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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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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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