40 NOVEL BIOMARKER ASSAYS FOR DETECTING LABYRINTHIN-POSITIVE ADENOCARCINOMAS FOR A PHASE I/II TRIAL OF PEPTIDE VACCINE LABVAX 3(22)-23 ALONE OR IN COMBINATION WITH PEMBROLIZUMAB

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Background Adenocarcinomas represent nearly 40% of all cancer types, and account for more than 70% of cancer-related deaths. Next generation sequencing (NGS) has been increasingly used for precision treatment in patients with adenocarcinomas. Labyrinthin (LAB) is a novel cancer neoantigen expressed on the surface of adenocarcinoma cells of various cancer types including lung adenocarcinoma (LUAD) and breast cancer. LabVax 3(22)-23 is a novel anti-tumor vaccine that contains four synthetic labyrinthin-based peptides designed to elicit both B-cell and T-cell responses. The objective of this study is to establish biomarker assays to identify candidate patients for a *first-in-human* phase I/II trial of peptide vaccine LabVax 3(22)-23 alone or in combination with pembrolizumab (NCT051013560).

Methods IHC assay for LAB expression on archived clinical tumor specimens was developed using a mouse monoclonal anti-LAB antibody MCA 44–3A6 (HB-8986TM, ATCC). LAB expression was scored on tumor cells by percentage and intensity on sections of tissue microarrays (TMAs) derived from 256 non-small cell lung cancer (NSCLC) and 97 breast cancer tissue blocks. LAB-specific mRNA expression was assessed in The Cancer Genome Atlas (TCGA) LUAD dataset by averaging expression of LAB-specific exons, excluding the related splice variant aspartyl/asparaginyl beta-hydroxylase (ASPH). The results were validated in an independent clinical NGS dataset of adenocarcinoma patients and selected tumor samples by IHC expression.

Results We found that LAB was expressed in 105/128 (82.0%) of LUAD by IHC. LAB expression is an independent poor prognostic factor for LUAD.[1] High prevalence of LAB expression was also found in breast cancer samples (95.8%, 93/97). There was no significant difference in the LAB expression among the ER, PR, and HER2 positive subgroups. IHC assay was used to detect LAB expression on 11 out of 12 (91.7%) patients screened for the phase I trial. Tumor origins included colon or rectum (8), ovarian (1), scalp (1), and prostate (1). LAB RNA was expressed in both oncogene-driven and non-oncogene-driven adenocarcinomas. Furthermore, LAB RNA expression was positively correlated with PD-L1 RNA expression across these LUAD subgroups. There was a good correlation between RNA seq expression with IHC expression in the initial 10 patients. Ongoing studies are validating these results with more patients with NGS data.

Conclusions We have established IHC and RNA assays to identify patients with LAB-positive adenocarcinomas in the ongoing phase I/II study (UCDCC#296, NCT051013560) evaluating the safety and efficacy of the LAB vaccine in combination with pembrolizumab.

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Trial Registration NCT051013560

REFERENCE

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Ethics Approval The 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).

Consent Patient consent was waived with the IRB approval.

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