A PHASE 1/2 OPEN LABEL STUDY OF LABVAX 3(22)-23 AND ADJUVANT GM-CSF ALONE OR IN COMBINATION WITH PEMBROLIZUMAB IN SUBJECTS WITH LABYRINTHIN-POSITIVE ADENOCARCINOMAS

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Background Adenocarcinomas account for more than 70% of cancer-related deaths. Labyrinthin (LAB) is a novel tumor-specific protein expressed on the cell surface of the majority of adenocarcinomas of various cancer types. We hypothesize that vaccination against LAB can elicit strong immune responses against the LAB-expressing adenocarcinomas in cancer patients. LabVax 3(22)-23 is a novel anti-tumor vaccine that contains 4 synthetic LAB-based peptides designed to elicit both B-cell and T-cell responses. Sargramostim, a recombinant granulocyte macrophage colony-stimulating factor (GM-CSF), is given as an immunostimulator with LabVax 3(22)-23 to boost the anti-tumor immune response. Preclinical studies showed that LabVax 3(22)-23 significantly inhibited tumor growth that was augmented by GM-CSF without any significant toxicity in C57/BL6 transgenic mice expressing human PD-1/PD-L1 implanted with the murine colon adenocarcinoma cell line MC-38-huPD-L1. In phase I first-in-human LabVax 3(22)-23 and GM-CSF were well tolerated in 10 heavily pre-treated patients with LAB-expressing, refractory adenocarcinomas. LAB expression was positively associated with the expression PD-L1 on lung adenocarcinoma (LUAD). Based on preclinical synergism with pembrolizumab, this dose and injection schedule will be tested in a phase II open label study of LabVax 3(22)-23 and GM-CSF in combination with pembrolizumab in patients with refractory LAB-positive adenocarcinomas.

Methods The primary objective is to assess the safety and objective response rate (ORR) by RECISTv1.1 in participants with advanced/metastatic or recurrent lung adenocarcinoma who have received at least one line of immune checkpoint inhibitor therapy (Cohort A) or non-lung adenocarcinomas (Cohort B). Secondary endpoints include adverse effects and clinical laboratory abnormalities per CTCAEv5.0; median progression-free survival (PFS), 6-month PFS, overall survival. Exploratory objectives measure the effect of LabVax 3(22)-23 on various immune responses (cytokines, anti-LAB antibody production to each peptide) and the correlation between the level of LAB expression and the efficacy of LabVax 3(22)-23. Eligible patients are required to have labyrinthin expression on their tumor cells by IHC and adequate organ function. Patients receive sargramostim subcutaneously and LabVax 3 (22)-23 intradermally on weeks 1, 2, 4, 8, and 12 and pembrolizumab 200 mg IV every 3 weeks up to 17 treatments in the absence of disease progression or unacceptable toxicity. For the Phase 2 lead-in part of the study, 6 participants of various adenocarcinomas will be enrolled. If ≤2 subjects have a DLT, then the study will proceed to phase 2 expansions of 18 participants in each cohort. In Cohort A, if ≥2 LUAD patients respond, an additional 25 patients will be enrolled.

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Trial Registration Clinical trial information: NCT05101356.

Ethics Approval The human tumor specimen study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of the University of California, Davis (UC Davis Cancer Center Biorepository Protocol# 293828, and date of approval: 18 January 2012). The clinical trial was approved by UCD IRB.

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