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OP0059

PROFOUND ANTICOAGULANT EFFECTS OF INITIAL ANTIRHEUMATIC TREATMENTS IN EARLY RHEUMATOID ARTHRITIS PATIENTS: A NORD-STAR SPIN-OFF STUDY

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Background: Patients with rheumatoid arthritis (RA) are at an increased risk of venous thromboembolism. Thus far, there have not been any comparative studies investigating the effects of initial antirheumatic treatments in (very) early RA patients.

Objectives: To assess the effects of different initial treatments on hemostatic parameters in patients with early RA.

Methods: NORD-STAR is an international, multicentre, open-label, assessor-blinded, phase 4 study where patients with newly diagnosed RA started methotrexate (MTX) and were randomised 1:1:1:1 to a) conventional treatment (either prednisolone tapered to 5mg/day, or sulfasalazine combined with hydroxychloroquine and intra-articular corticosteroids), b) certolizumab pegol, c) abatacept, d) tocilizumab[1]. This study is a spin-off from the main NORD-STAR study extensively investigating hemostatic system in 24 per protocol consecutive Dutch participants at baseline, 12 weeks and 24 weeks after the start of the treatment. Statistical analysis was done using paired samples t-test in SPSS version 28.

Results: The mean age of investigated patients was 51.8 (± 12.7) years and 58.3% were female. At baseline patients had an average DAS28 score of 4.6 (± 0.9) and had elevated levels of investigated coagulation biomarkers: Factor 1+2, fibrinogen, D-dimer and parameters of the two global hemostatic assays, i.e. endogenous thrombin potential (ETP) and overall hemostasis potential (OHP). These biomarkers decreased significantly at 12 and 24 weeks in patients in all groups (Table 1). Overall fibrinolytic potential (OFP) was decreased and clot lysis time (CLT) was prolonged at baseline, demonstrating impaired fibrinolytic activity in early RA. The reduction of coagulation parameters was significantly higher in biological treatment arms in comparison to the standard MTX treatment arm. In addition, tocilizumab was more effective compared to certolizumab and abatacept, (Figure 1), which was expected considering the direct inhibitory effect of this drug on the IL-6 synthesis and consequently the coagulation activation as well. After 24 weeks of treatment with methotrexate and tocilizumab, the average fibrinogen of patients was reduced by 63% vs 31% and 36% in the certolizumab and abatacept groups, respectively. The changes in DAS-28 and the changes in fibrinogen had a correlation of 0.385 which did not reach statistical significance.

Table 1. ***Measurements are marked with * if p<0.05, ** if p<0.01 and *** if p<0.001***

	Baseline	W12	W24
Factor 1+2 (pmol/L)	270.25 (149.4)	190.36 (108.6)**	179.52 (85.3)***
Fibrinogen (g/L)	4.64 (1.5)	3.61 (1.6)**	2.63 (1.2)***
D-dimer (mg/L)	2.17 (3.0)	0.33 (0.23)**	0.29 (0.2)**
OHP (Abs-sum)	157.38 (64.9)	120.62 (68.7)*	100.49 (53.8)***
OCP (Abs-sum)	369.52 (58.8)	305.04 (101.7)*	275.91 (83.1)***
OFP (%)	57.97 (13.1)	63.20 (12.7)*	65.25 (11.4)***
Lag time (s)	304.5 (71.1)	306.8 (71.8)	312.7 (65.4)
Slope	0.07 (0.02)	0.066 (0.03)	0.094 (0.12)
Max Abs	1.17 (0.3)	1.00 (0.4)*	0.91 (0.3)**
CLT (s)	1405 (356)	1317 (377)	1231 (320)**
ETP (nM*min)	1480 (471)	1395 (395)*	1337 (429)*
Peak (nM)	231 (78)	223 (68)	223 (74)
Lagtime (min)	4.06 (2.1)	3.28 (1.2)**	2.87 (1.0)***
ttPeak (min)	7.40 (2.2)	6.61 (1.5)*	6.13 (1.4)**

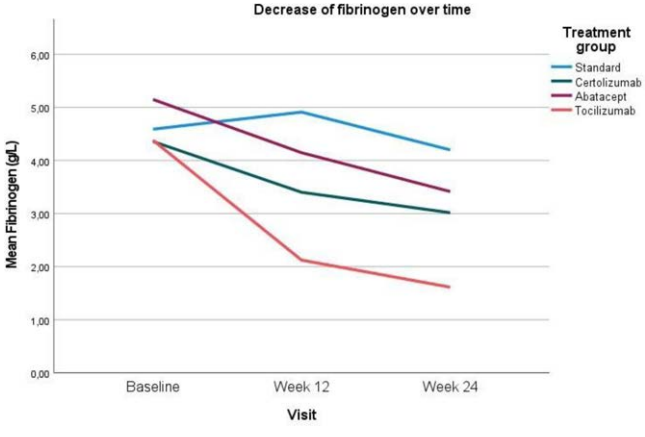

Figure 1.

Conclusion: Our results indicate an enhanced coagulation and fibrinolytic impairment in newly diagnosed RA patients. Effective antirheumatic treatments reduce this hemostatic imbalance, with significantly more pronounced effects of biologic drugs compared to conventional (MTX+glucocorticoids) treatment.

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OP0060 EXPOSURE TO SPECIFIC TUMOR NECROSIS FACTOR INHIBITORS AND RISK OF DEMYELINATING AND INFLAMMATORY NEUROPATHY IN PATIENTS WITH INFLAMMATORY ARTHRITIS. A COLLABORATIVE OBSERVATIONAL STUDY ACROSS FIVE NORDIC RHEUMATOLOGY REGISTERS

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Background: Though rare, studies have reported increased risk of neurological events including demyelinating disease of CNS (DML), multiple sclerosis (MS), and inflammatory neuropathy (INP) in patients with inflammatory joint disease treated with tumor necrosis factor inhibitors (TNFi).[1,2] More in-depth investigations are required to elucidate the association between TNFi and neurological events in these patients, especially whether rates differ across type of TNFi mode of action.

Objectives: To estimate the incidence of neurological events in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA, including axial spondyloarthritis and psoriatic arthritis) starting treatment with TNFi across five Nordic countries. To compare the incidence of neurological events in etanercept (ETN)-treated patients to patients treated with other TNFi (oTNFi).

Methods: We defined treatment cohorts of patients initiating TNFi between 2001 through 2018 from clinical rheumatology registers in Denmark (DK), Finland (FI), Iceland (IS), Norway (NO), and Sweden (SE). One patient could contribute to more than one treatment episode. Demographic data (sex, age), co-medication (methotrexate) and clinical variables (CRP, disease duration (<1 year, 1 to 5 years, >5 years) were extracted and used as covariates. We estimated crude incidence rates (IR) for neurological events and subtypes (ICD-10 codes: MS: G35, DML: G35, G36.0, G36.8-9, G37.1, G37.3, G37.5, G37.8-9, H46, H48.1, G04.8-9, INP: G61.0, G61.8-9), all countries pooled. We compared risk of neurological events between patients treated with ETN and oTNFi using Cox regression with time since treatment start, adjusted for the above covariates, robust standard errors, and stratified by country.

Results: We included 52,682 treatment starts, in 33,885 RA patients (DK 8,259, FI 3,765, IS 723, NO 1353, SE 19,785; 75% women, mean age 56 years) and 46,549 treatment starts in 28,772 SpA patients (DK 7,000, FI 2,885, IS 962, NO 2,684, SE 15,241; 47% women, mean age 45 years).

Numbers of DML, MS, INP and all neurological events, person-years (pyrs), and IRs in RA and SpA patients, for the two treatment groups are displayed in Figure 1. IRs for these neurological events showed some variation by diagnosis (RA vs. SpA), with rates of DML (and MS) in SpA patients around two (and three, respectively) times higher than the corresponding rates in RA (p<0.01), but similar rates for INP in RA and SpA patients. Comparing oTNFi to ETN, all Cox regression hazard ratios (HR) were statistically non-significant and close to one, whatever the outcome and the group of patients (Figure 1), with the adjusted HR (95%CI) for developing any neurological event in oTNFi compared to ETN being 1.08 (0.91-1.28) in RA patients and 0.96 (0.78-1.19) in SpA patients.

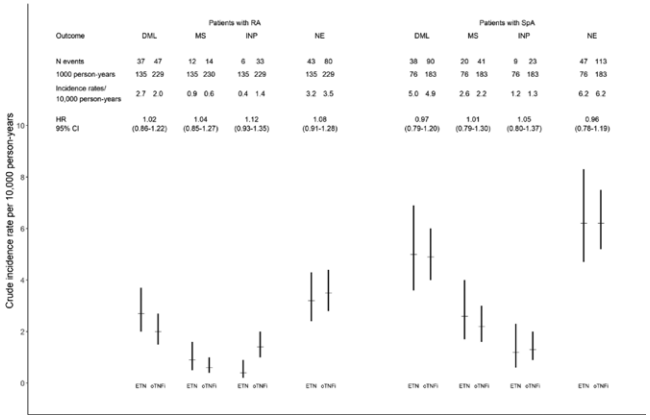

Figure 1. Number of events, pyrs and IRs of DML, MS, INP and all neurological events (NE) in RA and SpA patients, treated with ETN or oTNFi. HRs (95%CI) comparing oTNFi to ETN.

Conclusion: The incidences of DML and MS were lower in RA compared to SpA patients, while rates of INP were similar in both patients' groups. There was no evidence of differences in these rates between ETN and oTNFi. The findings are of importance from a safety perspective for patients starting TNFi.

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[1] Kopp T ARD 2020;79(5):566

[2] Kunchok A JAMA Neurol 2020;77(8):937

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