be useful as a practical and informative surrogates for outcomes, suggesting number of EN sites involvement assessed by CT and PET-CT as feasible clinical surrogate for outcomes in this population. New biomarkers are essential to better stratify patients with PTCL. Still, in practice, it is also necessary to have ways to stratify these patients using clinical data, mainly in regions with low-income resources. These indicators reflect distinct biological characteristics that merit further molecular investigation, potentially enhancing tailored therapies. Registries are essential given the rarity and poor prognosis associated with these diseases as well as generate hypotheses.

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NANATINOSTAT WITH OR WITHOUT VALGANCICLOVIR IN PATIENTS WITH RELAPSED/REFRACTORY EBV-POSITIVE PERIPHERAL T-CELL LYMPHOMA (NAVAL-1 STAGE 1)

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Introduction: Epstein-Barr virus-positive (EBV +) lymphomas are a heterogeneous group of malignancies that harbor latent EBV within the lymphoma cells and are associated with variable clinical features. Outcomes of EBV + Peripheral T-Cell Lymphoma (PTCL) patients are typically inferior to their EBV − counterpart, and thus represent an unmet medical need. Nanatinostat (Nstat) is a potent Class-I histone deacetylase inhibitor. With a novel mechanism of action, Nstat induces expression of the lytic BGLF4 protein kinase, which activates the nucleoside analog ganciclovir (GCV), derived from valganciclovir (VGCV) via phosphorylation. Incorporation of phosho-GCV into cellular DNA results in termination of DNA replication and apoptosis. **Materials and methods:** NAVAL-1 (NCR05011058) is an adaptive Phase 2, open-label, single-arm, two-stage, basket trial. In Stage 1 of the relapsed/refractory (R/R) EBV + PTCL cohort, 20 patients were randomized 1:1 to receive Nstat (20 mg orally once daily, 4 days/week) alone or in combination with VGCV (900 mg orally once daily, 7 days/week) and followed for efficacy and safety. Results: As of 28 June, 2024, the investigator-assessed overall response rate (ORR) by Cheson 2007 in the 10-patient Nstat+VGCV arm was 50% (with a duration of response that is maturing) with a complete response rate (CRR) of 20% in the intent-to-treat (ITT) population (ORR 71% and CRR 29% in the efficacy-evaluable population). One responding patient discontinued Nstat+VGCV to undergo allogeneic stem cell transplantation and remains lymphoma-free over 1 year. In the 10-patient Nstat monotherapy arm, the ORR and CRR were 10% and 0%, respectively, in the ITT population. Five patients without monotherapy response crossed over to combination therapy, including one who had a partial response and another with stable disease for 24+ weeks, both still ongoing. Most TRAEs have been hematological or gastrointestinal in nature and primarily Grade 1-2 in severity. Most Grade ≥3 TRAEs have been generally manageable or reversible except for one patient with Grade 5 TRAE of sepsis in the context of severe cytopenias. **Conclusion:** Combination Nstat+VGCV is a promising, generally well-tolerated treatment for patients with R/R EBV + PTCL that has shown improved efficacy over Nstat monotherapy in the challenging scenario of R/R PTCL.

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A GLOBAL PHASE 2 TRIAL OF NANATINOSTAT AND VALGANCICLOVIR IN PATIENTS WITH RELAPSED/REFRACTORY EBV-POSITIVE PERIPHERAL T-CELL LYMPHOMAS (NAVAL-1 STAGE 1-2)

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