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Introduction: Patients with Epstein-Barr virus-positive (EBV+) lymphoma are currently faced with challenging outcomes and represent an unmet medical need. Clinical outcomes in this population may be inferior to the EBV− counterpart in different lymphoma subtypes, including Peripheral T-Cell Lymphoma (PTCL). With a novel mechanism of action, nanatinostat (Nstat, a potent Class-I histone deacetylase inhibitor) induces expression of the lytic BGLF4 protein kinase, which activates the nucleoside analog ganciclovir (GCV), derived from valganciclovir (VGCV) via phosphorylation. Incorporation of phospho-GCV into cellular DNA results in termination of DNA synthesis causing apoptosis. **Materials and methods:** NAVAL-1 (NCR05011058) is an adaptive Phase 2, open-label, single-arm, two-stage, basket trial. Each lymphoma subtype cohort where ≥2 of 10 patients in Stage 1 responded to Nstat (20 mg orally once daily, 4 days/week) and VGCV (900 mg orally once daily, 7 days/week) continued to enroll 11 patients in Stage 2, for a total of 21 patients in each cohort. Efficacy and safety data from the 21-patient relapsed/refractory (R/R) EBV + PTCL cohort are presented herein. **Results:** As of 28 June, 2024, the investigator-assessed overall response rate (ORR), as assessed by Cheson 2007, in 21 patients treated with Nstat+VGCV was 33% (with a median duration of response that has not yet been reached) with a complete response rate (CRR) of 19% in the intent-to-treat population (ORR 41% and CRR 24% in the efficacy-evaluable population), including 2 patients who were able to proceed to allogeneic hematopoietic stem cell transplant. Patients receiving the combination in the second-line treatment setting had higher ORR (60%), with a CRR of 30% (efficacy-evaluable ORR 67% and CRR 33%). Most TRAEs have been hematological or gastrointestinal in nature and primarily Grade 1-2 in severity, and most Grade ≥3 TRAEs have been generally manageable or reversible except for one Grade 5 TRAE of sepsis in the context of severe cytopenias. Serious TRAEs have included influenza, pneumonia, upper respiratory tract infection, pancytopenia and sepsis (1 each). **Conclusion:** Nstat+VGCV is emerging as a promising, generally well-tolerated treatment for patients with R/R EBV + PTCL, particularly in the second-line treatment setting. Enrollment in the PTCL expansion is ongoing.

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UNVEILING THE PROGNOSTIC CHALLENGES OF NODAL PERIPHERAL T-CELL LYMPHOMAS: A MULTICENTER REAL-WORLD STUDY

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Introduction: Peripheral T-cell lymphomas (PTCL) are a rare group of malignancies derived from mature T-cells or natural killer cells, characterized by significant clinical-biological heterogeneity despite being grouped together. These entities have unique clinical, morphological, phenotypic, and molecular signatures. The predominantly nodal presentation group includes the histological variants ALK-positive anaplastic large cell lymphoma (ALK1+ ALCL), ALK-negative anaplastic large cell lymphoma (ALK1- ALCL), angioimmunoblastic T-cell lymphoma (AITL), and PTCL, not otherwise specified (PTCL-NOS). The central pillar of treatment for this subgroup of lymphomas is based on anthracycline-containing polychemotherapy regimens and upfront consolidation with autologous hematopoietic stem cell transplantation, although unfavorable outcomes such as primary refractory disease and early relapses are still common, except for the ALK1+ ALCL subgroup. **Methodology:** Hence, a multicenter, real-world, ambispective study was conducted, involving reference institutions in Brazil and two in the USA, to evaluate the main clinical-demographic characteristics associated with the outcomes of 179 patients diagnosed with nodal PTCL. **Results and discussion:** Individuals with nodal PTCL often presented at diagnosis with unfavorable clinical features, including a high frequency of advanced disease (stages III and IV), high tumor burden, poor performance status (ECOG ≥ 2 points), and frequent allocation in high-risk categories of the IPI and PIT prognostic indices. Patients with nodal PTCL included in this study globally exhibited low Complete Response rates, as well as shortened Overall Survival (OS) and Progression-Free Survival (PFS). In this cohort, we did not identify a robust survival benefit from the intensification of the CHOP regimen with the addition of etoposide (CHOEP protocol) or with BV-CHP. Age ≥ 60 years, ECOG ≥ 2, and lack of complete remission after primary therapy centered on CHOP-like chemotherapy were identified as independent prognostic factors associated with worse survival in this cohort represented by the four main histopathological subtypes of nodal PTCL. **Conclusion:** This analysis demonstrated a high frequency of unfavorable clinical features and poor OS and PFS outcomes in patients with nodal PTCL, regardless of the frontline chemotherapy regimen.

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REVEALING HIDDEN PATTERNS: HOW UNSUPERVISED MACHINE LEARNING AND MCA PREDICT SURVIVAL IN NODAL PERIPHERAL T-CELL LYMPHOMA PATIENTS

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