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

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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

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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.

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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

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Background: Around 40% of peripheral T-cell lymphomas (PTCL) are linked to Epstein-Barr virus (EBV), which is associated with poor prognosis and 5-year overall survival rates as low as 20%. EBV is latent in tumors: most viral genes, bar those driving host cell growth and apoptosis blockade, are silenced. However, novel therapeutics aim to target EBV-positive (EBV+) tumors by reinstating viral gene expression to activate the nucleoside analogue ganciclovir (GCV) that inhibits viral and tumor DNA synthesis and prompts cell death. The safety and efficacy of this strategy was evaluated here with the histone deacetylase inhibitor nanatinostat (Nstat) and the oral pro-drug of GCV, valganciclovir (VGCV), in patients (pts) with EBV+ PTCL. **Methods:** This Phase 1b/2 study (NCT03397706) assessed Nstat+VGCV in pts aged ≥18 years with EBV+ relapsed/refractory lymphoid malignancies who had ≥1 prior systemic therapy and no viable curative treatment options. EBV status was determined by the site or central laboratory on a specimen representative of the current disease. Phase 1b evaluated safety (from first drug administration until 28 days post-last dose or until the start of a new anticancer therapy) and established the recommended Phase 2 dose. Phase 2 assessed efficacy (overall response rate [ORR]). Here, subgroup analysis data from pts with PTCL (angioimmunoblastic T-cell lymphoma [AITL] and PTCL not otherwise specified [PTCL-NOS]), are reported. **Results:** Thirteen patients with nodal PTCL (8 AITL, 5 PTCL-NOS) were enrolled. The median age was 68.4 years, 69% were male, and 92% had stage 3–4 disease. At data cut-off (May 4, 2023), all pts had ≥1 treatment-emergent adverse event (TEAE). The most common (reported in ≥10% of pts) any-grade TEAEs were decreased white blood cell (WBC)/lymphocyte count (n = 6, 46%), fatigue and diarrhea (both n = 5, 38%) (Table 1). Grade ≥3 TEAEs included decreased WBC/lymphocyte count (n = 4, 31%) and decreased neutrophil count (n = 3, 23%). The most common any-grade, study drug-related TEAEs were nausea and increased blood creatine (both n = 4, 31%); anemia, fatigue, diarrhea, decreased neutrophil count, decreased appetite and decreased WBC/lymphocyte count were the next most common (all n = 3, 23%). Of the most common study drug-related TEAEs, most (76%) were grade 1/2. Three pts had ≥1 serious TEAE, including infection, gastrointestinal disorders and new neoplasm. No serious adverse reactions or deaths due to events related to the study drugs were reported. Eight pts were evaluable for efficacy (5 pts non-evaluable due to TEAEs [n = 3], investigator decision [n = 1] and EBV− status [n = 1]). Three pts (37.5%) had complete responses (CR), 1 (12.5%) had a partial response (PR), 1 had stable disease (SD) and 3 had progressive disease. The ORR was 50%, with a 62.5% disease control rate (DCR [CR+PR+SD]). The median duration of response (DoR) was 17.3 months (mos). ORR and DCR were similar in AITL and PTCL-NOS, but DoR was longer in pts with AITL (n = 2, 38.3 mos) compared with PTCL-NOS (n = 2, 6.1 mos). **Conclusions:** Encouraging safety and efficacy findings were observed with Nstat+VGCV in PTCL. Hematologic toxicities were consistent with the VGCV safety profile. An ongoing Phase 2 study (NCT05011058) will provide further data on this novel therapy for EBV+ lymphomas. Editorial support for this abstract was funded by Viracta.

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LINFOMA ANAPLÁSICO DE GRANDES CÉLULAS ASSOCIADO A IMPLANTE MAMÁRIO COM ACOMETIMENTO SISTÊMICO E MANIFESTAÇÕES ARTICULARES

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Introdução: O linfoma anaplásico de grandes células associado a implante mamário (BIA-ALCL), é um linfoma não-Hodgkin de células T relacionado à colocação de próteses mamárias, com origem no fluído e tecido cicatricial (cápsula fibrosa) ao redor do implante. Apresenta-se frequentemente como seroma tardio ao redor no implante. Menos de 10% dos pacientes apresentam disseminação linfonodal e sintomas sistêmicos. **Objetivo:** Relatar um caso de linfoma anaplásico de grandes células associado a implante mamário com disseminação sistêmica e sintomas predominantemente articulares. **Relato de caso:** Paciente de 60 anos, sexo feminino, branca, iniciou quadro de dores articulares em pequenas e médias articulações com evolução de cerca de 6 meses. Recebeu tratamento com cetoprofeno, hidroxicloroquina, metotrexato e prednisona com controle parcial das dores. Após 4 meses de sintomas, começou a apresentar febre vespertina, sudorese e emagrecimento. Encontrava-se em regular estado geral, hipocorada +/4, sem linfonodomegalias palpáveis ou alterações relevantes ao exame físico. Apresentava discreta anemia, elevação de PCR e VHS, com marcadores reumáticos e outros exames normais. A tomografia de tórax evidenciou linfonodos mediastinais (2,1 cm) e pequeno volume de líquido envolvendo a prótese mamária esquerda. O PET CT Scan que demonstrou linfonodos e linfonodomegalias localizados em fossa supraclavicular, paratraqueal, pre-vascular, subcarinal (15 mm, SUVmax 9,5), além de imagem de densidade líquida (seroma) envolvendo a prótese mamária esquerda (SUVmax 3,9). Foi submetida a cirurgia de explante da prótese mamária. O exame histopatológico e imunohistoquímico da cápsula e linfonodo axilar foi compatível com BIA-ALCL, CD30 positivo, ALK negativo. Apresentava estadiamento III (T4N2M0). Foi submetida a tratamento quimioterápico com BV-CHP (brentuximab vedotin, ciclofosfamida, doxorrubicina e prednisona), atingindo resposta completa, mantida há 2 anos. **Discussão:** O BIA-ALCL é uma neoplasia linfoide rara que, segundo dados da FDA, até 04/2022 foram totalizados 1130 casos no mundo. Sua patogênese tem como hipótese o processo inflamatório desencadeado pela resposta dos macrófagos frente ao tecido do implante, liberando citocinas com quimiotaxia e expansão clonal de linfócitos T CD30 reativos e aberrantes. As apresentações clínicas mais comuns são localizadas, com massa ao redor do implante, dor mamária, retração de cápsula e seroma. Nesses casos, o tratamento envolve a explantação da prótese com excisão completa da cápsula e qualquer massa adjacente. Por outro lado, a doença avançada corresponde cerca de 9% dos casos, com sobrevida global em 5 anos de 75%, significativamente menor quando comparado com 97,9% naqueles com doença localizada. Como a grande maioria dos pacientes com BIA-ALCL