Viagenpumatucel-L (HS-110) with Nivolumab in the Ongoing DURGA Trial

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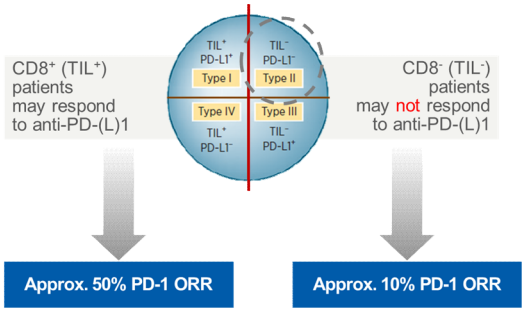
Key Points

- "DURGA" multi-arm trial is ongoing with nivolumab + viagenpumatucel-L, an allogeneic whole cell vaccine
- Treatment arms are assigned based on the patient's baseline CD8+ Tumor Infiltrating Lymphocyte (TIL) status in collaboration with Yale University Translational Immuno-Oncology Laboratory
- Protocol allows for up to 9 patients (2nd line or greater NSCLC adenocarcinoma) per arm, with potential expansion to 30 patients per arm

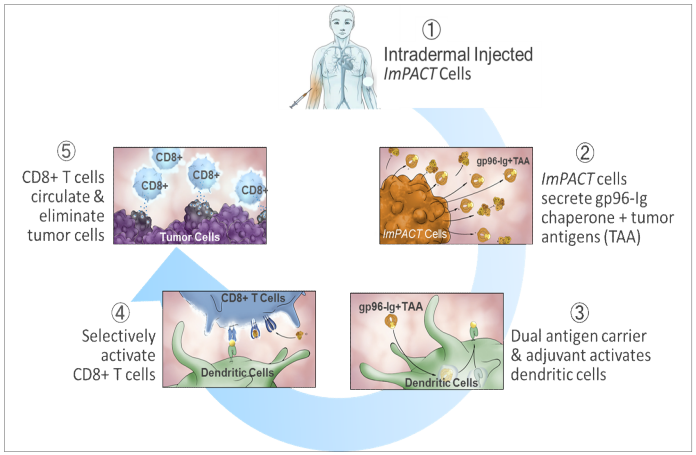
Background and Rationale

Non-small cell lung cancer (NSCLC) is the deadliest and third most-common malignancy in the US.[1] More than 50% of patients have advanced disease at diagnosis, and stage IV of the disease is almost uniformly fatal.[2] Recent clinical data with anti PD-1/PD-L1 monoclonal antibodies (mAbs) nivolumab, pembrolizumab, and atezolizumab have delivered objective responses in approximately 20% of an unselected population, with impressive duration in a subset of patients, and patients that express the highest levels of PD L1 on their tumors tend to respond best.[3] PD-L1 expression often occurs in response to T-cell activation, and therefore patients without existing tumor-infiltrating lymphocytes (TILs) may be less likely to respond to checkpoint inhibition without concomitant induction of TIL.[4] In fact, approximately 60% of patients are TIL-negative, perhaps accounting for the majority of patients who are currently underserved by single-agent checkpoint inhibitors.[5,6]



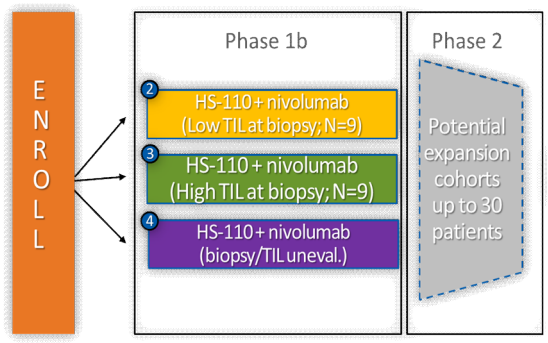
Viagenpumatucel-L is an allogeneic cell based vaccine being investigated in advanced NSCLC. Cell-secreted gp96-Ig delivers these cell-derived antigens directly to a recipient's own antigen presenting cells, resulting in highly selective activation of CD8+ cytotoxic T cells. Prior studies with viagenpumatucel-L (and related gp96-Ig vaccines) have shown a correlation between increases in CD8+ tumor infiltrating lymphocytes (TIL) and tumor response. Since the presence of TILs is one of the predictors for response to checkpoint inhibitors, the DURGA trial combining HS-110 with nivolumab was designed to explore the preclinical synergy between the two types of immunotherapy in an attempt to increase tumor inflammation and augment the population of patients benefiting from anti-PD-1 therapy. ClinicalTrials.gov identifier NCT02439450

Viagenpumatucel-L Mechanism of Action

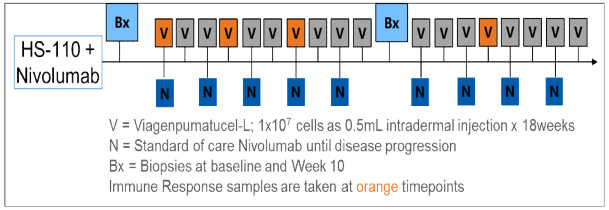


Viagenpumatucel-L is derived from a human lung adenocarcinoma cell line. The vaccine expresses a repertoire of multiple tumor antigens (including but not limited to MAGE-A3, survivin, LAGE-1, etc.) that are chaperoned by plasmid-transfected gp96-Ig. gp96 has dual antigen binding and adjuvant activity and delivers these cell-derived antigens directly to a patient's antigen presenting cells and shuttles those antigens to MHC-I. Preferential trafficking to MHC-I leads to exclusive activation of CD8+ cytotoxic T cells.

Trial Design



Trial Design and Regimen



Key Inclusion/Exclusion Criteria

- 2nd line or greater non-small cell lung **adenocarcinoma**
- Documented disease progression at study entry
- Adult patients with ECOG performance status (PS) ≤ 1
- CNS metastases may be permitted but must be treated and neurologically stable
- Adequate organ function
- No systemic anticancer therapy or radiation therapy within the previous 21 days
- No known immunodeficiency disorder or concurrent systemic immunosuppressive therapy
- No prior treatment with a cancer vaccine or checkpoint inhibitor for this indication

Trial Endpoints

Primary Endpoints

Phase 1b: Safety and Tolerability
Phase 2: Objective Response Rate (ORR)

Secondary Endpoints

Phase 1b: ORR, Peripheral blood immune response (IFNg-positive CD+ cells by ELISPOT), Overall survival (OS), PFS
Phase 2: Safety and tolerability, Peripheral blood immune response (IFNg-positive CD+ cells by ELISPOT), OS, PFS

Exploratory Endpoints

Characterization of **T-cell receptor (TCR) repertoire**, peripheral blood **immune response** by flow cytometry, total PBMC counts including lymphocyte subsets, evaluation of **biopsy tissue** for shared tumor **antigen expression**, presence of tumor infiltrating lymphocytes (TILs), correlation of **pre and post treatment TIL** levels with clinical outcomes, and expression of immunosuppressive molecules, **Disease control rate**, **OS** at 6 and 12 month

References

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