Objectives: To test the hypothesis that low or absent ERAP1 activity alters CD8 T cell immunogenicity through changes in the HLA-B51 peptidome and shapes the CD8 T cell immune response in affected subjects.

Methods: We generated HLA-B51* ERAP1 KO LCL clones using CRISPR-Cas9, performed mass spectrometry of the immunoprecipitated MHC-class I peptidome with subsequent computational deconvolution for HLA-B51-binding peptides. We then assessed single cell (ICS), bulk (ELISA) and proliferative (CFSE) CD8 effector (IFN γ , granzyme B, perforin) T cell responses through stimulation of allogeneic donor cells with WT vs KO LCL and determined ERAP1 haplotypes in 49 untreated Turkish BD subjects with ocular and/or major vascular involvement as well as healthy donors (HD) whose PBMC were profiled using 6 multicolour flow cytometry panels.

Results: WT and KO peptidomes differed significantly ($p < 0.0005$ Fisher's exact test) with a distinctive shift of peptide length frequencies exceeding 9-mer (binding optimum) in the KO vs WT. This held true for computationally deconvoluted HLA-B51 binders. IFN γ secretion from CD8 T cells stimulated with KO LCL was significantly different from WT (ICS, $p = 0.0006$; ELISA, $p = 0.0059$) as were CD8 T cell proliferation and ICS of perforin/granzyme B* CD8 T cells. Analysis of 133 T, B, NK and monocyte cell populations revealed predominance of CD8 T and NKT cell subset in HLA-B51+/Hap10+ BD vs HLA-B51+/Hap10- BD and HD, accounting for 80% of all populations reaching significance ($p < 0.05$, Mann-Whitney). Naive and effector memory CD8 T cell subsets were inversely correlated. Cohen's effect sizes were large (> 0.8) or very large (> 1.2).

Conclusion: We show that absence of functional ERAP1 alters human CD8 T cell immunogenicity. This is mediated by an HLA-class I peptidome with propensity for longer peptides above 9mer and suggests loss or de-novo presentation of peptide-HLA-B51 complexes to cognate CD8 TCR. The reciprocal changes in antigen-experienced vs naive CD8 T cell subsets in affected subjects point to biologic significance of HLA-B51/Hap10 in BD. Collectively, our findings suggest that an altered HLA-B51 peptidome modulates immunogenicity of CD8 effector T cells in ERAP1-Hap10 carriers with BD and identify targets for future drug development.

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OP0033

OPTIMIZATION OF TOCILIZUMAB THERAPY IN GIANT CELL ARTERITIS. A MULTICENTER REAL-LIFE STUDY OF 134 PATIENTS

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Background: Tocilizumab (TCZ) is the only biological agent approved in Giant Cell Arteritis (GCA). There is general agreement on the initial and the standard maintenance dose of TCZ. However, information on duration and optimization of TCZ in GCA is scarce.

Objectives: Our aim was to assess efficacy and safety of TCZ therapy optimization in an unselected wide series of GCA in clinical practice.

Methods: Multicenter study, 134 patients with GCA who received TCZ due to inefficacy/adverse events of previous therapy. Once complete remission was reached and based on a shared decision between patient and physician TCZ was optimized in some cases. Optimization was done by decreasing the dose and/or prolonging the TCZ dosing interval progressively.

Results: 134 GCA patients treated with TCZ (101w/33m); mean age 73.0±8.8 years. TCZ was administered IV to 106 (79.1%) patients and SC to 28 (20.9%). TCZ was optimized in 43 (32.1%) patients. No demographic, clinical manifestations or laboratory data differences had been found at TCZ onset (TABLE). After a follow up of 12 [6-15.5] months, and a

complete remission for 6 [3-12] months; the first TCZ optimization was performed. Median prednisone dose at first TCZ optimization was 2.5 [0-5] mg/day. TCZ IV was optimized from 8 to 4mg/kg/4weeks in 12 of 106 (11.3%) and from 162mg/SC/week to 162mg/SC/2weeks in 9 of 28 (32.1%) cases. Five (11.6%) of the 43 optimized cases relapsed. In 4 cases, the relapses were treated increasing TCZ up to the pre-optimization dose, in 1 case the route of administration was change (4mg/kg/4week to 162mg/SC/week). In 8 of 43 optimized patients (18.6%), it was possible to withdraw TCZ after complete remission for 30 [16.25-45.75] months. Regarding adverse events and severe infections were similar in both groups. The mean TCZ treatment costs were lower in the optimized group.

Conclusion: Once remission is reached in GCA patients under TCZ treatment, optimization of TCZ may be performed. Based on our experience it could be performed by reducing the dose with IV TCZ or by prolonging dosing interval with SC TCZ.

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TABLE

	OPTIMIZED-TCZ GROUP (n=43)	NON-OPTIMIZED TCZ GROUP (n=91)	p
BASAL FEATURES AT TCZ ONSET			
GENERAL FEATURES			
Age, years, mean± SD	68.9±8.7	71.4±8.5	0.125
Sex, female/male n(%)	32/10	68/24	0.779
Time from GCA diagnosis to TCZ onset (months), median [IQR]	19.5[7.75-45]	10.5[4-25]	0.047
SYSTEMIC MANIFESTATIONS			
Fever, n(%)	1(2.4)	8(8.7)	0.176
Constitutional syndrome, n(%)	11(26.2)	19(20.7)	0.476
PMR, n(%)	18(42.9)	56(60.9)	0.052
ISCHEMIC MANIFESTATIONS			
Visual involvement, n(%)	5(11.9)	23(25)	0.084
Headache, n(%)	26(61.9)	42(45.7)	0.081
Jaw claudication, n(%)	1(2.4)	11(12)	0.072
CORTICOSTEROIDS AT TCZ ONSET			
Prednisone dose, mg/d mean (SD)	15.1±11.1	25±17.4	0.001
FOLLOW-UP ON TCZ THERAPY (MONTHS), MEDIAN [IQR]	24[18-27]	6 [3-18]	0.000
RELAPSES			
Relapses, n(%)	5(11.6)	5(5.5)	0.207
End follow-up remission, n(%)	40(93)	84(92)	0.99
Severe side effects, n(%)	14(32.6)	22(24.2)	0.307
Serious infections, n(%)	6(14)	10(11)	0.878
Cost, (mean) euros per year			
IV	7 538.4	11 726.4	-
SC	7 329.0	11 726.4	-

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Lung diseases and other comorbidities in RA

OP0034

DOES THE RISK OF VENOUS THROMBOEMBOLISM VARY WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS?

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Background: Patients with rheumatoid arthritis (RA) are at increased risk for venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) (1). Several established risk factors of VTE, such as age, immobilization and comorbid conditions, occur more often patients with RA (2). In addition, inflammation may in itself also increase VTE risk by upregulating procoagulatory factors and causing endothelial damage (3). Recent reports indicate an increased risk of VTE in RA patients treated with JAK-inhibitors (4), pointing to the need to better understand how inflammation measured as clinical RA disease activity influences VTE risk.

Objectives: To investigate the relationship between clinical RA disease activity and incidence of VTE.

Methods: Patients with RA were identified from the Swedish Rheumatology Quality Register (SRQ) between July 1st 2006 and December 31st 2017. Clinical rheumatology data for these patients were obtained from the visits recorded in SRQ, and linked to national registers capturing data on VTE events and comorbid conditions. For each such rheumatologist visit, we defined a one-year period after the visit and determined whether a VTE event had occurred within this period or not. A visit followed by a VTE event was categorized as a case, all other visits were used as controls. Each patient could contribute to several visits. The DAS28 score registered at the visit was stratified into remission (0-2.5) vs. low (2.6-3.1), moderate (3.2-5.1) and high (>5.1) disease activity. Logistic regression with robust cluster standard errors was used to estimate the association between the DAS28 score and VTE.

Results: We identified 46,311 patients with RA who contributed data from 320,094 visits. Among these, 2,257 visits (0.7% of all visits) in 1345 unique individuals were followed by a VTE within the one-year window. Of these, 1391 were DVT events and 866 were PE events. Figure 1 displays the absolute probabilities of a VTE in this one-year window, and odds ratios for VTE by each DAS28 category, using DAS28 remission as reference. The one-year risk of a VTE increased from 0.5% in patients in DAS28 remission, to 1.1% in patients with DAS28 high disease activity (DAS28 above 5.1). The age- and sex-adjusted odds ratio for a VTE event in highly active RA compared to RA in remission was 2.12 (95% CI 1.80-2.47). A different analysis, in which each patient could only contribute to one visit, yielded similar results.

Figure 1. Odds ratios (OR) comparing the odds of VTE for DAS28 activity categories versus remission. Grey estimates are from unadjusted logistic regression models, black estimates are from logistic regression models adjusted for age and sex. Absolute one-year risk of VTE are estimated from unadjusted models.

Conclusion: This study demonstrates a strong association between clinical RA inflammatory activity as measured through DAS28 and risk of VTE. Among patients with high disease activity one in a hundred will develop a VTE within the coming year. These findings highlight the need for proper VTE risk assessment in patients with active RA, and confirm that patients with highly active RA, such as those recruited to trials for treatment with new drugs, are already at particularly elevated risk of VTE.

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OP0035

EXAMINATION OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS – PREVALENCE, TIME TO ONSET, AND CLINICAL CHARACTERISTICS

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Background: Interstitial lung disease (ILD) is a known extraarticular manifestation of rheumatoid arthritis (RA). Previous studies have shown variability in the prevalence of RA-ILD, as well as clinical characteristics and risk factors of RA-ILD.

Objectives: To evaluate the prevalence and time to onset of ILD and compare the clinical characteristics between RA patients (pts) with or without ILD using a large US electronic medical record (EMR)-based dataset.

Methods: Pts with an initial RA diagnosis (ICD-9-CM code: 714.0; ICD-10-CM codes: M05 & M06) during the study period (01JAN2009-20SEP2019) were included from the Discus Analytics JointMan database. The initial RA diagnosis date was defined as the index date. Pts with ILD were identified by ICD diagnosis codes or by provider indication in the JointMan record. Pts who developed ILD before RA were excluded from this analysis. The prevalence and time to onset of ILD were reported. Pt demographics, comorbidities, RA characteristics and disease activity scores were compared for 6 months prior to or on the index date (baseline period) for selected adult RA pts with available information.

Results: Among 8,963 identified RA pts, 337 (3.8%) were diagnosed with ILD on or after RA diagnosis. The median time to ILD onset post-RA was 2.3 years, and 47% had ILD within 2 years after RA diagnosis. RA-ILD pts were significantly older than those without ILD (65.8 years vs. 59.1 years; $p < 0.001$; Table 1). At baseline, a higher percentage of RA-ILD pts had history of chronic obstructive pulmonary disease, positive rheumatoid factor, rheumatoid nodules, erosive joint disease, positive anti-cyclic citrullinated peptide antibody, and joint swelling compared to RA-only pts (Table 2). The mean ESR and RA disease activity scores were also significantly higher for RA-ILD pts.

Table 1. Patient Demographics

Patient demographics	RA-ONLY Cohort (N = 5,612)	RA-ILD Cohort (N = 205)	P-value
Age, Mean $\pm$ SD, years	59.1 $\pm$ 14.2	65.8 $\pm$ 11.8	<.001
Male, N (%)	1,375 (24.5%)	72 (35.1%)	0.001
Race, N (%)			
White	4,014 (71.5%)	165 (80.5%)	0.005
African American	365 (6.5%)	9 (4.4%)	0.226
Other/Missing	1,233 (22.0%)	31 (15.1%)	0.020

Table 2. Baseline Clinical Characteristics

Clinical Characteristics	RA-ONLY Cohort (N = 3,846)	RA-ILD Cohort (N = 115)	P-value
History of Chronic Obstructive Pulmonary Disease, N (%)	102 (2.7%)	8 (7.0%)	0.006
Hypertension, N (%)	900 (23.4%)	23 (20.0%)	0.395
Serious Infection, N (%)	38 (1.0%)	3 (2.6%)	0.091
Rheumatoid Factor Positive, N (%)	1,388 (36.1%)	69 (60.0%)	<.001
Joint Stiffness, N (%)	1,092 (28.4%)	39 (33.9%)	0.197
Rheumatoid Nodules, N (%)	153 (4.0%)	17 (14.8%)	<.001
Erosive Joint Disease, N (%)	459 (11.9%)	23 (20.0%)	0.009
Anti-CCP Antibody Positive, N (%)	858 (22.3%)	45 (39.1%)	<.001
Joint Swelling*, N (%)	2,861 (58.0%)	123 (68.0%)	0.008
Joint Tenderness*, N (%)	3,728 (75.6%)	138 (76.2%)	0.851
ESR**, Mean $\pm$ SD, mm/hr	22.0 $\pm$ 22.6	30.1 $\pm$ 25.5	<.001
CRP**, Mean $\pm$ SD, mg/L	22.5 $\pm$ 13.0	60.6 $\pm$ 25.0	0.086
CDAI, Mean $\pm$ SD	16.4 $\pm$ 12.3	18.9 $\pm$ 15.7	0.044
DAS28-CRP, Mean $\pm$ SD	2.6 $\pm$ 1.2	3.1 $\pm$ 1.4	<.001
DAS28-ESR, Mean $\pm$ SD	3.3 $\pm$ 1.4	3.9 $\pm$ 1.5	<.001
SDAI, Mean $\pm$ SD	20.2 $\pm$ 29.3	28.6 $\pm$ 40.2	0.048

* A total of 4,929 non-ILD and 181 ILD patients had joint swelling and tenderness data.

** Variables were calculated among patients who had available information.

Conclusion: This large real-world RA population provides insight into the burden of ILD in RA pts. Pts with ILD had a higher proportion of comorbidities and RA-related conditions and higher RA activity. Further analysis is warranted to assess the risk factors of ILD and its prognosis.

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