AB0410 THE INTERPLAY BETWEEN C3 AND C4 AND DISEASE ACTIVITY IN PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS DURING TREATMENT WITH ANTI-IL6 RECEPTOR

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Background: The complement system (CS) is involved in the pathogenesis of rheumatoid arthritis (RA). Evidence reported that high C3 levels C3 in RA patients might reflect a pro-inflammatory status and represent a negative prognostic factor for TNF-inhibitors therapy.

Objectives: We evaluated CS in a cohort of RA patients treated with tocilizumab (TCZ) to explore whether there was any correlation between CS and both disease activity and response to therapy.

Methods: Consecutive outpatients affected by RA who started TCZ treatment i.v. at the Rheumatology Unit of "Policlinico Tor Vergata" in Rome (Italy) were enrolled (n=25) (Table I). We included 25 healthy subjects as controls. Disease activity was assessed by using DAS28 ESR-based while clinical response to therapy by EULAR response criteria. Peripheral blood samples were obtained from all patients at the time of each infusion. Laboratory assessment included ESR, CRP, RF, ACPA, C3, C4, CH50 assay. Clinical and laboratory data were registered at baseline (T0), after 1 (T1), 3 (T3), 6 (T6), 9 (T9), and 12 (T12) months from the beginning of the TCZ treatment.

Results: At baseline, both C3 and C4 were significantly higher in RA than in controls (Table I).

	RA (N=25)	Controls (N=25)	P value
Female (N%)	23/92	23/92	N.S.
Age (years)	65.4±11.5	60.1±9.3	N.S.
Disease duration (years)	13±8.2	N.A.	N.A.
DAS28	6.5±1.3	N.A.	N.A.
HAQ	1.9±0.8	N.A.	N.A.
Positivity of RF (N%)	17/68	N.A.	N.A.
Positivity of ACPA (N%)	20/80	N.A.	N.A.
ESR (mm/h)	58±28	N.A.	N.A.
CRP (mg/l)	8.5±7.6	N.A.	N.A.
C3 (mg/dl)	119.4±22.4	104±18	0.04
C4 (mg/dl)	26±6.7	22±4	0.013
CH50 (%)	108±24	100±18	N.S.
Therapy:		N.A.	
PDN ≤7.5 mg/die (N%)	9/36		
At least one DMARD (N%)	13/52		
– MTX (N%)	9/69.2		
– HCQ (N%)	4/30.7		
– SSZ (N%)	2/15.4		
– LEF (N%)	2/15.4		
I line TCZ (N%)	3/12		
II line TCZ (N%)	3/12		
III line TCZ (N%)	9/36		
IV line TCZ (N%)	7/28		
V line TCZ (N%)	3/12		

No difference in C3 and C4 resulted between ACPA positive and ACPA negative patients during the follow up. ESR, CRP and DAS28 levels were significantly reduced at T1, T3, T6, T9, and T12 with the respect to T0 (Figure 1A-C). C3 levels were significantly reduced at T3, T6, and T9 with the respect to T0 while C4 levels were significantly reduced at T3, T6, T9, and T12 with the respect to T0 (Figure 1D-E). Positive correlations resulted between DAS28 and both C3 and C4 at T1 and T3 (Figure 1F-I). C3 and C4 were directly related with ESR at T1 (C3: P 0.002; C4: P 0.005), T3 (C3: P 0.04; C4: P 0.03), and T6 (C3: P<0.0001; C4: P 0.002) and with CRP at T1 (C3: P 0.03; C4: P 0.01) and T6 (C3: P<0.0001; C4: P 0.03). When stratifying patients in accordance with the EULAR response to therapy, C3 decreased significantly in responders than in no-responders at T1; moreover, responders showed lower levels of both C3 and C4 at T1 and T3 with the respect to T0 (Figure 1L-O).

Conclusions: In RA patients, treatment with TCZ is able to reduce C3 and C4

levels in an early and sustained way. The disease activity is directly related with the reduction of C3 and C4 serum levels. RA patients with a good/moderate clinical response show significantly lower C3 and C4 levels than no-responder patients. Our preliminary data suggest that C3 and C4 can be a reliable marker of both the disease activity and the response to therapy in RA patients treated with TCZ.

Disclosure of Interest: None declared

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AB0411 COMPARISON OF TUBERCULIN SKIN TEST AND INTERFERON-GAMMA RELEASE ASSAY SCREENING IN PATIENTS WITH RHEUMATOID ARTHRITIS STARTING ANTI-TUMOR NECROSIS FACTOR THERAPY

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Background: Biologic agents provide clinical benefits in patients with Rheumatoid Arthritis (RA) but they are associated with an increased risk of tuberculosis (TB) infection.

Objectives: We investigated the accordance between the tuberculin skin test (TST) and the interferon-gamma (IFN-γ) release assay (IGRA) for the diagnosis of latent tuberculosis infection (LTBI) in patients with RA. The objective of our study was a direct comparison between the IGRA and the TST regarding LTBI diagnosis in RA patients before starting anti-TNF agents and at least one year after the initiation of treatment.

Methods: RA consecutive patients have been included in the study both before and after 1 year of the initiation of TNF-α antagonist therapy. A standard questionnaire was completed for each patient, including basic demographic data and concurrent immunosuppressive therapy (corticosteroids, disease-modifying anti-rheumatic drugs [DMARDs], synthetic and biologics). The patients were screened for LTBI using IGRA and TST methods.

All analyses were performed with IBM-SPSS Statistics for Windows (version 21). The kappa coefficient (κ) was calculated to determine the concordance between the two tests: TST and IGRA. The strength of the agreement was considered "poor" for κ ≤0.20, "low-moderate" for 0.20 < κ ≤0.40, moderate for 0.40 < κ ≤0.60, "substantial" for 0.60 < κ ≤0.80, and "optimal" for 0.80 < κ ≤1.

Results: 78 patients (67 female, 11 male) have been screened with TST and IGRA. The accordance between TST and IGRA was 89.7% (κ 0.514, κ<0.001). A κ value of 0.514 represents a moderate accordance between the two tests. 6 female patients converted TST (4 became positive, and 2 became negative). No patient developed active tuberculosis.

Conclusions: A moderate accordance between the two methods (TST and IGRA) was obtained. In the absence of a diagnostic gold standard for LTBI, different issues should be taken into consideration regarding the two methods (cost, laboratory expertise and equipment etc). More studies are needed in the field in order to elucidate the cost-effectiveness but also the appropriateness of both methods.

Disclosure of Interest: None declared

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AB0412 LESS THAN 5% OF REAL-LIFE PATIENTS WHO SWITCH FROM IV TO SC ABATACEPT IN REAL-WORLD CLINICAL PRACTICE SUBSEQUENTLY SWITCH BACK TO THE IV FORMULATION

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Background: Patients (pts) with RA may be able to switch from IV to SC abatacept with no loss of efficacy or safety concerns, but data are inconclusive.¹⁻⁴ In the ACTION (AbataCepTIn rOutiNe clinical practice; NCT02109666) study, a 1-year interim analysis showed that switching had no adverse clinical effect.⁵

Objectives: To examine treatment patterns and explore abatacept formulation switching over 2 years in ACTION.

Methods: ACTION is a 2-year, prospective, observational study of pts with moderate-to-severe RA who initiated IV abatacept in Europe and Canada between May 2008 and December 2013. Assessments in biologic-naïve and biologic-failure pts were: baseline characteristics, rates of and reasons for switching (IV to SC), and re-switching to IV over 2 years. Descriptive data were generated: mean (SD) for continuous variables and n (%) for categorical variables. Rates of switching were estimated by Kaplan-Meier analysis. Cohorts were pooled to analyse further pts who switched owing to low numbers.

Results: In the ACTION cohort, 2350/2364 pts (99.4%) were evaluable for this analysis (673 [28.6%] biologic naïve, 1677 [71.4%] biologic failure). A total of 729

(43.4%) biologic-failure pts had received 1, and 948 (56.6%) had received ≥ 2 previous biologics. Baseline characteristics in biologic-naïve and biologic-failure pts, respectively, were: mean (SD) age 59.9 (12.7) and 56.9 (12.5) years; RA duration 7.2 (8.22) and 12.1 (9.13) years; 496 (73.7%) and 1379 (82.2%) were women; 621 (92.3%) and 1552 (92.5%) had received prior MTX; and 533 (79.2%) and 1386 (82.6%) had received corticosteroids. Over 2 years, 195 pts switched from IV to SC abatacept (57 biologic naïve, 138 biologic failure; Fig.). Reasons for switching were available for 172 pts (51 biologic naïve, 121 biologic failure; some had >1 reason); biologic naïve/biologic failure: pt wish 54.9%/62.0%, physician choice 31.4%/19.8%, safety 5.9%/9.9%, remission/major improvement 3.9%/5.0%, poor compliance 0%/4.1%, lack of efficacy 2.0%/3.3%, surgery 2.0%/0.8%, weight adjustment 2.0%/0%, other 49.0%/36.4%. Only eight pts (2.6%) re-switched to IV abatacept (2 biologic naïve, 6 biologic failure). Reasons for re-switching were: pt wish (n=4), lack of efficacy (n=4), safety issue (n=1) and other (n=2).

Figure. Patients Who Switched From IV to SC Abatacept Over 2 Years (Kaplan-Meier Analysis)

Conclusions: Less than 5% of pts who switched formulation from IV to SC abatacept in real-world clinical practice re-switched to the IV formulation, suggesting that switching has no adverse clinical impact. A change in formulation was mainly due to pt wish, reflecting their involvement in decision-making.

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AB0413 INDUCTION AND PROGRESSION OF SUBCUTANEOUS NODULOSIS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

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Background: Tocilizumab (TCZ) is a monoclonal antibody (moAb) directed against the IL-6 receptor approved for moderate-to severe rheumatoid arthritis (RA) treatment. Some authors have reported a beneficial effect of TCZ in preventing lung and subcutaneous nodulosis in RA patients. On the contrary, to our knowledge no data concerning the acceleration of subcutaneous nodulosis under TCZ therapy are currently available.

Objectives: We report a small case series of 5 RA patients experimenting an evident worsening of subcutaneous nodulosis during the treatment with intravenous tocilizumab.

Methods: Our cohort included 5 patients (1 male and 4 females, mean age $\pm$ Standard Deviation (SD) 64 $\pm$ 10.6 years, mean disease duration $\pm$ SD 21.8 $\pm$ 10.9 years). Four patients were rheumatoid factor and anti-citrullinated peptide antibodies positive. Each patient had been previously treated with several conventional and biologic drugs. At the time of observation, three subjects were practicing methotrexate (MTX), two patients were taking hydroxychloroquine (HCQ) and one patient was taking prednisone. Intravenous tocilizumab 8 mg/kg every 4 weeks was administered for a mean $\pm$ SD of 43.4 $\pm$ 32.4 months, with

a good disease control in 3 cases. All the patients had a previous history of subcutaneous nodulosis that considerably worsened during the treatment with tocilizumab. Patients experimented the development of new subcutaneous nodules localized at the fingers, elbows or the inframammary fold, tending to ulceration. The management of this medical event included the tapering of MTX, the administration of steroids, the addition of HCQ, the use of antibiotics and surgery. However, neither pharmacological nor surgical treatment was completely effective, as nodules tended to recur and to increase in number and dimensions.

Results: To our knowledge this is the first report describing an accelerated subcutaneous nodulosis in a small cohort of RA patients treated with tocilizumab.

Disclosure of Interest: None declared

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AB0414 THE USE OF RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: IN WHICH INFUSION INTERVALS WERE GIVEN AND HOW DID THEY RESPOND? HUR-BIO REAL LIFE RESULTS

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Background: Rituximab is one of the treatment options in rheumatoid arthritis (RA) patients and officially recommended as a maintenance treatment given every 6 months after the initial loading of first course.

Objectives: In this real life study, it was aimed to investigate the infusion frequency of rituximab maintenance treatment and possible effects on disease activity.

Methods: The HUR-BIO is a single-center biologic registry of Hacettepe University which is established in Ankara and in which patients have been prospectively recorded since 2012. This database has 1235 RA patient records as of August 2016. Rituximab was prescribed at least once in 273 (22.1%) patients. The residence address of 85 those patients was within the boundaries of center city (Ankara) and they were included in to the study. In our clinic, the dates and the DAS-28 scores at the time of rituximab courses were recorded. Rituximab infusion compliance was classified as; "regular" if there is less than one month delay, "slightly irregular" if less than 3 months delay and "irregular" if more than 3 months delay.

Results: The mean age of the 85 patients (80% female) was 59.1 (10.1), the mean disease duration was 12.9 (8.6) years and 74.1% of patients were seropositive. 39/85 (46%) patients previously used at least one biological agent (46 (54%) patients were biologic naïve before Rituximab therapy). Median rituximab course number was 3 (1–8). A total of 211 rituximab courses were given to 85 patients. Rituximab course number and percentage is shown in figure. The mean interval time between rituximab courses was 7.9 (2.8) months. Total of 102 (52.6%)