Background Intratumoral B-cells are associated with improved survival with ICB in sarcomas.1 We investigated the dynamics of intratumoral and peripheral BCR repertoire and their association with survival in dedifferentiated liposarcoma (DDLPS, n=17) and undifferentiated pleomorphic sarcoma (UPS, n=10) patients treated in a neoadjuvant ICB trial of nivolumab +/- ipilimumab.2-4

Methods Tumor and peripheral blood mononuclear cells (PBMCs) were collected at baseline and surgery. Intratumoral and peripheral BCR heavy (IgH) and light (IgL) chain repertoires were evaluated using bulk RNA sequencing and the TRUST4 algorithm.5 IgH and IgL repertoire diversity and clonality were assessed by inverse Simpson and Gini index, respectively. Comparisons of continuous variables were done using Wilcoxon Rank-Sum test. High and low categories were defined by median values. Comparisons of progression-free survival (PFS) and overall survival (OS) curves were performed by log-rank method. Correlations were assessed using Spearman’s correlation.

Results Tumor transcriptomic data was available for 23 and 20 patients at baseline and surgery, respectively. PBMC transcriptomic data was available for 19 and 23 patients at baseline and surgery, respectively. BCR repertoire diversity increased with ICB, which was significant only in PBMCs (tumor: IgH p=0.077, IgL p=0.11; PBMC: IgH p=0.0065, IgL p=0.029; figures 1 and 2). Neither intratumoral nor peripheral BCR repertoire clonality was impacted by ICB treatment (figures 3 and 4). At baseline, patients with higher IgH BCR diversity had longer PFS (intratumoral: not reached [NR] vs 19 months, p=0.15; peripheral: NR vs 37 months, p=0.25). However, at surgery, patients with higher intratumoral IgH BCR diversity had shorter PFS (17 vs NR months, p=0.024), while peripheral BCR diversity was not associated with PFS (p=0.98). At baseline, patients with higher intratumoral IgH BCR clonality had longer PFS (p=0.19) and significantly longer OS (p=0.022) while neither intratumoral nor peripheral BCR clonality at surgery was associated with survival.

Conclusions ICB is associated with increases in intratumoral and peripheral BCR diversity but not with changes in clonality. Overall, neither the intratumoral IgL nor peripheral IgH and IgL BCR repertoires were associated with survival. Greater diversity of the intratumoral IgH repertoire was a favorable prognostic factor at baseline but a negative one after ICB. These findings warrant future investigations.

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Trial Registration NCT03307616

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Ethics Approval This study was approved by MD Anderson Cancer Center Institutional Review Board. IRB approval 2017-0143. All participants gave written informed consent.

Abstract 542 Figure 1 Intratumoral BCR repertoire diversity
A-B. Comparison of intratumoral BCR diversity at baseline and at surgery in heavy chains (C) and light chains (D), p-values are Wilcoxon rank test. A-B, Comparison of intratumoral BCR diversity at baseline and at surgery. C-D, Kaplan-Meier survival curves of PFS by intratumoral diversity at baseline and at surgery in heavy chains (A) and light chains (B), p-values are log-rank test.

A-B, Comparison of peripheral BCR diversity at baseline and at surgery in heavy chains (C) and light chains (D), p-values are Wilcoxon rank test. A-B, Comparison of peripheral BCR diversity at baseline and at surgery.
in heavy chains (A) and light chains (B), p-values are Wilcoxon tests. C-D, Kaplan-Meier survival curves of PFS by peripheral diversity at baseline and at surgery in heavy chains (C) and light chains (D), p-values are log-rank tests. E-F, Kaplan-Meier survival curves of OS by peripheral diversity at baseline and at surgery in heavy chains (C) and light chains (D), p-values are log-rank tests.

Abstract 542 Figure 3  Intratumoral BCR repertoire clonality.
A-B, Comparison of intratumoral BCR clonality at baseline and at surgery in heavy chains (A) and light chains (B), p-values are Wilcoxon tests. C-D, Kaplan-Meier survival curves of PFS by intratumoral clonality at baseline and at surgery in heavy chains (C) and light chains (D), p-values are log-rank tests. E-F, Kaplan-Meier survival curves of OS by intratumoral clonality at baseline and at surgery in heavy chains (C) and light chains (D), p-values are log-rank tests.

Abstract 542 Figure 4  Peripheral BCR repertoire clonality.
A-B, Comparison of peripheral BCR clonality at baseline and at surgery in heavy chains (A) and light chains (B), p-values are Wilcoxon tests. C-D, Kaplan-Meier survival curves of PFS by peripheral clonality at baseline and at surgery in heavy chains (C) and light chains (D), p-values are log-rank tests. E-F, Kaplan-Meier survival curves of OS by peripheral clonality at baseline and at surgery in heavy chains (C) and light chains (D), p-values are log-rank tests.