

A PHASE 1, FIRST-IN-HUMAN, OPEN-LABEL STUDY EVALUATING THE SAFETY, TOLERABILITY, PHARMACOKINETICS, PHARMACODYNAMICS, AND PRELIMINARY EFFICACY OF PRJ1-3024 IN SUBJECTS WITH ADVANCED SOLID TUMORS

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Background PRJ1-3024 is a small molecule hematopoietic progenitor kinase 1 (HPK1) inhibitor designed to enhance T-cell function and anti-tumor responses. HPK1 is an immunosuppressive regulatory kinase with a restricted expression profile in hematopoietic compartment.^{1, 2} HPK1 kinase activity suppresses immune functions of a wide range of cells including cluster of differentiation CD4⁺ T cells, cluster of differentiation CD8⁺ T cells, and dendritic cells (DCs). Inactivating kinase domain of HPK1 is sufficient to elicit anti-tumor immune responses.³ It was demonstrated that HPK1 mediates T-cell dysfunction and is a potential therapeutic target for T-cell-based immunotherapies.⁴ These results strongly support a small molecule inhibitor of HPK1 functioning as a cancer immunotherapy agent.

Methods Phase 1, multicenter, non-randomized, open-label study to evaluate the safety, tolerability, and preliminary efficacy in patients with advanced solid tumors. The primary objective is to determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D). The secondary objectives are to evaluate safety, PK, pharmacodynamics of PRJ1-3024, and evaluate preliminary efficacy of PRJ1-3024. PRJ1-3024 is administered orally once daily (QD). Each cycle is 21 days with dose-limiting toxicity (DLT) assessment to be completed after 21 days on treatment in Cycle 1. Changes in multiple cytokines and chemokines in plasma and effects on phosphor-SLP-76 and proinflammatory cytokines in activated PBMCs will be evaluated. Pre- and Post-dose tumor tissue samples will be used for isolation of tumor-infiltrating lymphocytes to investigate the effects on the activation, expansion and migration of immune cells.

Results As of June 01, 2023, 16 patients with advanced solid tumors were enrolled in 5 dose cohorts: 80, 160, 300, 500, and 600mg. Median age was 64.7 years (range 42–84). Diagnoses were NSCLC(3 pts), Small Cell Lung Carcinoma (3 pts), Urothelial Carcinoma (3 pts), Gastroesophageal Junction (1), Cutaneous Melanoma (1), Cutaneous Squamous Carcinoma (1), HCC (1), HNSCC (1), TNBC (1), and Prostate Cancer (1). Eleven patients (69%) had ≥ 4 prior cancer therapies, 14 patients had prior treatment with immune checkpoint inhibitors. The most common TEAEs (in >2 patients) were diarrhea (7 pts), nausea (6 pts), blood creatinine increased (3 pts), fatigue (3 pts), and vomiting (3 pts). PK and PD assessments will be updated at time of presentation.

Conclusions PRJ1-3024 is a potent inhibitor of HPK1 that is shown to be well tolerated. Further safety and efficacy results will be presented at the meeting including additional cohorts if available.

Trial Registration Clinicaltrials.gov: NCT05315167

REFERENCES

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Ethics Approval Advarra IRB Approval: MOD01175260

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

All participants gave informed consent before taking part in this clinical trial.

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