

with a greater number of CD4+/OX40+ or CD8+/OX40+ T-cells had a longer OS ( $p = 0.021$ ;  $p = 0.009$ ), while the CD8+/OX40+ T-cells also maintained independent prognostic value for survival (HR = 0.517; CI = 0.276-0.968;  $p = 0.039$ ).

**Conclusions:** Overall, our findings provide insights for the application of targeting OX40, or a combined OX40 agonists and first-line immunochemotherapy in DLBCL patients.

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**Keywords:** Basic and Translational Science - Other, Aggressive B-cell non-Hodgkin lymphoma

No conflicts of interests pertinent to the abstract.

### 297 | A WIDE T-CELL EXHAUSTION PATTERN IS FREQUENT IN THE TUMOR MICROENVIRONMENT OF RELAPSED/REFRACTORY B-CELL LYMPHOMA PATIENTS AND COULD BE CIRCUMVENTED BY PDL1 BLOCKADE

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**Background:** Relapsed/refractory (R/R) B-cell non-Hodgkin lymphomas (B-NHL) remain incurable diseases and need novel therapeutic approaches. In the LYSA trial GATA (NCT03276468), 58 DLBCL and 58 FL R/R patients were treated by obinutuzumab (OBI) combined with BCL-2 inhibitor venetoclax (VEN) and anti-PDL1 atezolizumab (ATE) in order to test the synergy of chemo-free tumor-targeted therapies. The goal of the present study was to evaluate the influence of tumor microenvironment (TME) on the efficiency of this novel drug combination.

**Methods:** A centralized pathological review was mandatory for all enrolled cases. As a result, 67 cases including 35 DLBCL (16 GC and 19 non-GC subtypes) and 32 FL (grade 1-2) with sufficient relapse material were selected for evaluating TME composition and immune checkpoints (ICP) expression using standard and/or multiplexed IHC analyses. All stainings have been scored manually, and when possible validated using a computer-assisted software. Biopsy samples at diagnosis were also analyzed in 60% of cases. Non-parametric tests were used to test correlations between TME parameters and clinical responses assessed by Lugano criteria at the end of induction (EOI) after 8 cycles of ATE, OBI and VEN.

**Results:** R/R FL exhibited a higher amount of CD3<sup>+</sup> T-cells, CD4<sup>+</sup> T-cells and CTL than R/R DLBCL ( $p < 0.001$ ,  $p = 0.03$  and  $p < 0.001$ ). By contrast, R/R DLBCL contained more CD163<sup>+</sup> macrophages than R/R FL ( $p = 0.029$ ). TIM3 expression was higher in R/R DLBCL vs R/R FL ( $p = 0.036$ ), whereas PD1 expression was higher in R/R FL than R/R DLBCL ( $p = 0.008$ ). ICP expression and ME composition did not significantly vary between GC and non-GC DLBCL subtypes. As compared to the initial diagnosis, expressions of TIM3 in FL and TIGIT in DLBCL had a tendency to be increased at relapse, but no difference in terms of immune cell composition was observed. PD1/PDL1 expression was not correlated with clinical response, whereas higher expression of TIM3 and TIGIT (>15%) was associated with better response in R/R FL (50% versus 33% of CR) and R/R DLBCL (40% versus 0% of CR), respectively.

**Conclusions:** We show herein that TME composition and ICP expression are distinct between R/R FL and R/R DLBCL and remain mostly unchanged after R-chemotherapy compared to initial biopsies, except for higher TIM3 and TIGIT expression levels. This preliminary study indicates that high expression of TIGIT in R/R DLBCL and TIM3 in R/R FL patients are correlated with responsiveness following OBI-VEN-ATE therapy. Thus, TIGIT and TIM3 expression could predict the efficacy of PD1/PDL1 blockade in these settings. Overall, these data may reflect the triggering of a global T-cell exhaustion program in R/R B-NHLs, which can be at least in part circumvented by anti-PDL1 therapy. In future trials, targeting TIM3 and TIGIT might be considered as a synergistic strategy to enhance the benefit of PD1/PDL1 blockade in these patients.

**Keywords:** Diagnostic and Prognostic Biomarkers

No conflicts of interests pertinent to the abstract.

### 298 | MICROENVIRONMENT IMMUNE CELLS IN BONE MARROW AND LYMPH NODE MEASURED BY FLOW CYTOMETRY CAN PREDICT SURVIVAL IN DIFFUSE LARGE B CELL LYMPHOMA

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**Introduction:** Tumor microenvironment (TME) in diffuse large B-cell lymphoma (DLBCL) has recently been in the spotlight. The predictive role of immune cells (IC) in peripheral blood (PB), bone marrow (BM) and lymph nodes (LN) has been individually assessed, often using techniques not widely available. However, data regarding the relative prognostic impact of TME in each compartment evaluated simultaneously in DLBCL is still lacking.