were associated with high serum levels of inflammatory markers IL-6 (over 5.5 pg/ml, $p=0.0006$) and IL-1b (over 4 pg/ml, $p=0.0005$), however the level of these markers was not affected by the smoking status of the patients. We found 14 times lower sPD-L1 levels in smoking RA patients that did not receive TNF-inhibitors ($p=0.0092$), but treatment with TNF-inhibitors normalised levels of sPD-L1.

Furthermore, aCCP positivity in RA patients was associated with higher levels of sPD-L1 ($p=0.0036$). We speculate that the presence of antibodies might influence the levels of sPD-L1 through the stimulation of Fc-receptors expressed by PD-L1 producing cells. In PBMC depleted of T cells, we saw that smokers had lower mRNA expression of the stimulatory FcγRIIIA ($p=0.028$) and predominance of the inhibitory FcγRIIB in the FcγRIIB/FcγRIIIA ratio ($p=0.0004$).

Conclusions Smoking decreases the serum levels of the inflammation limiting protein sPD-L1, but levels were restored by treatment with TNF-inhibitors. aCCP positive RA patients had higher levels of sPD-L1, possibly due to activation of Fc-receptors expressed by PD-L1 producing cells.

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Disclosure of interest None declared

P024

COMPARISON OF CCP2 AND CCP3 ASSAYS IN A LARGE COHORT OF ESTABLISHED RHEUMATOID ARTHRITIS AND CONTROLS

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Introduction Rheumatoid Factor (RF) and anti-citrullinated protein antibodies (ACPA) are important serological marker in the diagnosis of rheumatoid arthritis (RA) and are part of the classification criteria. ACPA are generally detected using anti-cyclic citrullinated peptide (CCP) antibody assays. The first generation of the CCP test uses a peptide derived from the filaggrin protein as the antigen, whereas, the second and third generation CCP (CCP2, CCP3) are based on peptides specifically designed and optimised (mimotypes) to detect ACPA, thereby enhancing the immunoreactivity of the citrulline-containing epitope.

Objectives The goal was to compare the performance of CCP2 and CCP3 assays.

Methods 1655 samples including 968 RA patients and 687 controls (450 ankylosing spondylitis (AS) and 237 psoriatic arthritis (PsA) patients), all derived from the Swiss Clinical Quality Management in Rheumatic Diseases Foundation (SCQM) were included. ACPA were determined by CCP2 ELISA (Eurodiagnostica, Sweden), CCP3 ELISA (QUANTA Lite CCP3 IgG) and CCP3 CIA (QUANTA Flash CCP3 IgG) (both Inova Diagnostics, US). RF IgM was measured by ELISA (QUANTA Lite RF IgM, Inova Diagnostics, US).

Results The CCP2 ELISA showed a high sensitivity (71.1%) and a moderately high specificity (86.9%) with a corresponding Odds ratio (OR) of 16.3 (95% CI: 12.5 to 21.1). The two CCP3 assays showed lower sensitivities (61.8% for the ELISA and 61.4% for the CIA), but significantly higher

specificities (98.4% and 98.5% respectively), resulting in much higher predictive values, with OR of 99.3 (95% CI: 54.4 to 181.2) and 107.5 (95% CI: 57.4 to 201.5), respectively. When compared at the same specificity (95%), the sensitivities were 61.3% for the CCP2 ELISA, 68.1% for the CCP3 ELISA and 66.1% for the CCP3 CIA. When multi-parametric analyses were performed by combining ACPA with RF IgM, combining different markers resulted in higher OR than the individual markers. The combination of CCP3 and RF IgM resulted in a higher OR (OR=187.0, 510/1655) than the combination of CCP2 with RF IgM (OR=36.7, 565/1655). The addition of CCP2 to the combination of CCP3 and RF IgM resulted in a lower OR (OR=175.0, 494/1655).

Conclusions CCP3 showed a better overall performance than CCP2 in this cohort of RA and controls, when analysed individually as well as in combination with RF IgM.

Disclosure of interest None declared

P025

THE DIAGNOSTIC AND PROGNOSTIC VALUE OF AUTOANTIBODIES IN RHEUMATOID ARTHRITIS

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Introduction Rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) are important diagnostic tools in rheumatoid arthritis (RA). These antibodies are predominantly of the IgM (RF) or IgG (ACPA) isotype. Other isotypes of both antibodies – like IgA – and other antibodies – like anti-RA33, which is directed to the nuclear antigen hnRNP-A2 – have been repeatedly reported but their diagnostic and prognostic value has still not been fully elucidated.

Objectives Here we investigated (i) the prevalence of IgA-RF and IgA-ACPA as well as isotypes IgA, IgG and IgM of anti-RA33 antibody in patients with RA and (ii) their predictive value regarding therapeutic response to methotrexate (MTX).

Methods Sera from 290 RA patients, 261 disease controls and 100 healthy subjects were tested for the presence of RF, ACPA and anti-RA33 IgG/A/M isotypes by EliATM (Thermo Fisher Scientific). RF and ACPA were routinely measured by nephelometry and the anti-CCP EliATM, respectively. For finding associations with American College of Rheumatology (ACR)20 and simplified disease activity score (SDAI)50 therapeutic responses, an inception cohort of 165 RA patients was analysed.

Results Diagnostic specificity of antibodies was at least 95%. 185 (63.4%) of 290 RA patients tested positive for at least one routine marker (RF or ACPA) while 107 were negative for both antibodies (seronegative). Among these, 24 (8.2%) patients tested positive for IgG/A/M anti-RA33 and/or IgA-RF/ACPA. To determine the prognostic value regarding therapeutic responses a cross-validated combined model with an accuracy of 77% and an estimated p -value ($k=10$) of 0.00034 showed high levels (>133 IU/ml) of IgM-RF to be associated with a favourable response to methotrexate (MTX). In case of low or no RF, the presence of IgG-RA33 antibody on the one hand, and the absence of IgA-ACPA on the other hand was associated with a favourable response.