without active disease and 19% still experiencing active disease. 32% were still receiving GCs - 22% of them receiving > 5mg/ day. There was negative impact on functional status with 14% reducing working hours, 13% restricted social life, 6% leaving employment, 6% registered as disabled and 2% leaving full time education.

**Conclusion:** The start of maintenance treatment in AAV is variably defined but typically at 6 months after start of remission induction therapy. Achieving full remission and preventing relapse are still clinical problems and many patients require ongoing GC therapy to maintain remission. Infectious complications and adverse events are common and there is significant negative impact on patient functional status over time.

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OP0030      **GRANULOMATOSIS WITH POLYANGIITIS SUSTAINED REMISSION OFF-THERAPY: DATA FROM THE FRENCH VASCULITIS STUDY GROUP REGISTRY**

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**Background:** Data on granulomatosis with polyangiitis (GPA) sustained remission off-therapy (SROT) are limited and it is unknown whether disease characteristics or treatment regimen may affect it.

**Objectives:** This study aimed to assess SROT of GPA patients from the French Vasculitis Study Group registry, and identify factors associated with its occurrence and durability during follow-up.

**Methods:** GPA had to satisfy the 1990 ACR classification criteria and/or revised Chapel Hill Nomenclature for study inclusion. SROT was defined as remission (BVAS=0) without glucocorticoids (GC) or immunosuppressants (IS), the latter for ≥6 months (ie 2 consecutive visits). SROT and its duration were extracted from the database. Data from patients with 3-, 5- and 10-year SROT were analyzed. Baseline characteristics of patients with 3-year GPA SROT were compared to those of registry GPA patients with available data at 3 years but not in SROT (controls), and 3-year SROT achieving 5-year SROT vs those who relapsed between 3 & 5 years. Patients with 3-year GPA SROT follow-up +7 years were analyzed according to maintained SROT or not.

**Results:** Among 795 database patients with new-onset GPA, 259 achieved at least 1 SROT at some time during their disease, after a median [IQR] of 36 [28–63] months post-diagnosis. The first SROT lasted a median of 14 [I8-32] months. Among 202 of those patients who had follow-up, 73 (36%) remained in SROT for a median follow-up of 34 [14-45] months post-SROT. Among 434 (54%) patients followed for ≥3 years post-diagnosis, 82% had received GC and cyclophosphamide induction therapy. At 3 years post-diagnosis, 92 (21%) patients in SROT were compared to 342 (79%) controls who had relapsed or were still taking GC or IS. Patients achieving 3-year SROT vs controls, respectively, had more frequently received intravenous cyclophosphamide as induction therapy (89% vs 77%, P=0.01), with a higher median number of infusions (7.5 vs 6; P=0.05); no other clinical or biological baseline difference was found. Among those 92 3-year SROT patients, 74 had ≥2 years of additional follow-up: 46 (62%) attained 5-year SROT and 28 (38%) had relapsed after a mean follow-up of 13 months. Baseline clinical and biological characteristics of patients achieving 5-year SROT did not differ from those of 3-year SROT patients who relapsed. Among those 92 3-year SROT patients, 16 had ≥7 additional years of follow-up: 6 (38%) achieved 10-year SROT, ie 8% of 75 GPA with available data at 10 years, and 10 (63%) had relapsed a mean 35 ± 28 months after achieving 3-year SROT.

**Conclusion:** Only 8% of GPA patients achieved 10-year SROT after conventional induction and maintenance therapies. No baseline clinical or biological characteristics helped distinguish patients achieving or maintaining SROT and those who relapsed. However, patients achieving 3-year SROT had received more intensive induction therapy than those who relapsed or were still on GC or IS at 3 years.

**Disclosure of Interests:** None declared

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OP0031      **AN INCREASE IN SERUM CALPROTECTIN LEVEL IN ANCA-ASSOCIATED VASCULITIDES PATIENTS DURING MAINTENANCE THERAPY IS ASSOCIATED WITH MORE RELAPSE AND ACCELERATED RENAL FUNCTION DECLINE**

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**Background:** Calprotectin (S100A8/A9), a protein secreted by activated neutrophils and monocytes in inflammatory conditions, is upregulated in active ANCA-associated vasculitides. Serum calprotectin level variation during induction therapy is associated with disease relapse in PR3-ANCA-associated vasculitides (1). However, the place of this biomarker during maintenance therapy is unknown.

**Objectives:** To demonstrate whether variation in serum calprotectin level during maintenance therapy could be used as a biomarker predicting subsequent relapse in ANCA-associated vasculitides.

**Methods:** Patients with ANCA-associated vasculitides in complete remission (BVAS=0) after induction therapy with cyclophosphamide and included in the MAINRITSAN trial (2) were analyzed. Patients were randomized to receive rituximab or azathioprine as maintenance therapy. Relapse was defined as the re-occurrence or new onset of disease attributable to active vasculitis. Accelerated decline renal function (estimated Glomerular Filtration Rate (eGFR) assessed using the MDRD equation) was defined in concordance with NICE 2015 guideline (3) as "a decrease in eGFR of 25% or more and a change in GFR category or a sustained decrease in eGFR of 15 ml/min/1.73m² over 12 months". Calprotectin was assessed in the serum at inclusion and 6 months by ELISA (IDK® Calprotectin ELISA kit, Immunodiagnostik). We defined an increase in serum levels of calprotectin as a positive variation of calprotectin level at M6 compared to baseline.

**Results:** Of all, 96 patients (female 45.8%, mean age 55.3±13.5, 69.8% PR3+, 62.5% ANCA positive at inclusion) had at least a calprotectin dosage (86 at baseline, 86 at M6 and 76 patients at this 2 time-point). Calprotectin level at baseline or 6 months was not significantly different between relapsing patients and those without relapse after 18 months of follow-up, whereas the calprotectin variation at M6 compared to baseline was higher in relapsing patients (n=10) (mean (SD) 17991 (±28972) ng/ml) than in patients not experiencing any relapse (n=66) (9419 (±50002) ng/mL; p=0.03). An increase in serum calprotectin level at 6 months was significantly associated with an increased risk of relapse in PR3-ANCA patients (OR=5.6 (95%CI, 1.0-31.3; p=0,049) but not in the whole study group (OR=3.3 (95%CI, 0.8-14.1; p=0.1), and identified patients with accelerated renal function decline (all cohort: OR=10.6 (95%CI, 2.9-39.6; p=0.002; PR3+ patients: OR=5.909 (95%CI, 2.9-39.6; p=0.01)), whereas calprotectin level did not correlate with glomerular filtration rate (r = -0.07, p=0.35).

**Conclusion:** An increase in serum calprotectin during the first 6 months of maintenance therapy in ANCA-associated vasculitides is a useful biomarker predicting vasculitis relapse and accelerated renal function deterioration in the following 12 months.
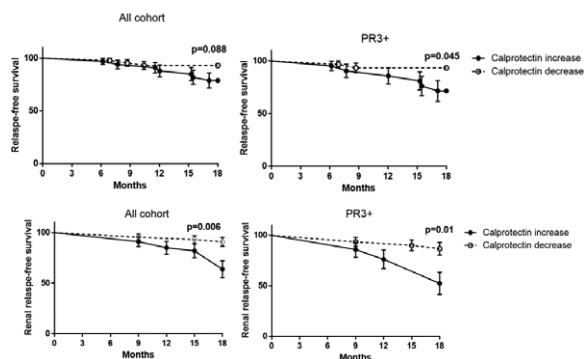


**Increase calprotectin serum at 6 months identify relapser and accelerated decline renal function at 1 year.** Kaplan-Meier survival curves of ANCA-associated vasculitis patients with an increase in serum calprotectin at 6 months (solid line) or not (dotted line) remaining total relapse-free or accelerated decline renal function-free. Gehan-Beslow-Wilcoxon test.

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OP0032      **ERAP1-MEDIATED IMMUNOGENICITY AND IMMUNE-PHENOTYPES IN HLA-B51+ BEHÇET'S DISEASE POINT TO PATHOGENIC CD8 T CELL EFFECTOR RESPONSES**

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**Background:** HLA-B51 is a definite risk factor for Behçet's disease (BD). A coding variant of ERAP1, Hap10 – with low peptide-trimming activity – vastly potentiates this risk, but is mechanistically unclear[1,2].

**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 (IFNg, 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. IFNg 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, n(%) | 5(11.6) | 5(5.5) | 0.207 |
| End follow-up remission, n(%) | 40(93) | 84(92) | 0.99 |
| Severe side efects, n(%) | 14(32.6) | 22(24.2) | 0.307 |
| Seriuos 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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