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 $\pm$ 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 $\geq$ 65 years (baseline)	2.96	1.94 4.52
CRP $\geq$ 5 ml	2.09	1.39 3.14
> 5 mg and $\leq$ 10 mg glucocorticoids/day	1.04	0.55 1.98
> 10 mg and $\leq$ 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.

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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, Physical Interacting Cell 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.

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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

regarding axial inflammation in spondyloarthritis (SpA), better efficacy regarding cutaneous psoriasis, but is inferior in inflammatory bowel disease (IBD). However, the efficacy of SEC compared to TNFi in anterior uveitis (AU) has not been extensively studied.

Objectives: To compare the occurrence of AU in patients with SpA treated with SEC, adalimumab (ADA), infliximab (IFX) or etanercept (ETN), in clinical practice.

Methods: Patients with ankylosing spondylitis or undifferentiated SpA starting either SEC, ADA, IFX or ETN, in 2015 through 2017, were identified in the Swedish Rheumatology Quality register, and were linked to the national patient register for identification of AU. AU-flares were defined as the number of visits with an AU diagnosis, separated by a ≥ 60 days penalty interval, within ophthalmology outpatient care, during the respective bDMARD treatment.

Follow-up started at the bDMARD initiation, and ended at the first of Dec 31st 2017, death, emigration or discontinuation date of the bDMARD.

To assess and accommodate treatment channeling, crude incidence rates for AU-flares were determined (A) for all bDMARD treatment starts, (B) excluding patients with an AU diagnosis during the year prior to the bDMARD start, and (C) in addition, excluding all first line bDMARD treatment starts.

Hazard ratios (HR) for time until a first on-treatment AU diagnosis were estimated using Cox regression (ADA=reference), adjusted for sex, age, and any history of AU, and estimating robust confidence intervals to account for the individuals contributing multiple lines of treatment.

Results: In total, 2,684 patients (52% women) contributed 3,255 treatment initiations. SEC was less frequently used as first line bDMARD and there was channeling of patients with previous AU, towards treatment with ADA, and away from ETN (Table 1). Further, AU occurred almost exclusively in patients with a pre-treatment history of AU (data not shown).

Table 1.

Analysis	Treat-ment starts, N	Previous AU ¹	Age at treatment start, mean (sd)	N Previous bDMARD, median	HR (95% CI) for first AU-diagnosis	AU flares, N	Follow-up ² , years
A. All treatment starts, N=3255							
SEC	333	21%	48 (13)	2	2.0 (1.2-3.3)	52	241
ADA	872	34%	44 (12)	1	Ref	175	973
IFX	714	21%	43 (14)	0	0.9 (0.6-1.4)	68	677
ETN	1336	17%	44 (14)	0	0.9 (0.7-1.3)	102	1290
B. Excluding patients with prior AU within 1 year before treatment start, N=2907							
SEC	304	13%	47 (13)	2	3.1 (1.4-7.3)	10	212
ADA	711	19%	44 (13)	1	Ref	18	792
IFX	633	11%	43 (14)	0	1.0 (0.4-2.3)	8	599
ETN	1259	12%	44 (14)	0	1.8 (1.0-3.4)	43	1204
C. Excluding patients with prior AU within 1 year before treatment start and first line bDMARD, N=1288							
SEC	284	14%	48 (13)	2	2.5 (1.0-6.2)	10	198
ADA	374	18%	45 (13)	1	Ref	11	384
IFX	185	12%	45 (14)	2	1.3 (0.4-4.0)	4	166
ETN	445	17%	47 (14)	1	1.9 (0.9-4.0)	23	439

1) Anterior uveitis between 2001 and treatment start; 2) Total follow-up time for analyses of incidence rate.

The incidence rates of AU-flares were higher for SEC and ETN compared to ADA and IFX, in the analyses (B, C) accommodating for channeling, figure 1.

Compared to ADA, the adjusted HRs of a first on-treatment AU-diagnosis were also higher for SEC and ETA, Table 1.

Table. Multivariable hazard ratios for all-cause and cause-specific mortality in NHANES III and 1999-2007.

Men						
Serum urate range (mg/dL)	<4	4-5	5-6	6-7	7-8	>8
Deaths (N)	325	934	1513	1412	872	658
All-cause	1.33 (1.17, 1.51)	1.17 (1.07, 1.28)	1.00**	1.04 (0.96, 1.13)	1.13 (1.04, 1.24)	1.52 (1.37, 1.69)
Cardiovascular	0.97 (0.75, 1.27)	1.10 (0.93, 1.30)	1.00	0.93 (0.80, 1.08)	1.13 (0.96, 1.34)	1.22 (1.00, 1.49)
Chronic lower respiratory disease	0.92 (0.51, 1.68)	0.96 (0.64, 1.43)	1.00	1.01 (0.69, 1.47)	0.86 (0.53, 1.38)	1.91 (1.18, 3.10)
Alzheimer's disease	1.13 (0.50, 2.55)	0.88 (0.48, 1.61)	1.00	1.14 (0.69, 1.91)	0.87 (0.45, 1.69)	0.23 (0.05, 0.99)
Diabetes mellitus	3.39 (1.89, 6.09)	1.81 (1.10, 3.00)	1.00	0.86 (0.51, 1.44)	0.93 (0.51, 1.69)	1.60 (0.87, 2.95)
Women						
Serum urate range (mg/dL)	<3	3-4	4-5	5-6	6-7	>7
Deaths (N)	181	750	1321	1170	776	703
All-cause	1.11 (0.93, 1.31)	1.03 (0.93, 1.14)	1.00 (0.92, 1.09)	1.00	1.11 (1.00, 1.22)	1.45 (1.31, 1.61)
Cardiovascular	1.23 (0.88, 1.71)	1.11 (0.92, 1.34)	0.94 (0.80, 1.11)	1.00	1.06 (0.89, 1.28)	1.16 (0.95, 1.41)
Chronic lower respiratory disease	1.26 (0.62, 2.57)	1.11 (0.72, 1.72)	0.87 (0.58, 1.30)	1.00	0.66 (0.39, 1.12)	0.85 (0.49, 1.45)
Alzheimer's disease	1.38 (0.57, 3.36)	0.97 (0.54, 1.73)	1.15 (0.73, 1.81)	1.00	0.79 (0.44, 1.41)	0.54 (0.25, 1.15)
Diabetes mellitus	1.69 (0.71, 4.02)	1.50 (0.89, 2.53)	0.91 (0.56, 1.46)	1.00	1.11 (0.68, 1.82)	1.66 (1.02, 2.71)

Conclusion: In clinical practice, SEC and ETN are associated with a higher incidence of AU than ADA and INF, suggesting a poorer protective effect of SEC and ETN against AU. These preliminary results should be interpreted in light of pronounced treatment channeling, which was only partly accommodated for.

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OP0015 SEX-SPECIFIC U-SHAPED RELATIONSHIP BETWEEN SERUM URATE AND MORTALITY IN THE UNITED STATES GENERAL POPULATION

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Background: A U-shaped relationship may exist between serum urate (SU) and cardiovascular events, although the relationship between SU and mortality is unclear. The most recent EULAR recommendations for gout advise against maintaining SU <3mg/dl for prolonged periods.

Objectives: To examine the relationship between SU and all-cause and cause-specific mortality in large cohorts in the United States (US).

Methods: We examined National Health and Nutrition Examination Survey (NHANES) data from 1988-1994 (NHANES III) and 1999-2007 including subjects