provide important insights into divergent and shared mechanistic features of RA and serve as a template for future studies to guide drug target discovery by synovial molecular signatures and de-sign stratified approaches for patients with RA.

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Figure 1 Identification of RA patients using non-negative matrix factorization, functional enrichment, and immune cell infiltration in the differentially expressed genes set. (A-D) The consensus map of NMF clustering results in the total RNA sequencing dataset. Patients were divided into cluster 1-5 according to the expression profiles of 576 DEGs. Heatmap of five clusters defined by the cluster-based genes expression. (E-F) Gene Ontology (GO) terms and KEGG pathway related to common cluster-based gene signatures. (G-H) Cell subset enrichment score according to RA subgroup. (I-J) Distribution of the five RA subgroups by clinical phenotypes (the positivity of ACPA). (ns, not significant; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$)

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OP0185

RADIOGRAPHIC PROGRESSION DESPITE PERSISTENT LDA OR REMISSION IS INFLUENCED BY CURRENT SMOKING RATHER THAN THE RESPECTIVE DAS 28 LEVEL, RESULTS OF THE SWISS RHEUMATOID ARTHRITIS REGISTER (SCQM)

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Background: The therapeutic aim for rheumatoid arthritis (RA) is to control disease activity and prevent radiographic progression. Various clinical scores are utilized to describe disease activity in RA patients. The DAS28 score can define states of low disease activity (LDA) and remission. Despite achieving LDA or remission, radiographic progression may nevertheless occur. However, the rates and frequency of this occurrence have not been analyzed in detail.

Objectives: To describe the frequency and rate of radiographic progression in patients with persistent LDA or remission.

Methods: Analysis of RA patients from the SCQM cohort. Persistent LDA or remission were defined as DAS 28 ≤ 3.2 or < 2.6 respectively, at two subsequent follow up time points in the database. We included patients with at least two sets of radiographs within these intervals of LDA and/or remission. Radiographic progression was measured with the Raitingen-score (range 0-190), which describes joint erosions numerically. Repair was defined as an improvement in the Raitingen score > 5 points/year and progression as > 2 or > 5 points change in the Raitingen score within one year.

Results: Among 10'141 RA patients, 4'342 episodes of remission occurred in 3'927 patients with 1'776 sets of X rays available within these episodes. Similarly, 8'136 episodes of LDA in 6'765 patients and 2'358 sets of X rays were present within these intervals. For patients in LDA or remission, rates of repair were 5.5% and 4.8%, respectively, while for radiographic progression > 5 points in the Raitingen score/year were 10.3% in both groups and for > 2 points change of Raitingen score/year were 27.7 and 25.4%, respectively.

No differences for demographic factors or measures of disease activity, rheumatoid factor or ACPA were found comparing patients with radiographic progression or non-progression despite LDA or remission at the beginning of the episode of LDA and/or remission.

Interestingly, 42.9% of patients in LDA with progression of > 5 points in the Raitingen score/year were current smokers vs 29.4% among the non-progressors ($X^2 = 6.55$, $p = 0.01$). This significant difference vanished when the cut-off for radiographic progression was set at > 2 points yearly change in Raitingen score or in patients in remission.

Conclusion: Radiographic progression despite LDA or remission are more frequent than expected. No differences in radiographic progression were found comparing LDA and remission suggesting that the goal of LDA is appropriate. Smoking seems to be an independent risk factor for radiographic progression despite LDA. Why the effect of smoking could was not demonstrated in patients in remission, remains unclear.

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Oncorheumatology: the crossroads of cancer and musculoskeletal diseases

OP0186

CHANGES IN CIRCULATING B CELL LEVELS AND IMMUNOPHENOTYPE ARE ASSOCIATED WITH DEVELOPMENT OF ARTHRITIS FOLLOWING TREATMENT WITH CHECKPOINT INHIBITORS

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Background: Inflammatory arthritis (IA) is frequent among rheumatic side effects induced by checkpoint inhibitor (CPI) therapy for metastatic malignancies¹. While T cells are likely to sustain the inflammatory process², fewer data are available concerning the role of B cells³.

Objectives: To investigate the phenotype of circulating B cells in patients who develop CPI-induced IA (CPI-IA) and to compare it with features of B cells in patients not developing immune-related adverse events (irAE) upon CPI treatment.

Methods: B cell subsets at baseline (before CPI initiation) and during CPI treatment were analyzed in CPI-IA patients and in patients receiving CPI but who did not develop irAE (non-irAE). Peripheral blood mononuclear cells (PBMC) were analyzed by flow cytometry and B cells were identified as CD19⁺ and divided into naïve (CD27⁺IgD⁺), memory (CD27⁺IgD⁺), double negative (CD27⁺IgD⁻) and transitional (CD10⁺CD24⁺CD38^{hi}) B cells. Levels of CD21, an activation marker on transitional B cells, were also analyzed. Non-parametric tests were used for analysis of differences between groups.

Results: Six CPI-IA and 7 non-irAE patients matched for age, gender and CPI treatment were included, who had received CPI treatment due to metastatic melanoma. Flow cytometry revealed a significant increase of circulating B cells ($p=0.002$) (Figure 1A) and especially of transitional B cells in CPI-IA patients vs. non-irAE (median %, range: 7.8 (4.5-11.4) vs. 3.2 (1.6-4.3), $p=0.007$) (Figure 1B), while no remarkable changes were seen across other subsets. Transitional B cell levels significantly decreased from active to quiescent CPI-IA in all patients ($p=0.008$). In two CPI-IA patients for whom baseline sampling was available, the increase of transitional levels occurred early after CPI treatment and before CPI-IA onset. Levels of expression of CD21 on transitional B cells were increased in CPI-IA vs. non-irAE ($p=0.01$).

Figure 1. B cells (CD19⁺) and transitionals are significantly increased in CPI-IA patients. Mann-whitney U test, ** $p<0.01$

Conclusion: Transitional B cells are expanded in CPI-IA patients and seem to increase early after start of CPI therapy. Monitoring this B cell subset might lead to closer follow-up and earlier diagnosis of CPI-IA.

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OP0187

INCIDENCE OF MALIGNANCY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE JAPANESE IORRA PATIENT REGISTRY

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Background: The risk of some types of malignancy is increased in patients (pts) with rheumatoid arthritis (RA), compared with the general population. We have previously reported the incidence of malignancy in Japanese pts with RA.¹⁻⁴

Objectives: This analysis further evaluated the incidence of malignancy in Japanese pts with RA using recent data from the large prospective observational study, IORRA.

Methods: This analysis included all pts with RA aged ≥ 18 years who were enrolled in IORRA from April 2013 to October 2018, with follow-up through October 2019, and participated in ≥ 2 surveys. Index was defined as the date of the first entry in the IORRA database, with baseline defined as the 6-month period prior to the index date. Malignancies were identified in pt reports of biannual IORRA surveys and confirmed using medical records. Age- and sex-standardised incidence ratios (SIRs) and 95% confidence intervals (CIs) were calculated.

Results: In total, 8020 pts were included. At baseline, the majority (85.0%) of pts were female; mean disease duration was 12.8 years, 5.8% and 4.8% of pts had a past history of malignancy or comorbid malignancy at baseline, respectively, and the majority (75.9%) of pts were receiving methotrexate (Table). The SIR (95% CI) was 0.90 (0.80, 1.01). SIRs (95% CI) of site-specific malignancies were: breast cancer, 0.91 (0.69, 1.18); lung cancer, 0.67 (0.44, 0.97); colon cancer, 0.93 (0.62, 1.32); stomach cancer, 0.82 (0.56, 1.14); and lymphoma, 3.74 (2.73, 4.96).

Table 1. Patient demographics and baseline disease characteristics

Patients with RA (N=8020)	
Age (years), mean (SD)	59.3 (13.8)
Female, n (%)	6816 (85.0)
Duration of RA (years), mean (SD)	12.8 (10.3)
Never smoked, n (%)	5086 (66.2)
DAS28, mean (SD)	2.8 (1.1)
J-HAQ, mean (SD)	0.60 (0.72)
Malignancy status, n (%)	
Past history of malignancy	467 (5.8)
Comorbid malignancy at baseline	386 (4.8)
Medication use, n (%)	
MTX	6088 (75.9)
Tacrolimus	787 (9.8)
Corticosteroids	2641 (32.9)
bDMARD use	1508 (18.8)
TNFi	1163 (14.5)
Tocilizumab	311 (3.9)
Abatacept	106 (1.3)
JAK inhibitors	4 (0.05)

bDMARD, biological disease-modifying antirheumatic drug; DAS28, Disease Activity Score in 28 joints; JAK, Janus kinase; J-HAQ, Japanese Health Assessment Questionnaire; MTX, methotrexate; N, the number of patients included in the analysis, the number of patients assessed for each characteristic may be fewer than N; n, the number of patients with each characteristic; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

Conclusion: Overall risk of malignancy was similar to that in the general Japanese population, although a significantly higher risk of lymphoma was identified.

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