Phase 1 First-In-Human Trial Of LV305 In Patients With Advanced Or Metastatic Cancer Expressing NY-ESO-1

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I. ABSTRACT

Background: Development of immunotherapies using oncolytic viruses for cancer treatment is based on the hypothesis that infected tumor cells are killed by viral replication and are presented on the cell surface to the immune system. The NY-ESO-1 tumor antigen has been shown to be immunogenic in a subset of patients.

Methods: LV305 is a novel hybrid viral vector gene delivery system (http://www.cta.lncc.br/index.php) and is composed of a modified vaccinia virus variant (MVA) virus that encodes the NY-ESO-1 antigen and a naked plasmid expressing the NY-ESO-1 antigen. LV305 was tested in a first-in-human trial in which patients with advanced or metastatic cancer expressing NY-ESO-1 were treated with escalating doses of LV305. A phase 1B trial comparing LV305 + pembrolizumab to pembrolizumab alone in patients with NY-ESO-1 expressing tumors was also conducted.

Results: LV305 induced T cells that recognized NY-ESO-1 and two additional NY-ESO-1 peptides in an NY-ESO-1-negative patient. In sarcoma patients, LV305 induced specific CD8+ T cells against NY-ESO-1, which were associated with clinical response. In patients with melanoma, LV305 induced T cells that targeted NY-ESO-1 and two additional NY-ESO-1 peptides. These agents may be synergistic with checkpoint inhibitors like anti-PD-1/L1 antibodies.

Conclusion: These results support further development of LV305 as a potential adoptive cellular therapy for NY-ESO-1 expressing tumors.

II. RATIONALE / BACKGROUND

- NY-ESO-1 is a novel viral vector gene delivery system (Zvex) that expresses the NY-ESO-1 tumor antigen to generate and expand anti-cancer CTLs. LV305 is a novel hybrid viral vector gene delivery system (LV305).

III. III. LV305 TRIAL DESIGN AND RESULTS

- LV305 INDUCED NEW T CELLS AND INCREASED THE FREQUENCY OF TILS AND NY-ESO-1-PRESENTING EFFECTIVE CELLS.

IV. SUMMARY

- LV305 is a novel viral vector gene delivery system that targets and transduces DCs with NY-ESO-1, which has been shown to be immunogenic in some patients.

V. FUTURE PLANS

- LV305 is an NY-ESO-1-specific T cell line that targets and transduces DCs with NY-ESO-1, which has been shown to be immunogenic in some patients.

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LV305 Induced New T Cells And Increased The Frequency Of TILs And NY-ESO-1-Presenting Effective Cells (P=1-1)

Clinical Outcome: LV305 Stabilized Tumor Growth

- LV305 is a novel viral vector gene delivery system that targets and transduces DCs with NY-ESO-1, which has been shown to be immunogenic in some patients.

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