investigação adequada foram fundamentais para o diagnóstico e início do tratamento em tempo hábil.

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FIRST INTERIM RESULTS OF THE REAL-LIFE STUDY EVALUATING THE EFFICACY AND SAFETY OF BELINOSTAT

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Introduction: Belinostat is a Pan-Histone Deacetylase Inhibitors (HDACi) that increases histone acetylation leading with anti-angiogenic and antitumor properties as cell cycle retardation, changes in cell microtube dynamics, apoptosis ultimately reducing cancer cell proliferation, indicated in the treatment of in refractory or relapsed (R/R) Peripheral T- Cell Lymphoma (PTCL) as monotherapy. BELBRA is the real-life observatory study initiated in Brazil with the participation of around 90 lymphoma reference centers, with 97 patients to date. Representing one of the largest real-life Belinostat studies in the world. **Objectives:** BELBRA is the real-life observatory study to evaluate Belinostat's option for Brazilian PTCL R&R previously submitted to multiple conventional chemotherapy regimens. **Material and methods:** Methods: to date, 97 R/R PTCL patients treated with Belinostat in Brazil have been mapped. Of these 97, we received data from 20 patients. In this interim analysis, the demographic characteristics of the 97 mapped patients were analyzed, including sex, age, and subtype. Furthermore, more detailed analyzes of the 20 patients were carried out including overall response (OR), complete and partial responses (CR and PR), assessment of disease-free progression (DFP), as well as the safety profile of Belinostat therapy. Data collection and statistical analyzes continue to be carried out. **Results:** Overall, 53.9% (41) were female and 46.1% (35) male, with a median age of 60 years. Ninety-seven (97) patients diagnosed as R/R PTCL with the following classification subtype: lymphoma NOS 46.7% (35) Not Otherwise Specified (NOS), LACG 21.3% (16), MF 12 16.0% (12), ATLL 8.0% (6%), AITL 6.7% (5), LLPC 1.3% (1). Following a more detailed analysis of twenty patients (20): As first line CHOP or CHOP like therapies 16 (80.0%) and other therapies for 4 (20.0%) of patients. As for R/R PTCL Belinostate was used as monotherapy as 2nd or ≥ 3rd lines in 6 (30.0%) and 14 (70%) respectively. The overall response rate was ORR 45% (CR 10.0% and PR 35.0%) and Stable Disease SD 2 (10.0%) with a Disease Progression in 8 (45.0%) of patients. Also, in those 20 patients, Belinostate treatment with an average of 5,4 cycles (2 to 17) was well tolerated with all patients remaining in the full 1,000 mg/m2 dosage intravenously during 30 minutes on days 1 to 5 every 21 days. **Discussion and conclusion:** So far Real-world evidence from this Brazilian registry shows that Belinostat has a favorable efficacy and safety profile and supports its use in PTCL patients who are refractory or has relapsed to previous therapies.

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GENOMIC PROFILING AND TARGETED THERAPY IN BRAZILIAN LARGE B-CELL LYMPHOMAS: A HIGH-RISK MOLECULAR LANDSCAPE

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Introduction: Diffuse large B-cell lymphoma (DLBCL) is biologically heterogeneous, with its genomic landscape mapped in high-income countries but scarcely characterized in low- and middle-income countries (LMICs) like Brazil. Distinct demographics, healthcare settings, and ancestry-related backgrounds may influence disease biology, limiting the applicability of existing risk models and targeted therapies. Incorporation of next-generation sequencing (NGS) into routine practice enables precise molecular classification, improved risk stratification, and identification of actionable alterations, directly informing clinical management. **Objectives:** To report a molecular characterization of a Brazilian DLBCL cohort and illustrate how NGS-guided decisions can shape therapeutic strategies. **Material and methods:** We retrospectively analyzed Brazilian patients with DLBCL or high-grade B-cell lymphoma who underwent a targeted NGS for lymphoid malignancies. Mutational data were classified according to the LymphPlex algorithm. **Results:** Twenty-two patients (median age 66) harbored ≥ 1 molecular alteration. Median tumor mutational burden was 11.4 mut/Mb (range 1.6

−191); microsatellite instability was detected in one patient. Frequently mutated genes included TP53 (32%), PIM1 (23%), MYD88 (18%), CD79B (18%), SOCS1 (18%), KMT2D (18%), and CREBBP (18%). Mutations predominantly involved epigenetic/chromatin remodeling (64%), TCR/BCR/NF-κB signaling (59%), and apoptosis/DNA damage pathways (59%). LymphPlex classification identified Others (36%), TP53Mut (32%), MCD-like (14%), EZB-like without MYC rearrangement (14%), and EZB-like with MYC rearrangement (4.5%). High-risk categories (TP53Mut + MCD-like) accounted for 46% of patients. As expected, MCD-like was restricted to non-GCB tumors and EZB-like to GCB tumors, while the heterogeneous "Others" group included recurrent alterations such as TET2, GNA13, NOTCH2, BTK, and CDKN2A deletion. Two patients exemplify the clinical impact of these findings. One, a 60-year-old woman with relapsed/refractory non-GCB DLBCL and CNS involvement, harbored MYD88 (L265P) and CD79B mutations, defining the MCD subtype. Given its known sensitivity to BTK inhibition, acalabrutinib was initiated, inducing a rapid metabolic complete remission and enabling consolidation with anti-CD19 CAR-T therapy; she remains disease-free after two years. The other, a 50-year-old woman with CNS-involved DLBCL ineligible for ASCT, was also classified as MCD subtype and received maintenance ibrutinib, achieving and sustaining complete remission for 1.5 years. **Discussion and conclusion:** This Brazilian DLBCL cohort shares key oncogenic drivers with global series but shows a notable enrichment for high-risk subtypes, particularly TP53Mut and MCD-like, which are associated with poor prognosis. The case examples highlight how NGS not only refines molecular classification but also directly informs targeted therapy selection—enabling durable remissions in patients with advanced, refractory disease who otherwise have limited options. In conclusion, targeted NGS in DLBCL offers dual value: generating population-level insights that reveal a high prevalence of aggressive molecular subtypes in Brazil, and providing actionable data that can refine treatment selection and improve outcomes in individual patients. These findings underscore the need for robust local genomic datasets to guide precision oncology in LMIC settings.

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HISTOPLASMOSE DISSEMINADA MIMETIZANDO RECIDIVA PARA LINFOMA DIFUSO DE GRANDES CÉLULAS B

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Introdução: O Linfoma Difuso de Grandes Células B (LDGCB) é uma doença linfoproliferativa agressiva, mas com potencial de cura. Devido à imunossupressão secundária à doença e à quimioterapia, esses pacientes são passíveis de complicações infecciosas atípicas. Relatamos caso de paciente com LDGCB que, 1 ano após término do tratamento quimioterápico, evoluiu com linfadenomegalias que, biopsiadas, resultaram no diagnóstico de Histoplasmose disseminada, mimetizando progressão de doença linfoproliferativa. Metodologia: Estudo descritivo tipo relato de caso, incluindo histórico clínico, tratamento prévio, evolução e exames referentes à internação em hospital público de Brasília-DF. Dados provenientes do prontuário. **Descrição do caso:** Paciente, 61 anos, sexo feminino, portadora de LDGCB, subtipo centro germinativo, Lugano III, IPI III. Realizou 6 ciclos de R-CHOP, última sessão em 15/07/2024, com resposta completa por PET. Durante acompanhamento ambulatorial, surgiram adenomegalias cervicais, axilares e inguinais, associadas a sudorese noturna e perda ponderal de 16 kg em 3 meses. PET-CT em 15/05/2025 mostrou linfonodomegalias difusas com hipermetabolismo, sugestivas de recaída. Biópsia de linfonodo axilar: linfadenite granulomatosa fúngica compatível com Histoplasmose. Internada em 13/06/25 para tratamento com Anfotericina B lipossomal (5 mg/kg) por 14 dias e posterior Itraconazol por 12 semanas. Após 10 dias, evoluiu com choque séptico e disfunção múltipla de órgãos. Apresentava citopenia, febre e hiperferritinemia, aventando-se hipótese de linfohistiocitose hemofagocítica (LHH) secundária; iniciada corticoterapia empiricamente (10 mg/m^2). Exames posteriores descartaram hipótese (Hscore <1%). Apesar do tratamento antifúngico e suporte, evoluiu a óbito em 18/06/2025. Discussão: Histoplasmose é infecção fúngica sistêmica pelo Histoplasma capsulatum, fungo dimórfico transmitido por inalação de microconídios de solos contaminados com dejetos de aves e morcegos. Revisão sistemática de 34 casos (2001-2024) observou 73,5% relacionados a neoplasias hematológicas, potencializada quando associada ao HIV. Por manifestações como febre indeterminada, adenomegalias e perda ponderal, pode mimetizar progressão de doença, retardando tratamento. Discutir diagnósticos diferenciais é essencial. A LHH secundária, adquirida, afeta adultos, desencadeada por doenças autoimunes (12%), câncer (28%) ou infecções (50%), como Histoplasmose. Descartá-la impacta diretamente o tratamento e prognóstico. **Conclusão:** O desfecho desfavorável evidencia a complexidade no manejo de doenças hematológicas, em que imunossupressão severa favorece infecções graves e atípicas. Neutropenia funcional e defeito de linfócitos citotóxicos ocasionam complicações imunológicas severas. Suspeita precoce, acesso a exames e laudos rápidos, aliados a uso inteligente de Scores diagnósticos direcionando início imediato do tratamento, são determinantes para melhor prognóstico.

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IMPACTO DO MOMENTO DE INTRODUÇÃO DO RITUXIMABE NO TRATAMENTO DO LINFOMA DIFUSO DE GRANDES CÉLULAS B: ANÁLISE DE SOBREVIDA

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