Conclusions Thus, these data suggest that determination of multiple antibodies increases the diagnostic power of serological testing and may be a feasible tool for the prediction of MTX response especially in combined models.

Disclosure of interest D. Sieghart: None declared, A. Platzer: None declared, F. Alasti: None declared, P. Studenic: None declared, M. Grundhuber Employee of: Thermo Fisher Scientific – Phadia GmbH, S. Swiniarski Employee of: Thermo Fisher Scientific – Phadia GmbH, S. Blueml: None declared, T. Perkmann: None declared, J. Smolen: None declared, G. Steiner: None declared

P026 BASELINE AUTOANTIBODY PROFILE IN RHEUMATOID ARTHRITIS ASSOCIATES WITH EARLY TREATMENT RESPONSE BUT NOT LONG-TERM OUTCOMES

[1]EC de Moel*, [1]VF Derksen, [1]LA Trouw, [2]H Bang, [3]RJ Goekoop, [4]I Speyer, [1]TW Huizinga, [1]CF Allaart, [1]RE Toes, [1]D van der Woude. *[1]Rheumatology, Leiden University Medical Centre, Leiden, Netherlands; [2]Orgentec Diagnostika, Mainz, Germany; [3]Rheumatology, Haga Hospital; [4]Rheumatology, Haaglanden Medical Centre, The Hague, Netherlands*

10.1136/annrheumdis-2018-EWRR2018.51

Introduction The autoantibody profile of seropositive rheumatoid arthritis (RA) is very diverse and consists of various isotypes and antibodies to multiple post-translational modifications. It is yet unknown whether this varying breadth of the autoantibody profile is clinically relevant and associates with treatment outcomes.

Objectives To investigate whether the composition of the autoantibody profile in RA, as a marker of the underlying immunopathology, influences initial and long-term treatment outcomes.

Methods In sera of 399 seropositive RA patients in the IMPROVED study[1] drawn at baseline and at the moment of drug tapering, we measured IgG, IgM, and IgA isotypes for anti-cyclic citrullinated peptide-2 and anti-carbamylated protein antibodies, IgM and IgA rheumatoid factor, and reactivity against 4 citrullinated and 2 acetylated peptides (anti-modified protein antibodies (AMPAs)). We investigated the effect of the breadth of the autoantibody profile on;

- change in disease activity score (DAS)–44 between 0 and 4 months,
- initial drug–free remission (DFR: drug–free DAS44<1.6) achieved between 1 and 2 years of follow–up, and
- long–term sustained DFR until last follow–up.

Results Corrected for age, gender, smoking, BMI, and baseline Health Assessment Questionnaire score, patients with a broad autoantibody profile at baseline had a significantly better early treatment response: ΔDAS 0–4 months of 1–2, 3–4, and 5–6 vs 7–8 isotypes: −1.5 [p<0.001], −1.7 [p=0.003], and −1.8 [p=0.001] vs −2.2. Similar results were observed for AMPA-number; ΔDAS 0–4 months of 1–2, 3–4, and 5–6 vs 7–8 AMPAs, respectively: −1.7 [p=0.016], −1.5 [p<0.001], and −1.9 [p=0.22] vs −2.1. However, patients with a broad baseline autoantibody profile achieved less initial DFR. For long-term sustained DFR there was no longer an association with the breadth of the autoantibody response. When assessing autoantibodies at the moment of tapering, similar results were observed.

Conclusions A broad baseline autoantibody profile is associated with a better early treatment response and a worse chance of achieving DFR at early stages, but not later in the treatment regimen, suggesting that the relevance of the autoantibody profile for treatment outcomes diminishes over time. The breadth of the baseline autoantibody profile, reflecting a break in tolerance against several different autoantigens and extensive isotype switching, may indicate a more active humoral autoimmunity which could make the underlying disease processes initially more suppressible by medication.

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Disclosure of interest None declared

P027 ABSTRACT WITHDRAWN

P028 TREATMENT OF BAFF TRANSGENIC MICE WITH ANTI-TNF: MONOCLONAL ANTI-TNF ARE ASSOCIATED WITH A HIGHER RISK OF LYMPHOMA THAN ETANERCEPT

[1]G Nocturne*, [2]B Ly, [2]S Boudaoud, [2]S Bitoun, [2]A Paoletti, [1]R Seror, [3]C Nicco, [4]F Mackay, [5]F Vincent, [1]S Ferlicot, [6]L Stimmer, [7]S Roulland, [1]R krzysiek, [1]S Hacein Bey, [3]F Batteux, [1]X Mariette. *[1]Université Paris Sud; [2]INSERM, Le Kremlin Bicetre; [3]Paris Descartes University, Paris, France; [4]Melbourne Univeristy, Melbourne; [5]Monash Univeristy, Monash, Australia; [6]CEA, Fontenay aux Roes; [7]Marseille University, Marseille, France*

10.1136/annrheumdis-2018-EWRR2018.52

Introduction Risk of lymhoma in patients with rheumatoid arthritis (RA) and disease activity is the main risk factor. The impact of treatment, notably of anti-TNF, is unclear: decreasing the risk of lymphoma by controlling activity or alterring anti-tumour immunosurveillance. Anti-TNF are not associated with an increased risk of lymphoma in large epidemiologic studies. However, the risk might vary according to the type or to the dose of anti-TNF.

Objectives To assess if the risk of lymphoma might differ according to the type of anti-TNF, comparing monoclonal anti-TNF to the soluble receptor. For that, we used BAFF transgenic (Tg) mice as a model of autoimmunity-associated lymphomas. They develop lupus and Sjögren and 3% of them spontaneously developed lymphoma at 12–18 months.

Methods Six months aged BAFF-Tg mice were treated with anti-TNF for 12 months: etanercept (ETA) (n=15, 8 mg/kgx3/week), monoclonal anti-mouse TNF: TN3 19.12 (n=15, 20 mg/kg/week), adalimumab (ADA) (n=12, 20 mg/kg/week) or controls (n=22). Sera were assessed monthly. Crude mortality was compared among the different groups. Histological examination of the spleen was performed. The Fisher's exact test was used to compare the incidence of lymphoma among the groups.

Results Adjunction of low dose of methotrexate during the 3 first days of treatment prevented immunisation in the 3 groups for life. Using L929 cells, a cell line sensitive to TNF induced death, we confirmed that ADA was 8 to 12 times less efficient than ETA to inhibit soluble murine TNF. As expected, the mean level of ETA, TN3 and ADA were 7 µg/ml, 69 µg/ml and 105 µg/ml, respectively. The level of autoantibodies and serum Ig did not significantly differ among the groups. However, crude mortality was significantly higher in mice treated with monoclonal anti-TNF compared to controls (p=0.0001 for ADA and p=0.0003 for TN3) but not for mice treated with ETA. Incidence of lymphoma was higher in