Background: The first-in-class, oral, small-molecule agonist of retinoid acid receptor–related orphan receptor γ (ROγ), LYC-55716, is an investigational agent under development as an immunotherapy for solid tumors. A Phase 1/2a trial demonstrated the safety of LYC-55716 as monotherapy and provided evidence of clinical activity, including a confirmed partial response in a patient with non–small cell lung cancer (NSCLC). Based on pre-clinical testing, the combination of ROγ agonist and a PD-1 inhibitor may enhance immune activation and the favorable effects of PD-1 inhibition on the tumor microenvironment. This ongoing open-label, multicenter Phase Ib trial is assessing the safety as well as clinical and biologic activity of LYC-55716 in combination with pembrolizumab (L+P) in patients with NSCLC.

Methods: A run-in cohort of patients (n = 3) is receiving L+P to monitor for safety signals. After determining a dose for further study, 1 main cohort (n = 15) will receive L+P until disease progression or unacceptable toxicity. Pre- and post-treatment biopsies will be obtained for patients in the main study cohort. Primary endpoints are safety (monitoring of adverse events, physical examination, lab results) and incidence of dose-limiting toxicities during the run-in period and ongoing treatment. Secondary endpoints include cellular and molecular immune response and biomarkers, objective response rate, duration of response determined via response evaluation criteria in solid tumors (RECIST) v1.1 and immune-related RECIST, and pharmacokinetics. Immune biomarkers are being assessed by immunohistochemistry (IHC) and a comprehensive gene profiling panel using a NanoString platform.

Results: Enrollment of patients in the run-in cohort is pending. IHC assay validation for ROγ and other immune markers is complete. Results of safety, preliminary efficacy, and biomarker evaluation will be available for patients initially enrolled at the time of presentation.

Conclusions: The LYC-55716 safety profile and clinical activity as a monotherapy agent support investigation of L+P to treat patients with metastatic NSCLC.

Clinical trial identification: NCT03396497.

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