Full-Length Variant Survivin Vaccine Potentiates Autologous Hematopoietic Stem Cell Transplantation in Multiple Myeloma

A new cancer vaccine consists of dendritic cells transduced with a full-length double mutant survivin gene delivered via an adenoviral vector. The vaccine will target survivin expressing tumors. The survivin protein is crucial for cancer cell function and is expressed in over 50% of patients in twelve distinct types of cancer. In a Phase I clinical trial, multiple myeloma patients were given this variant survivin vaccine prior to and post autologous stem cell transplantation with 4 out of 7 patients (57%) achieving a complete response (CR). Historical rates are expected to be closer to 17%. Patients with CRs have better survival outcomes years later.

COMMERCIAL OPPORTUNITY

- Survivin was designated a Top 25 tumor-associated (TAA) antigen by the NCI based on immunogenicity and differential expression in 50-80% of patients with more than 12 distinct cancer types. Survivin plays an essential role as an inhibitor of cancer cell death and promotes growth, metastasis, and treatment resistance of malignant cells.

- Multiple myeloma (MM) is an incurable cancer with an estimated 30,280 cases in the US in 2017. Over 40% of MM samples overexpress survivin and have significantly reduced T-cell responses against survivin protein. Approximately 5,000 MM patients receive high-dose chemotherapy and adoptive stem cell transplant (ASCT) each year in North America. Extensive clinical studies find that patients achieving CR post-transplant have significantly higher long-term overall survival (OS) and progression-free survival (PFS) at 12-15 years.

- The survivin vaccine market is attractive, as evidenced by two companies with ongoing clinical trials. MimiVax LLC has a synthetic peptide vaccine (SurVaxM) currently in Phase I/II trials for multiple myeloma, glioblastoma, and glioma. DPX-Survivac, a survivin-based peptide antigen produced by Immunovaccine Inc., is in Phase II trials for ovarian cancer, lymphoma, and glioblastoma. In contrast to DPX-Survivac and SurVaxM, the Moffitt full length variant survivin protein vaccine DC:AdmS should enable the presentation of multiple peptide epitopes, and recognition by a more diverse immune repertoire in patient populations.

TECHNOLOGY

An antigen presenting cell displaying a variant survivin polypeptide was produced through transfection of dendritic cells (DCs) with a double mutant (T34A and C84A) full-length survivin protein adenovirus construct. Co-culture of Multiple Myeloma (MM) patient-derived DCs with CD4+CD25- peripheral T cells *ex vivo* resulted in a significant increase in both the frequency and absolute number of survivin-reactive CD4+ T cells, with a fold expansion range of 0-270x and median of 42x. Additionally, T cells expanded with DCs presenting this variant survivin protein were survivin specific by IFNγ ELISpot analysis when re-stimulated with survivin peptide pools, producing about three times as many spots as an irrelevant peptide control. In a Phase I clinical trial, MM patients who did not achieve CR after induction therapy were administered the DC:AdmS pre- and post-autologous stem cell transplant. Results indicate that 4/7 (57%) of vaccinated patients achieved CR post-transplant compared with a historical CR rate of 9/51 (17.4%).

PUBLICATION

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