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PRELIMINARY ANALYSIS OF A PHASE 1 STUDY OF NEXI-002 AUTOLOGOUS MULTI-AGENT-SPECIFIC CD8+ T CELLS FOR THE TREATMENT OF RELAPSED OR REFRACTORY MULTIPLE MYELOMA (RRMM)

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Background: MM is an incurable malignancy that occurs predominately in older patients and is characterized by the growth of malignant plasma cells in the bone marrow. The median age of patients at diagnosis is 69 years and MM accounts for approximately 17% of all hematologic cancers. Despite substantial advances in therapy, virtually all patients relapse, emphasizing the need for additional effective treatments.

Aims: To characterize the safety and preliminary efficacy of NEXI-002, an HLA-restricted adoptive non-genetically modified and autologous cell product. The NEXI-002 product contains CD8+ T-cell memory subtypes that combine tumor potency with the potential for long-term immune persistence.

Methods: First-In-Human open-label phase 1/2 clinical trial. Safety, activity and correlative exploratory endpoints are evaluated and followed in patients during the study. HLA 02:01 patients underwent leukapheresis and artificial antigen presenting cells (aAPCs) were employed to isolate and expand CD8+ T-cell clonotypes expressing T cell receptors specific for HLA-restricted peptides from the WT1, CD138, CS1, and NY-ESO antigens. After expansion, the NEXI-002 product consists of γδ and CD8+ lymphocytes that are infused into the patient.

Results: Three patients were treated with single infusions of 80 to 100 million cells of NEXI-002 following lymphodepleting chemotherapy (fludarabine 30 mg/m^2 and cyclophosphamide 300 mg/m^2 on Days -5 to -3). All three patients have completed the dose-limiting toxicity (DLT) period. No cytokine release syndrome, neurotoxicity, infusion-related reaction, or other NEXI-002-related serious adverse events were observed. At the time of analysis, correlative studies demonstrate the NEXI-002 product is comprised mostly of CD8+ antigen-specific T cells that include stem-like central memory, central memory, and effector T cells. The infused CD8+ antigen-specific T cells were detectable by multimer staining in peripheral blood and the product phenotype was maintained over time. Flow cytometry studies of cells stained for antigen specificity determined that infused NEXI-002 cells contain T cell clones that were undetectable in the peripheral blood of patients at baseline but were detected in blood and persist over the current 3-4 weeks of follow-up. A robust lymphocyte recovery occurred quickly after the infusion of NEXI-002, demonstrating CD3 (CD4/CD8) reconstitution following lymphodepletion chemotherapy.

Summary/Conclusion: Early results indicate that NEXI-002 infusion is safe and well tolerated and is capable of proliferation and persistence within peripheral blood. NEXI-002 may have the potential to provide clinical benefit for patients with RRMM. Due to these encouraging findings, the trial will be expanded to gain greater safety and activity experience with NEXI-002. Updated data will be available.

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