A PHASE 1, FIRST-IN-HUMAN, OPEN-LABEL, MULTICENTER STUDY OF INCA32459, A BISPECIFIC ANTI–PD-1 AND ANTI–LAG-3 ANTIBODY, IN PATIENTS WITH SELECT ADVANCED MALIGNANCIES

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Background Anti–programmed cell death (PD)-ligand (L)1 therapies have improved clinical outcomes in patients with various cancers. However, many patients either do not respond or develop resistance, partly due to additional immune checkpoint receptors including lymphocyte activation gene-3 (LAG-3), which is frequently co-expressed with PD-1 on tumor-infiltrating lymphocytes. Combined anti–PD-1 and anti–LAG-3 therapy has demonstrated improvements in clinical outcomes compared with anti–PD-1 alone. Co-targeting PD-1 and LAG-3 with a bispecific antibody has the potential to demonstrate enhanced clinical activity compared with individual monoclonal antibodies by achieving synergistic blockade. Therefore, this study aims to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary clinical efficacy of INCA32459, a bispecific anti–PD-1 × anti–LAG-3 antibody, in patients with advanced malignancies.

Methods This first-in-human, multicenter, open-label, dose-escalation, dose-expansion phase 1 clinical study will enroll approximately 120 patients into separate dose-escalation (n=40) and dose-expansion phases (n=80; figure 1). Patients with select advanced malignancies will be eligible to participate in the dose-escalation phase and will receive intravenous INCA32459 starting at dose level 1 every 3 weeks. Dose escalation will proceed according to a protocol-defined statistical hybrid design to assess the safety and tolerability of INCA32459 and determine the maximum tolerated dose and/or the recommended doses for expansion. The dose-expansion phase will consist of 2 tumor-specific cohorts. Cohort 1 will enroll patients with unresectable or metastatic melanoma who have experienced disease progression after standard therapy (n=40). Cohort 2 will enroll patients with recurrent or metastatic PD-L1+ (combined positive score ≥1) squamous cell carcinoma of the head and neck who have experienced disease progression after standard therapy (n=40). Treatment will be administered in 3-week cycles up to a maximum duration of 2 years. The primary endpoints are safety and tolerability as assessed by occurrence of dose-limiting toxicities and incidence of treatment-emergent adverse events (TEAEs), including overall TEAEs and TEAEs that lead to treatment interruption or withdrawal. Secondary endpoints include objective response rate, disease control rate, and duration of response as determined by investigator assessment according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 or Lugano criteria (for patients with B-cell lymphomas); pharmacokinetic parameters; and PD-1 receptor occupancy in peripheral blood samples.

Trial Registration ClinicalTrials.gov registration pending

REFERENCES


Ethics Approval The study protocol was approved by institutional review boards or independent ethics committees at participating centers.

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