Figure 1. Mean RA-WIS by allocation group over 2 years of follow-up. Mean ± Standard Error are plotted.

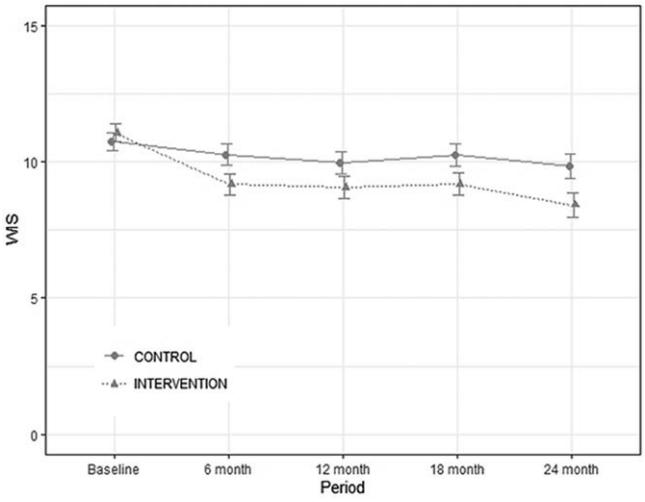
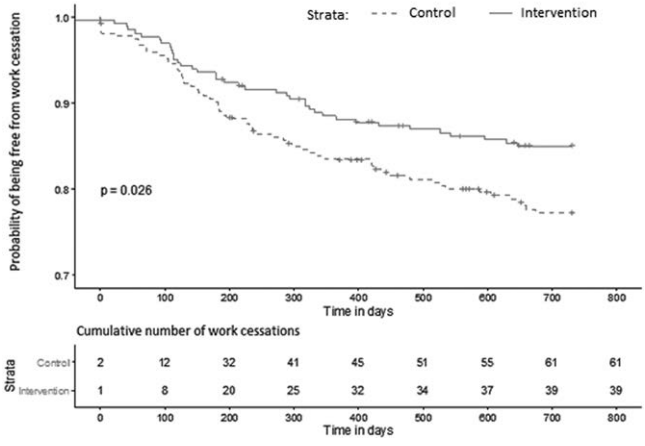


Figure 2. Kaplan Meier analysis of time to work cessation ≥2 months



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OP0011

A RANDOMIZED, DOUBLE-BLIND, ACTIVE-CONTROLLED STUDY OF AVACOPAN IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS

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Background: Complement fragment C5a is strongly linked to the pathogenesis of Anti-Neutrophil Cytoplasmic Antibody (ANCA)-associated vasculitis (AAV). C5a receptor (C5aR), present on neutrophils, is a G protein-coupled receptor for C5a. Avacopan (previously CCX168) is an orally-administered selective antagonist of C5aR which blocks C5a-induced cell activation. Two previous Phase 2 clinical trials provided evidence of effectiveness of avacopan in AAV and its potential to eliminate extensive use of glucocorticoids (GC) and GC-related toxicities.

Objectives: This Phase 3 study evaluated the efficacy and safety of avacopan for the treatment of AAV.

Methods: Eligible subjects were randomized 1:1 to receive either prednisone or avacopan in combination with either a) cyclophosphamide (oral or IV) followed by azathioprine or b) rituximab (four IV infusions). Randomization was stratified by the treatment regimen (rituximab, IV cyclophosphamide, or oral cyclophosphamide), ANCA serotype, and newly-diagnosed or relapsing disease. Treatment period was 52 weeks; primary efficacy endpoints were the proportion of subjects achieving disease remission at Week 26, and sustained disease remission at Week 52. Remission was defined as a Birmingham Vasculitis Activity Score (BVAS) of zero and not taking glucocorticoids for AAV within 4 weeks prior to Week 26. Sustained remission was defined as being in remission at Week 26 and also subsequently in remission as defined above at Week 52. Any relapse of AAV between Weeks 26 and 52 was considered not achieving sustained remission.

Results: 330 subjects were randomized and dosed: 166 in avacopan and 164 in prednisone arms. At Week 26, 72.3% subjects achieved remission in the avacopan arm compared to 70.1% in the prednisone arm ($p<0.0001$ for non-inferiority). At Week 52, 65.7% subjects achieved sustained remission in the avacopan arm compared to 54.9% in the prednisone arm achieving both non-inferiority and superiority to prednisone arm ($p=0.0066$ for superiority of avacopan).

The avacopan arm had a significant reduction in glucocorticoid-related toxicity compared to the prednisone arm as measured by the Glucocorticoid Toxicity Index (GTI) of Cumulative Worsening Score ($p=0.0002$) and Aggregate Improvement Score ($p=0.0082$).

In subjects with renal disease at baseline, the avacopan arm showed a mean increase in estimated glomerular filtration rate (eGFR) of 7.3 mL/min/1.73 m2 from baseline to week 52 as compared to 4.0 mL/min/1.73 m2 increase in the prednisone arm ($p=0.0259$).

Overall subject incidence of serious adverse events (SAEs) was generally consistent with previous AAV trials at 45.1% and 42.2% for prednisone and avacopan groups, respectively. Serious infections were 15.2% and 13.3%, serious hepatic adverse events 3.7% vs 5.4%, and SAEs of white blood cell count decreases were 4.9% vs 2.4% for prednisone and avacopan, respectively. No meningococcal infections were reported.

Conclusion: Avacopan treatment resulted in remission in AAV patients receiving rituximab or cyclophosphamide/azathioprine at a rate that was non-inferior to the active comparator prednisone at week 26 and superior to prednisone in sustained remission at Week 52. A significant reduction in glucocorticoid-related toxicity was observed in the avacopan vs. prednisone arms. Significant increase in eGFR in subjects with renal disease was also observed in avacopan vs. prednisone. The safety profile of avacopan appears acceptable for development in AAV. Avacopan treatment for AAV is efficacious and exhibits benefits not seen with chronic prednisone therapy.

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OP0012

TNF INHIBITORS ARE ASSOCIATED WITH A REDUCED RISK OF VENOUS THROMBOEMBOLISM COMPARED TO CSDMARDS IN RA PATIENTS

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Background: While the short-term use of bDMARDs up to 180 days has been associated with an increased risk of venous thromboembolism (VTE) compared to csDMARDs in patients with rheumatoid arthritis (RA), the long term use of more than 730 days has been associated with a decreased risk based on claims data [1]. Among patients with inflammatory bowel disease, observational data indicated that TNF inhibitors may have a protective effect regarding the VTE risk [2].

Objectives: To assess the effects of TNF inhibitors and newer bDMARDs (including abatacept, rituximab, sarilumab, and tocilizumab) on the VTE risk based on observational data from RA patients.
Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. This analysis comprises patients who were enrolled with start of a bDMARD between 01/2009 and 04/2019 and had at least one follow-up.
Cox regression models were used to calculate hazard ratios (HRs) for VTEs, for csDMARDs, TNF inhibitors and other bDMARDs. Propensity score weighting was used to adjust for confounding by indication.
Results: Patients receiving TNF inhibitors or other bDMARDs on average had higher CRP levels and a higher prevalence of cardiovascular diseases at baseline than patients receiving csDMARDs. They also received more often glucocorticoids (Table 1).

Table 1. Patient characteristics at baseline for DMARD groups

Parameter	csDMARDs	TNFi	Other bDMARDs
N	3500	5060	2534
VTE event	38 (1.1)	55 (1.1)	23 (0.9)
Age [years]	58.8 (12.6)	56.5 (12.9)	58.1 (12.4)
Female sex	2575 (73.6)	3734 (73.8)	1933 (76.3)
Disease duration [years]	6.2 (7.2)	9.4 (8.6)	11.9 (9.2)
Seropositivity	2189 (62.6)	3739 (73.9)	2048 (80.8)
Joint erosions	1024 (31.0)	2566 (52.4)	1523 (63.3)
Prior bDMARD therapies	0 (0.2)	0.3 (0.6)	1.2 (1.2)
CRP	8.8 (8.1)	11.6 (10.6)	12.4 (11.8)
DAS28-ESR	4.4 (1.3)	4.9 (1.2)	5.1 (1.3)
% of full physical capacity	71.3 (21.8)	66.2 (22.6)	62.1 (23.5)
Current glucocorticoid therapy	2564 (73.3)	3951 (78.1)	2036 (80.4)
Heart failure	36 (1)	113 (2.2)	93 (3.7)
Coronary artery disease	196 (5.6)	326 (6.4)	183 (7.2)
Cerebrovascular disease	60 (1.7)	86 (1.7)	44 (1.7)
Osteoporosis	400 (11.4)	771 (15.2)	530 (20.9)
Ever smoker	1875 (53.6)	2738 (54.1)	1402 (55.3)

Results are presented as mean ± SD or number (percentage).

The HR of patients receiving TNF inhibitors for a serious VTE event was 0.53 (95% CI: 0.33 – 0.86) compared to csDMARDs, while the HR for patients receiving other bDMARDs was 0.66 (95% CI: 0.40 – 1.09). A CRP level of more than 5 mg/L (HR 2.09, 95% CI: 1.39 – 3.14) and an age above 65 years (HR 2.96, 95% CI: 1.94 – 4.52) increased the risk for a serious VTE event. Better physical function was associated with a decreased risk for VTEs (Table 2).

Table 2. Hazard ratios for VTE events

Parameter (at time of event/end of observation unless specified otherwise)	Hazard ratio	95% confidence interval	
TNF inhibitors (reference: csDMARDs)	**0.53**	**0.33**	**0.86**
Other bDMARDs (reference: csDMARDs)	0.66	0.40	1.09
Age ≥ 65 years (baseline)	**2.96**	**1.94**	**4.52**
CRP ≥ 5 ml	**2.09**	**1.39**	**3.14**
> 5 mg and ≤ 10 mg glucocorticoids/day	1.04	0.55	1.98
> 10 mg and ≤ 15 mg glucocorticoids/day	2.35	0.81	6.79
> 15 mg glucocorticoids/day	2.03	0.76	5.41
% of full physical capacity (per 10 percentage points increase, time of event)	**0.85**	**0.78**	**0.92**
Current smoking (baseline)	0.98	0.61	1.55
Former smoking (baseline)	0.80	0.45	1.43

Conclusion: Treatment with TNF inhibitors (compared to csDMARDs) and better physical function significantly reduced the risk of serious VTE events, while age above 65 years and high CRP levels increased this risk.
References:
[1] Kim S. C. et al. Am. J. Med. 2015; 128(5): 539.e7–539.e17.
[2] Desaj R.J. et al. CMAJ 2017; 189:E1438-47.
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OP0013 SINGLE CELL PROFILE OF SKIN STROMAL AND IMMUNE CELLS AND PERIPHERAL BLOOD IMMUNE CELLS OF SCLERODERMA PATIENTS TOWARDS IDENTIFICATION OF DISEASE MECHANISM, PROGNOSTIC BIOMARKERS AND POTENTIAL THERAPEUTIC TARGETS

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Background: Despite many years of research, our understanding of Systemic Sclerosis (SSc) pathogenic processes, patient-to-patient variability, and diversity of stromal and immune cells within the involved tissues microenvironment, their interaction, as well as the genes and pathways leading to the pathogenesis remains largely unclear. Current technologies for characterizing SSc have limited depth and resolution, which needed for molecular define the small skin stromal and immune cells sub-populations supposed to drive SSc pathogenesis. Single-cell sequencing technologies hold a great potential in genomic medicine since they offer high resolution and sensitivity for unbiased profiling of disease versus normal niches.
Objectives: Comprehensive characterization of stromal and immune cells in the skin and blood of SSc patients, and healthy controls, their specific intra-skin cell states, pathways, cell-cell interactions, and unbiased characterization of cell types profile, biomarkers, drivers, and regulatory pathways associated with specific SSc patient subgroups.
Methods: We applied the massively parallel single cell RNA-seq (MARS-seq) developed in our laboratory to conduct a comprehensive single-cell genomics analysis of skin stromal and immune cells obtained through punch biopsy and blood immune cells from 73 SSc patients (39 DcSSc, 34 LcSSc) and 30 healthy controls. We used the MetaCell analytical method to identify homogeneous and robust groups of cells from single cell RNA-seq data. The perturbed signaling pathways, pathogenic stromal or immune cell subsets are characterized using CyTOF, immunohistochemistry, **P**hysical **I**nteracting **C**ell sequencing (**PIC**-seq), and *in vitro* functional assays.
Results: We collected data from a total of 46,742 high-quality skin stromal cells, and 57,475 high-quality blood and skin immune cells. Analysis of stromal cell compartment led to a detailed map of 261 meta cells organized into 16 broad lineages including: Fibroblasts, Pericytes, Vascular cells, and other cells. In the immune cell compartment, we found 361 meta cells organized into 14 broad lineages (e.g unique skin T, B, NK and dendritic cells). We observed a unique population of stromal and immune cells in the skin and blood of SSc patients as compared to controls. The major and dramatic changes were observed in the stromal cell compartment of the patient's skin compared to controls. In the fibroblast lineage we found a small cluster of cells that were significantly diminished in the SSc patients compared with control, expressed genes associated with fibrosis and vascular remodeling. Significantly higher number of specific subsets of pericytes and vascular cells was found in SSc patients compared to controls. Analysis of the immune cell compartment revealed only minor changes in the immune cell composition in patients compared with controls. Finally, we found known and novel pathways (e.g Wnt/Notch signaling, IFN type I/II, AP-1 pathway, complement cascade activation) and cell-cell interactions that play crucial roles in SSc pathogenicity.
Conclusion: Our study provides a detailed and unprecedented high-resolution atlas of the immune and stromal cells that make up the skin and peripheral blood in a large cohort of SSc patients with diverse disease duration and clinical settings. Our findings of candidate stromal and immune cell subpopulation, genes and pathways constitute the basis for understanding of SSc pathogenesis and heterogeneity and holds great potential to provide clinicians with new and powerful molecular tools for understanding of the immune-stromal cell crosstalk, for finding new biomarkers for SSc activity and complications and for tailoring and identification of new therapeutic targets.
Disclosure of Interests: Chamutal Gur: None declared, Alexandra Balbir-Gurman Consultant of: Novartis, Hagit Peleg: None declared, Suhail Aamar: None declared, Fadi Kharouf: None declared, Yolanda Braun-Moscovici: None declared, Shuang-Yin Wang: None declared, Ido Amit: None declared
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OP0014 COMPARISON OF ANTERIOR UVEITIS OCCURRENCE DURING TREATMENT WITH SECUKINUMAB, ADALIMUMAB, INFLIXIMAB AND ETANERCEPT IN SPONDYLOARTHRITIS

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Background: Randomized controlled trials indicate that compared to tumor necrosis factor inhibitors (TNFi), secukinumab (SEC) has similar efficacy