wide clinical and biological diversity, as well as a heterogeneous prognosis. It especially affects the elderly population, with an increasing incidence with advancing age. The DLBCL of elderly (≥ 60 years) and very-elderly (≥ 80 years) patients has numerous particularities, including high-risk molecular-genetic findings, greater association with Epstein-Barr (EBV) virus infection, lower tolerability to conventional immunochemotherapy, and poor clinical outcomes. Therefore, alternative therapeutic strategies have emerged for these patients, including immunochemotherapy in reduced doses and regimens without anthracyclines. Based on this premisse, the current study aims to describe clinical and laboratory characteristics, assess outcomes, determine survival predictors and compare responses and toxicities in a large cohort of elderly patients with DLBCL, NOS older than 70 years. **Methods:** This is a retrospective, observational and single-center study, involving 185 patients with DLBCL, NOS aged ≥ 70 years, diagnosed and treated at the Department of Hematology, University of São Paulo, Brazil, from January 2009 to December 2020. **Results:** The median age at diagnosis was 75 years (70-97) and 58.9% (109/185) were female. Comorbidities were prevalent, including 19.5% (36/185) of immobility, 28.1% (52/185) of desnutrition, and 25% (46/185) of polypharmacy. Advanced clinical stage (III/IV) was observed in 73.6% (134/185), 48.6% (90/185) had bulky disease ≥ 7 cm, 63.2% (117/185) had B-symptoms, 76.2% (141/185) had ≥ 1 extranodal site involved by lymphoma, 67% (124/185) had intermediate-high/high-risk IPI, and 52.3% (57/109) had GCB-like phenotype detected by IHC. Ninety-eight percent of patients (182/185) received at least one line of therapy, 65.9% (120/182) underwent cytoreduction, 50.5% (92/182) received intrathecal CNS chemoprophylaxis, and 41.8% (76/185) experienced radiotherapy. The R-miniCHOP elderly regimen had a lower overall response rate (ORR) (p = 0.040), however patients in this group had unfavorable clinical and laboratory characteristics, including higher rates of hypoalbuminemia (p = 0.001), IPI ≥ 3 (p = 0.013) and NCCN-IPI ≥ 3 (p = 0.002). For the entire cohort, ORR was 68.1% (95% CI: 60.8-74.8), 13.2% (95% CI: 8.6-18.9) were chemorefractory, early-mortality rate (< 100 days) was 18.7% (95% CI: 13.3-25.1), and overall mortality rate was 52.4% (97/185). With a median follow-up of 6.3 years (95% CI: 5.5-6.7), the estimated 5-year OS and PFS were 50.2% (95% CI: 42.4-57.5) and 44.6% (95% CI: 37.0-51.9), respectively. In multivariate analysis, age ≥ 75 years [HR 2.22, p = 0.001], advanced-stage III/IV [HR 2.36, p = 0.003], neutrophilia ≥ 7.0 × 109/L [HR 2.25, p = 0.001] and lymphocyte/monocyte ratio > 4 [HR 1.98, p = 0.01] were associated with decreased overall survival. Similarly, age ≥ 75 years [HR 2.33, p < 0.001], stage III/IV [HR 2.38, p = 0.002], B-symptoms [HR 1.62, p = 0.032], LDH ≥ 1.5 x UVN [HR 1.09, p = 0.047], neutrophilia [HR 2.25, p = 0.001] and high lymphocyte/monocyte ratio [HR 2.08, p = 0.005] predicted poor PFS. **Conclusion:** In the largest real-life Latin American cohort including patients with DLBCL, NOS older than 70 years, age ≥ 75 years, advanced clinical stage III/IV, neutrophilia and high lymphocyte/monocyte ratio were independent predictors associated with decreased overall survival.

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HIGH TUMOR MUTATION BURDEN IN EPIGENETIC REGULATORY GENES PREDICTS DECREASED OVERALL SURVIVAL IN NODAL PERIPHERAL T-CELL LYMPHOMAS

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Introduction: Nodal peripheral T-cell lymphomas (nPTCL) constitute a heterogeneous group of rare malignancies with aggressive biological behavior and poor prognosis. Epigenetic phenomena involving genes that control DNA-methylation and histone deacetylation, such as *IDH2*, *DNMT3A*, *TET2* and *RhoA*, play a central role in their pathogenesis. Tumor mutation burden (TMB) has emerged as a prognostic biomarker in numerous solid neoplasms. Furthermore, TMB reflects the process of clonal evolution, with progressive acquisition of additional molecular-genetic abnormalities. Recent studies were capable to establish a relationship between TMB and response to anti-cancer treatments. In 2021 Fachi et cols. established a correlation between high TMB in epigenetic regulatory genes and higher response rates to 5-azacytidine and romidepsin in nPTCL. However, the potential prognostic impact of epigenetic TMB remains unknown in nPTCL. Based on this premise, here we aimed, in a pioneering way, to search for a correlation between epigenetic high TMB and adverse prognosis in nPTCL. **Methods:** This is a retrospective, observational and single-center study, involving 59 patients with nPTCL diagnosed and treated at the Department of Hematology, University of São Paulo, Brazil, from January 2000 to December 2019. FFPE diagnostic tumor samples were submitted to Sanger sequencing with a target-panel, involving *IDH2*, *DNMT3A*, *TET2* and *RhoA* genes to search for recurrent mutations. **Results:** The median age was 50 years (IqR 38-61), and 57.6% (34/59) were male. Thirty-nine percent (23/59) had bulky disease ≥ 7 cm, 83% (49/59) had B-symptoms, 94.9% (56/59) had advanced stage III/IV, 27.1% (16/59) had ECOG ≥ 2, 27.1% (16/59) had ≥ 2 extranodal sites involved by lymphoma, and 55.9% (33/59) had intermediate-high/high-risk IPI. Seventy-six percent (45/59) received up-front therapy with CHOP-like regimens (CHOP or CHOEP), 23.7% (14/59) experienced radiotherapy, and 33.3% (20/59) were consolidated with ASCT. With a median follow-up of 3.7 years (95% CI: 0.9-12.4), the estimated 2-year OS and PFS were 57.1% (95% CI: 45.5-70.4) and 49.2% (95% CI: 34.0-59.2), respectively. *Missense*, *non-sense* or *frameshift* mutations in the *IDH2* gene were observed in 3.3% (2/59) of cases, *DNMT3A* in 3.3% (2/59), *RhoA* in 23.7% (14/59) and *TET2* in 37.2% (22/59). Among the 59 patients included, 23/59 (38.9%) had no mutations in the target-genes, 25/59 (42.4%) had 1 mutation, and 11/59 (18.6%) had two or more mutations. Therefore, the cases were categorized into low TMB (< 2 mutations) [n = 48/59 – 81.3%] or high TMB (≥ 2 mutations) [n = 11/59 – 18.7%]. The median overall survival was 51.4 months (95% CI: 0-124.1) for low TMB and only 3.1 months (95% CI: 3.1-15.2) for high TMB, p = 0.08. The estimated 2-year OS was 64.3% (95% CI: 50.6-78.0) for low TMB and 36.4% (95% CI: 8.0-65.0) for high TMB. Similarly, median

progression-free survival was 13.3 months (95% CI: 0-29.4) for low TMB and 6.3 months (95% CI: 0.9-11.6) for high TMB, p = 0.319. The estimated 2-year PFS was 46.1% (95% CI: 20.0-72.1) for low TMB and 25.0% (95% CI: 17.5-67.5) for high TMB. **Conclusion:** In a pioneering way, we demonstrated that the high epigenectic TMB, defined by the presence of 2 or more mutations involving epigenetic regulatory genes, was associated with decreased overall survival in Brazilian patients with nodal PTCL. Although preliminary, these data support the potential impact of epigenetic TMB as a prognostic biomarker in nPTCL.

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CLINICAL OUTCOMES, PROGNOSTIC FACTORS AND THERAPEUTIC MANAGEMENT IN EXTRANODAL NATURAL-KILLER/T-CELL LYMPHOMA, NASAL-TYPE (ENKTL-NT) – RESULTS OF THE MULTICENTER T-CELL BRAZIL PROJECT

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Introduction: Extranodal natural-killer/ T-cell lymphoma, nasal-type (ENKTL-NT) is an aggressive, angiocentric, and extensively necrotic malignancy, universally associated with Epstein-Barr virus (EBV) infection. Although highly prevalent in South America, few studies involving cohorts from this region have been published. Brazil is the largest and most populous country in South America, but Brazilian data on ENKTL-NT are extremely scare. In order to fill this gap, the current study aims to describe clinical and laboratory characteristics, assess clinical outcomes, determine predictors of survival and compare responses between different therapeutic modalities applied in a multicenter cohort of Brazilian patients with ENKTL-NT. **Methods:** This is a retrospective, observational and multicenter study, involving 98 patients with ENKTL-NT diagnosed and treated at 20 different Brazilian institutions between January 2000 and December 2021. Endpoints included overall response rate (ORR), overall survival (OS) and progression-free survival (PFS). Survival curves were constructed using the Kaplan-Meier method and the Log-Rank test was used to assess the relationship between variables and outcomes. Univariate analysis was performed using the semi-parametric Cox test and multivariate analysis by Cox regression method or proportional ratios model. **Results:** The median age was 50 years (IqR 40-58) and 60.2% (59/ 98) were male. Sixty-three percent (62/ 98) had B-symptoms, 26.5% (26/ 98) had ECOG ≥ 2, 16.3% (16/ 98) had extranasal disease, 34.7% had advanced-stage III/ IV, and 30.2% (29/ 98) had high-risk *PINK* score. With a median follow-up of 49.0 months (95% CI: 35.8-62.3), the estimated 2-year OS and PFS were 51.1% (95% CI: 40.4-61.6) and 17.7% (95% CI: 4.5-30.8), respectively. Among early-stage disease (IE/ IIE) patients, the estimated 2-year OS were 81.3% (95% CI: 64.8-97.7) for SCRT (sequential chemoradiotherapy) followed by CHOP-like, 53.2% (95% CI: 29.3-77.1) for CCRT (concurrent chemoradiotherapy) followed by VIPD, and 50.5% (95% CI:21.4-79.5) for SCRT followed by asparaginase-based regimens, p = 0.221. CCRT-VIPD was associated with higher early-mortality (p = 0.034), and higher rates of neutropenia (p = 0.075), febrile neutropenia (p = 0.043) and mucositis (p < 0.001). Among advanced-stage (III/ IV) disease, the estimated 2-year OS were 37.0% (95% CI: 8.9-65.0) for asparaginase-based regimens and 33.0% (95% CI: 1.9-68.5) for anthracycline-based regimens, p = 0.851. Chemoradiotherapy (CRT) was associated with benefit for OS (p = 0.001) and PFS (p = 0.007) compared to chemotherapy alone. In multivariate analysis, anemia (HR 2.052, p = 0.038), lymphopenia [HR 3.600, p = 0.012], advanced-stage disease (III/ IV) [HR 3.101, p = 0.007], bone marrow infiltration [HR 5.406, p = 0.034] and omission of RT in up-front therapy [HR 2.791, p = 0.023] were independent factors associated with decreased survival. **Conclusion:** High-dose EF-RT proved to be the cornerstone for the treatment of early-stage ENKTL-NT, and omission of this therapeutic modality was associated with decreased OS and PFS in Brazilian patients. In our real-life study, CCRT-VIPD regimen was poorly tolerated, and surprinsingly protocols based on anti-MDR agents were not associated with increased survival either in early- or advanced-stage disease. We also found that anemia, lymphopenia, advanced-stage (III/IV) and bone marrow involvement were independent predictors associated with poor clinical outcomes.

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LINFOMA DIFUSO DE GRANDES CÉLULAS B ESPLÊNICO E EM BASE DE LÍNGUA - RELATO DE CASO

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Introdução: O linfoma difuso de grandes células B (LDGCB), mesmo sendo um dos linfomas não-Hodgkin (LNH) mais comuns, tem sua apresentação linfonodal e extranodal de forma rara em literatura. Este artigo relata um caso atípico de LDGCB situado em baço e em base de língua em um paciente masculino de 28 anos, atendido em um hospital de referência no estado de Santa Catarina. **Relato de caso:** Homem de 28 anos deu entrada em hospital queixando-se de lombalgia, com irradiação para testículo direito, e dores abdominais há cerca de seis meses. Relata perda ponderal de 10 kg durante 1 mês, juntamente com disfagia para sólidos. Foi submetido a uma tomografia computadorizada (TC) de abdome total que