necessário o desenvolvimento de novos estudos, que possam permitir o uso de agentes direcionados ao tratamento.

https://doi.org/10.1016/j.htct.2023.09.664

SAFETY AND EFFICACY FINDINGS OF A PHASE 1B/2 STUDY OF NANATINOSTAT PLUS VALGANCICLOVIR FOR TREATMENT OF RELAPSED/REFRACTORY EPSTEIN-BARR VIRUS-POSITIVE DIFFUSE LARGE B-CELL LYMPHOMA

M Capra [a], P Scheinberg [b], J Pereira [c], B Haverkos [d], S Spruill [e], D Strickland [f], P Porcu [g]

[a] *Centro Integrado de Hematologia e Oncologia, Hospital Mãe de Deus, Porto Alegre, Brazil*
[b] *Division of Hematology, A Beneficência Portuguesa de São Paulo (BP), São Paulo, Brazil*
[c] *Division of Hematology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HCFMUSP), São Paulo, Brazil*
[d] *Division of Hematology, University of Colorado, Denver, United States*
[e] *Applied Statistics and Consulting, Spruce Pine, United States*
[f] *Viracta Therapeutics, Inc., Cardiff, United States*
[g] *Division of Hematologic Malignancies and Hematopoetic Stem Cell Transplantation, Department of Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, United States*

Background: Diffuse large B-cell lymphoma (DLBCL) is one of several lymphoid malignancies in which Epstein-Barr virus (EBV) can play a significant role in pathogenesis. An estimated 5–14% of DLBCL cases are linked to EBV, which is associated with poor prognosis and 5-year survival rates as low as 25%. EBV is an attractive and druggable, but largely untapped, non-host tumor target, partly due to its latency. Most EBV genes, including those of the lytic cycle, are epigenetically silenced, preventing effective viral targeting. However, reactivation of viral gene expression with a histone deacetylase inhibitor (HDACi), combined with a DNA synthesis inhibitor, such as ganciclovir and its oral prodrug valganciclovir (VGCV), is an effective strategy to induce EBV+ tumor cell apoptosis. The safety and efficacy of this novel therapeutic strategy was investigated here using the HDACi nanatinostat (Nstat) and VGCV in patients (pts) with EBV-positive (EBV+) DLBCL. **Methods:** This Phase 1b/2 study (NCT03397706) assessed Nstat +VGCV in pts aged ≥18 years with EBV+ relapsed/refractory lymphoid malignancies. For inclusion, pts must have had ≥1 prior systemic therapies and no viable curative treatment options. Phase 1b evaluated safety and defined the recommended Phase 2 dose of Nstat+VGCV. Safety was assessed from first drug administration until 28 days post-last dose or until the start of a new anticancer therapy. Phase 2 assessed efficacy (overall response rate [ORR]). Here, subgroup analysis data of pts with DLBCL are reported. **Results:** Ten pts with DLBCL were included in the Safety Analysis Set. The median age was 76 years, 70% of pts were male and 80% had stage 3–4 disease. At the data cut-off (May 4, 2023), all pts had reported ≥1 treatment-emergent adverse event (TEAE). The most common any-grade TEAEs were fatigue (n = 8, 80%), neutropenia (n = 6, 60%), anemia, and decreased platelet count/thrombocytopenia (both n = 5, 50%). The most common grade ≥3 TEAEs were neutropenia (n = 5, 50%), anemia (n = 3, 30%), and decreased white blood cell/lymphocyte count (n = 2, 20%). The most common any-grade TEAEs related to the study drugs were fatigue, neutropenia (both n = 6, 60%), anemia, and decreased platelet count/thrombocytopenia (both n = 4, 40%). Five pts (50%) reported ≥1 serious TEAE. Four pts (40%) experienced study drug-related serious adverse reactions, namely atrial fibrillation (n = 2, 20%), febrile neutropenia, and myelodysplastic syndrome (both n = 1, 10%). No deaths due to events related to the study drugs were reported. Nine pts were evaluable for efficacy (1 excluded due to an unrelated serious adverse event). Three pts (33.3%) had a complete response (CR) and 3 (33.3%) had a partial response (PR); 1 pt (11%) had stable disease (SD). The ORR was 66.7%, with a 77.8% disease control rate (CR+PR+SD). At data cut-off, the duration of response (DoR) was not evaluable, as 3 pts remained on study treatment with DoR values of 11.2 (CR), 42.5 (PR) and 49.7 (CR) months. **Conclusions:** Encouraging safety and efficacy findings were observed with Nstat+VGCV in DLBCL, with durable disease control in responders. Hematologic toxicities were consistent with the VGCV safety profile. An ongoing confirmatory Phase 2 study (NCT05011058) will provide further data on this novel treatment combination for EBV+ lymphomas. Editorial support for this abstract was funded by Viracta.

https://doi.org/10.1016/j.htct.2023.09.665

A PHASE 1B/2 STUDY EVALUATING THE SAFETY AND EFFICACY OF NANATINOSTAT PLUS VALGANCICLOVIR FOR TREATMENT OF RELAPSED/REFRACTORY EPSTEIN-BARR VIRUS-POSITIVE NODAL PERIPHERAL T-CELL LYMPHOMA

J Pereira [a], P Scheinberg [b], M Capra [c], P Porcu [d], S Spruill [e], D Strickland [f], B Haverkos [g]

[a] *Division of Hematology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HCFMUSP), São Paulo, Brazil*
[b] *Division of Hematology, A Beneficência Portuguesa de São Paulo (BP), São Paulo, Brazil*
[c] *Centro Integrado de Hematologia e Oncologia, Hospital Mãe de Deus, Porto Alegre, Brazil*
[d] *Division of Hematologic Malignancies and Hematopoetic Stem Cell Transplantation, Department of Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, United States*
[e] *Applied Statistics and Consulting, Spruce Pine, United States*
[f] *Viracta Therapeutics, Inc., Cardiff, United States*
[g] *Division of Hematology, University of Colorado, Denver, United States*