospective cohort studies: MTX-starters = Rheumatoid Arthritis Medication Study (RAMS); biologic-starters = Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS). Anti-CCP titre (Axis-Shield Anti-CCP test; U/ml; anti-CCP titre >5 U/ml = anti-CCP+) was measured at the co-ordinating centre from blood samples taken at baseline, 6 months and 12 months. Patients who were anti-CCP+ at baseline and had titre measured at one other assessment were included in the analysis. Patients completed the Health Assessment Questionnaire (HAQ) and the Disease Activity Score (DAS28) was calculated at each assessment. The association between anti-CCP titre and DAS28 and HAQ was assessed using linear random effects models, controlling for age, gender and disease duration (months). Anti-CCP titre was natural log-transformed. Missing data resulting from anti-CCP assay failure were imputed using multiple imputation.

Results: In total, 686 MTX-starters and 346 biologic-starters were included. Biologic-starters had worse disease at baseline compared to MTX-starter (Table). Median [IQR] titre decreased slightly over follow-up for MTX-starters (baseline = 147 [48, 416]; 6 months = 133 [47, 454]; 12 months = 124 [44, 421]; p=0.63) and biologic-starters (baseline = 138 [37, 492]; 6 months = 112 [30, 468]; 12 months = 103 [30, 451]; p=0.36) but this was non-significant. For MTX-starters, anti-CCP titre was statistically significantly associated with DAS28 and HAQ, but the effect sizes were small (mean difference [95% CI] per unit increase in log anti-CCP: DAS28 = 0.07 [0.02, 0.11]; HAQ = 0.06 [0.03, 0.08]). There was no significant association between anti-CCP titre and DAS28 and HAQ for biologic-starters (mean difference [95% CI] per unit increase in log anti-CCP: DAS28 = 0.03 [-0.05, 0.10]; HAQ = 0.02 [-0.01, 0.05]).

Conclusion: Time-varying anti-CCP titre level was not strongly associated with disease activity or disability over one year in either MTX-starters or biologic-starters who were anti-CCP+ at baseline, indicating repeat testing of anti-CCP level may not be necessary.