PB2056 ORBITAL LYMPHOMA: CLINICAL AND EPIDEMIOLOGICAL PATTERNS WITHIN THE UNITED STATES

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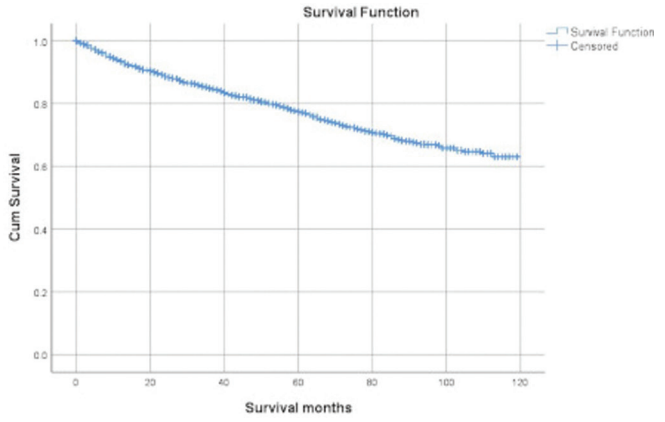
Background: Lymphomas are relatively common tumors that may affect the orbit through tissue infiltration. However, data available about tumors possibly originating in orbit (also called orbital lymphoma) are scarce.
Aims: In this study, we aimed to spotlight on this type of malignancy using the using data from American National Cancer Institute, Surveillance, Epidemiology, and End Results (SEER) Program.
Methods: We used SEER*Stat version 8.3.5, Microsoft Excel, as well as SPSS IBM SPSS Statistics for Windows, Version 25.0 for data analysis. In SEER*Stat, we used the (Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2017 Sub (1973–2015 varying)) database to obtain data. We included cases diagnosed with lymphoma between 2006 and 2015 at site related to orbital cavity C69.0-C69.9.
Results: A total of 2340 cases were identified with a median age of 65.2. Females and patients of white race represented the majority of the analyzed cohort (n = 1249, 53.4%; n = 1846, 78.9%, respectively). Age-adjusted Incidence rate was 3 per 10,000. 5-years observed survival was 82 % (95% CI: 79.8% - 84%) while the 5-years relative survival was 94.3 % (95% CI: 91.3% - 96.2%). The most common pathology of studied cases was extranodal marginal zone lymphoma of mucosal-associated lymphoid tissue (MALT) (n = 1310, 56%) [Table 1]. Median survival was not reached at the study cutoff (Figure 1).

Table 1: Different Pathological Subtypes for Eye / Orbit Lymphoma

Pathological Subtype	Number of Cases	Percentage
9670–9699: NHL - Mature B-Cell Lymphomas	2021	86.4 %
9590–9599: Malignant Lymphomas, NOS Or Diffuse	270	11.5 %
9820–9839: Lymphoid Leukemias (C42.1)	23	1 %
9700–9719: Nhl - Mature T And Nk-Cell Lymphomas	19	0.8 %
9650–9669: Hodgkin Lymphomas	3	0.1 %
9720:9729: Nhl – Precursor Cell Lymphoblastic lymphoma	2	0.1%



Summary/Conclusion: Orbital lymphoma has an incidence rate of 3 per 10,000. These tumors are more likely to occur in old age, females, and white race. Survival data are relatively good with the 5-years relative survival being 94.3%.

PB2057 PRE-CLINICAL BLOCKING OF PD-L1 MOLECULE, WHICH EXPRESSION IS DOWN REGULATED BY NF-κB, JAK1/JAK2 AND BTK INHIBITORS, INDUCES REGRESSION OF ACTIVATED B-CELL LYMPHOMA.

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Background: Escape from immune control must be important in the natural course of B-cell lymphomas, especially for those with activation of NF-κB.
Aims: To search for PD-L1 expression in mouse model L.CD40 that could explain the tumor B cells escape of immune surveillance.
Methods: The pre-clinical L.CD40 transgenic mouse model is characterized by B-cell specific CD40 signaling responsible for NF-kB continuous activation with a spleen monoclonal B-cell tumor after one year in 60% of cases. L.CD40 mice were injected with anti-PD-L1 antibody.
Results: L.CD40 tumors B-cells expressed high levels of PD-L1. This expression was dependent on activation of either NF-κB, JAK1/JAK2 or BTK pathways since ex vivo treatment with the inhibitory molecules PHA-408, ruxolitinib and ibrutinib led to decrease of its expression. Treatment of L.CD40 lymphomatous mice with an anti-PD-L1 monoclonal antibody induced tumor regression with decreased spleen content, activation and proliferation rate of B-cells as well as a marked increase in T cell activation, as assessed by CD62L and CD44 expression.
Summary/Conclusion: These results highlight the interest of therapies targeting the PD-1/PD-L1 axis in activated lymphomas with PD-L1 expression, with possible synergies with tyrosine kinase inhibitors.

PB2058 THE PROGNOSTIC ROLE OF MYOCYTE-SPECIFIC ENHANCER FACTOR 2C (MEF2C) IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMAS (DLBCL)

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Background: DLBCL is the most common subtype of non-Hodgkin's lymphomas. However, the pathogenesis of DLBCL is not fully understood. Transcription factors or signaling pathways involved in normal B cell development and function might represent future therapeutic targets. Such a transcription factor is MEF2C contributing to B cell activation and germinal center formation.
Aims: This study aims at investigating the role of MEF2C as prognostic biomarker in DLBCL.
Methods: 82 patients with DLBCL were enrolled in our study. We assessed the expression of MEF2C by performing immunohistochemistry (IHC) on paraffin slides of 62 tissue blocks and results were evaluated by using the H-score semiquantitative approach, with a range from 0 to 300. Additionally, we analyzed clinical [sex, age, stage of DLBCL, performance status, extranodal sites, B symptoms, International Prognostic Index (IPI), age-adjusted IPI, revised-IPI, National Comprehensive Cancer Network (NCCN)-IPI], laboratory [lactate dehydrogenase (LDH), hemoglobin (Hb), white blood cells (WBC), neutrophils, lymphocytes, monocytes, platelets and beta-2-microglobulin] and pathologic characteristics (CD10, BCL6, MUM-1, Ki-67) of patients in relation to overall (OS) and disease free survival (DFS).
Results: Mean and median value of MEF2C H-score was 120 ± 58. We observed a statistical significant correlation with age (p = 0.021) and a tendency to correlate with LDH (p = 0.18). The expression of MEF2C was not associated with other clinical or laboratory values. MEF2C positivity >80% was correlated with borderline inferior OS (p = 0.083). Among patients, who survived more than 12 months after initial diagnosis, those with MEF2C H score <120 had a significant better OS comparing with those with MEF2C H score >120 (p = 0.009).
Summary/Conclusion: High IHC expression of MEF2C showed a negative prognostic influence in patients with OS more than 12 months after initial diagnosis. However, these results should be confirmed in larger groups of DLBCL patients and the underlying oncogenic mechanism of MEF2C in DLBCL should be further explored.

PB2059 MYD88 L265P STATUS IN DIFFUSE LARGE B CELL LYMPHOMA, NOT OTHERWISE SPECIFIED. A SINGLE-CENTER STUDY FROM ARGENTINA.

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Background: Diffuse large B-cell Lymphoma (DLBCL) is a heterogeneous disease. Based on Hans' algorithm, DLBCL not otherwise specified (NOS) is classified by cell-of-origin into germinal center B-cell (GCB) and non-GCB subtypes. Non-GCB ones have frequently NF-kB pathway activation and worse prognosis compared to GCB cases. MYD88 is an

adaptor protein of toll-like and IL-1 receptor signalling, leading downstream NF-kB pathway activation. MYD88 L265P mutation confers the protein constitutional activation. This mutation is present in around 20% of non-GCB subtype, and rarely found in GCB subtype of DLBCL. The prognostic value of MYD88 L265P mutation in DLBCL has been matter of controversy.

Aims: The aim of the study was to determine the prevalence of MYD88 L265P mutation in DLBCL NOS cases of Argentina, and compare it with previous reports in the literature.

Methods: A retrospective cohort of 73 DLBCL NOS cases diagnosed in the Italian Hospital of Buenos Aires (Argentina) between 2010 and 2016 was studied. Complete clinical records, Hans' algorithm, and available material for molecular testing were inclusion criteria. Patients with prior diagnosis of low-grade lymphoma or diagnosis of immunodeficiency-associated, post-transplant, EBV+, primary mediastinal, primary testicular, primary CNS, primary effusion, leg-type or intravascular DLBCL were excluded. DNA was extracted from tissue blocks using QIAamp mini kit (Qiagen). MYD88 L265P was assessed using an in-house allele-specific probe-based Real-Time PCR assay. Positive (primary testicular DLBCL) and negative controls (tonsil) were added to each run. Every case was checked subsequently using qBiomarker MYD88 L265P Somatic Mutation Assay (Qiagen). Prevalences were expressed as percentage, confident intervals were calculated using Clopper-Pearson exact method. Kaplan Meier curves and Log-rank test were used to evaluate overall survival (OS).

Results: 36 patients (49,31%) were female, and median age at diagnosis was 66 years (range 26–89). 33 patients (45,20%) had extranodal involvement (gastrointestinal tract: 14 cases; liver: 5 cases; bone: 4 cases; other locations: 10 cases). 44 cases (60,27%) were GCB and 29 (39,73%) were non-GCB DLBCLs. MYD88 L265P mutation was present in 2 cases (2,74%; CI 95%: 0,33–9,55%) among all DLBCLs, including 1 GCB case (2,27%; CI 95%: 0,06–12,02%) and 1 non-GCB case (3,45%; CI 95%: 0,09–17.76%). There was no significant association between MYD88 L265P status, Hans´algorithm subtype, sex, age or Ki67 index and OS.

Summary/Conclusion: In the analyzed population, the prevalence of GCB and non-GCB subtypes among DLBCL NOS cases was similar to international reports, although we did not find significant difference between both groups regarding OS (p = 0,712). MYD88 L265P mutation was found only in 2 patients (1 GCB and 1 non-GCB), accounting for 2,74% (CI 95%: 0,33–9,55%) and 2,27% (CI 95%: 0,06–12,02%) of all DLBCL NOS and non-GCB cases, respectively. Both prevalences are significantly lower than those published in 2017 by Lee et al. in a meta-analysis, where they found that MYD88 L265P is present in 16% (CI 95%: 15–18,09%) and 20,63% (CI 95%: 18,41–23%) of patients among all DLBCLs and non-GCB subtype, respectively. However, MYD88 L265P prevalence in primary SNC, testicular and leg-type DLBCLs diagnosed in our institution are similar to the literature (data not shown).

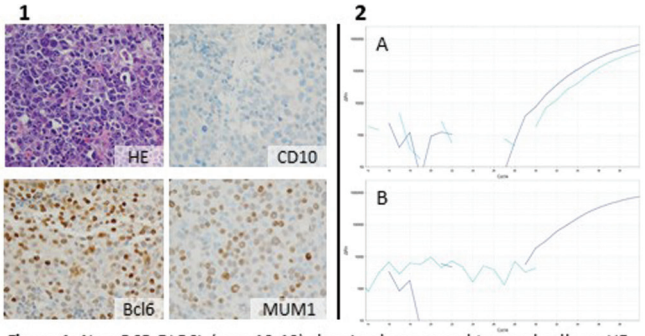

Figure 1: Non-GCB DLBCL (case 10-12) showing large round tumoral cells on HE staining. This case was negative for CD10, and positive for Bcl6 and MUM1.
Figure 2: Amplification plot showing MYD88 wild-type (blue line) and L265P amplification (cyan line). Plot A and B correspond to a positive (10-12) and a negative (16-24) case, respectively.

PB2060 THE UTILITY OF VARIABLE LEVELS OF CD39 EXPRESSION BY FLOW CYTOMETRY TO DISTINGUISHING B CELL LYMPHOMA SUBTYPES.

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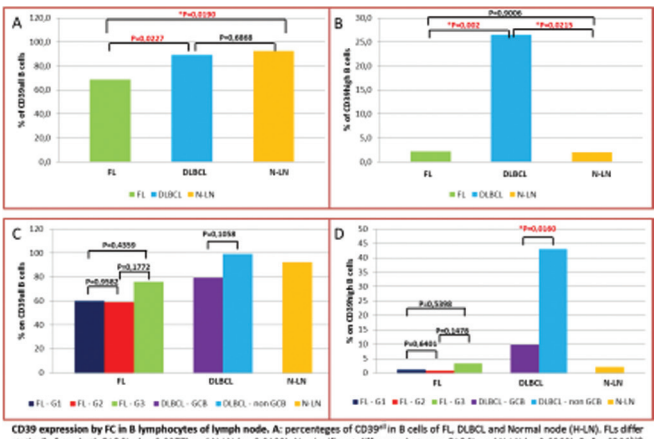
Background: B lymphocytes were considered to be positive regulators of humoral immune responses. Recently B-cell subsets named "regulatory B cells" (Bregs) have been describe. These subsets negatively regulate immune responses by inhibiting the activity of the effector T lymphocytes (Teff) and favoring that of the regulators T (Treg). The Bregs have been linked to not only inflammatory and autoimmune diseases, but also malignancies via suppressing anti-tumour immunity. It emerged that B-cells have regulatory properties having the ability to produce the immunosuppressive adenosine (ADO) via CD39, an ectoenzyme expressed on cells that cooperates to metabolize exogenous ATP to ADO. Studies have experimented that CD39 is upregulated ($CD39^{high}$) in subset of activated immunosuppressive B-cells. Unlike T and NK, greater than 90% of normal B-cells express CD39, while the neoplastic B-cells have an heterogeneous expression of CD39.

Aims: The aim of this study was to assess the expression of CD39 in neoplastic B cells of nodal Follicular lymphomas (FL) and Diffuse Large B Cell Lymphomas (DLBCL). Moreover, these were compare with background non-malignant B cells, when present.

Methods: We investigated the intensities of CD39 ($CD39^{all}$,$CD39^{hight}$) by flow cytometry (FC) in cell suspensions from dissociated tissues of 17 DLBCL, 22 FL and 10 normal lymph node (N-LN). According Hans algorithm, among DLBCL 8 case were classified as Germinal Center B (GCB) subtypes and 9 as non-GCB. The FL are subdivided according to the histological grade: 2 cases G1, 8 G2 and 12 G3.

Results: For $CD39^{all}$ there was no difference in expression between DLBCL and N-LN (p = 0,68), while there are significant differences between DLBCL and FL (p = 0,02) and between FL and N-LN (p = 0,019). There were statistical differences for $CD39^{high}$ expression in DLBCL compared with N-LN (p = 0,02) and with FL (p = 0,002). On the contrary, there were no statistically differences between FL and N-LN (p = 0,9). Within the DLBCL the two subgroups were similar for $CD39^{all}$ (p = 0,1) but presented different results for $CD39^{high}$: non-GCB subtypes had a stronger expression compared to GCBs (p = 0,01). In FL subgroups CD39 expression showed high heterogeneity with a trend to a greater intensity of the marker as the histological grade increases, although there is not a statistically significant difference



CD39 expression by FC in B lymphocytes of lymph node. A: percenteges of $CD39^{all}$ in B cells of FL, DLBCL and Normal node (N-LN). FLs differ statically from both DLBCLs (p= 0,0277) and N-LN (p= 0,0190). No significant difference between DLBCL and N-LN (p=0,6868); B: for $CD39^{high}$ significant difference between DLBCLs and FLs (p=0,002) and N-LN (p=0,0215), unlike between FLs and N-LN(p=0,9006); C: within the DLBCL and the FL, no statistical difference between the groups for the $CD39^{all}$; D: within the DBCLs non-GCB subtypes had a stronger expression compared to GCBs (p=0,016).

Summary/Conclusion: Analysis of CD39 by FC could be an useful tool to distinguishing between FL and DLBCL. In particular, in FLs the intensity of expression could be related to the histological grade. Furthermore, $CD39^{high}$ seems to differentiate GCB from non-GCB DLBCL, confirming in the latter the origin from activated B cell. The variable levels of CD39 by FC could contribute to orient in the defining entities that are not always easily and clearly differentiated. In addition, a variation of CD39 expression between neoplastic and normal cells was noted, particularly when clonal elements differ by FC for different sizes according to Side and Forward Scatter. Given that in Breg there is a variable levels of CD39 as a function of their immunosuppressive activity, it could be hypothesized that even in neoplastic B cells the different intensity of expression of the marker could suggest an active role of the B clone in producing immunosuppressive molecules and in characterizing the microenvironment favorable to the same lymphoma. Acknowledgments: This