P1275 PERCENTAGE OF TUMOR INFILTRATING T LYMPHOCYTES MEASURED BY FLOW CYTOMETRY AT DIAGNOSIS PREDICTS SURVIVAL AFTER SALVAGE CHEMOTHERAPY IN RELAPSED/REFRACTORY DIFFUSE LARGE B CELL LYMPHOMA PATIENTS.

**Topic:** 20. Lymphoma Biology & Translational Research

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**Background:**

Tumor microenvironment (TME) in diffuse large B-cell lymphoma (DLBCL) is considered to play a major role in lymphomagenesis and tumor progression. In relapsed/refractory (R/R) patients (pts), data regarding outcomes of salvage chemotherapy according to easily acquired TME variables such as percentage (%) of infiltrating T-lymphocytes (TL) is scarce. This information may be of particular interest in this era where standard of care in the 2nd line (2L) setting in DLBCL is being challenged.

**Aims:**

To determine the prognostic impact of the % of TL in lymph node (LN) biopsies at diagnosis, on event free and overall survival after 1st line (EFS₁ and OS₁) and 2nd line treatment (EFS₂ and OS₂) in a cohort of patients with R/R DLBCL.

**Methods:**

We identified pts with R/R DLBCL and available tissue biopsy flow cytometry (FC) data from diagnosis who received treatment at our center from 2012-2021.

FC analysis was performed with 8-color FC panels according to international Euroflow protocols. % of TL in LN biopsy by FC was compared to normal values determined by Battaglia et al (Immunology 2003) and analyzed as dichotomized variables: low vs. normal-high.

Survival analysis was estimated with Kaplan-Meier and Cox regression and the comparison between variables was performed with log-rank test.

**Results:**

43 pts were included in this retrospective study. At diagnosis, median age was 63 years. 79% had advanced stage disease and 69.5% poor R-IPI. All pts were treated with immunochemotherapy regimens. Complete response (CR) rate was 67.4%. Median EFS₁ was estimated at 12.3 months (m) and median OS₁ at 34.3 m, with a median follow up time of 27.8 m (range: 6-188). 44.2% had primary refractory disease or early relapse. All pts were treated with immunochemotherapy regimens as 2L. 24 pts (55.8%) achieved 2nd CR and the remaining were chemorefractory. Only 34.9% received consolidation with ASCT, 30/43 due to progressive disease and 11/43 for ineligibility. Median EFS₂ and OS₂ were 7.6 and 14.2 m, respectively.

Median EFS₁ did not statistically differ between pts with low LN TL % vs those with normal-high values (10 vs 13.6 m).

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In contrast, a low % of TL in LN biopsy samples was associated with inferior EFS2 (median of 5.4 vs. 47.3 m, p: 0.028, figure 1). The risk of progression or death after 2L treatment was 2.44 higher in pts with low LN TL % (CI 95%: 1.07-5.57, p: 0.03). Primary refractory pts had similar adverse outcomes to 2L therapy when stratified according to LN TL % (p: 0.8). Conversely, relapsed pts with low LN TL % had a median EFS2 of 6 vs 77 m for the normal-high subgroup (p: 0.017).

Low LN TL % was also associated with inferior OS1 (median 22.5 vs. 120.4 months, p: 0.007). Moreover, survival after 2L chemotherapy was significantly decreased in pts with low LN TL % with a median of 7.3 vs 101.6 m in those with normal-high values, p: 0.004. The risk of death after salvage treatment was 3.31 times higher in the low LN TL % subgroup, p: 0.007.

Summary/Conclusion:

Tumor infiltrating TL in LN in DLBCL measured by FC showed prognostic impact in our cohort of R/R pts. Although timing of progression or relapse did not significantly differ between subgroups, EFS2 and consequently OS were markedly decreased in pts with low LN TL. These results suggest that outcomes of 2L chemotherapy in this subgroup are disappointing with only a third of pts receiving consolidation with ASCT mainly due to refractory disease. Changing 2L treatment paradigms in DLBCL with the introduction of CAR-T cells may prove beneficial in this high risk subset of pts with low intratumoral immunity.