Background

Extensive Stage Small Cell Lung Cancer (ES-SCLC) and Large Cell Neuroendocrine of the lung (LCNEC) are aggressive neuroendocrine carcinomas with an exceptionally poor prognosis.\(^1\)\(^2\) Although the majority of patients experience response to first line of therapy, the durability of response is often limited. Delta-like ligand 3 (DLL3) is an inhibitory Notch ligand that is highly expressed on the cell surface in SCLC (~85% of the patients having positive staining in >25% tumor cells) and LCNEC (74% having positive staining in at least 1% of tumor cells).\(^3\)\(^4\) Preclinical studies of LB2102, an autologous DLL3-directed CAR-T cell, have demonstrated DLL3-specific antitumor effects with a low risk of on-target/off-tumor toxicities and off-target/off-tumor toxicities.

Methods

This phase 1, open-label, multicenter, dose-escalation and cohort expansion study of LB2102 will treat up to 41 subjects with ES-SCLC or LCNEC (NCT05680922). Part A will enroll and treat 12–24 subjects, and Part B will treat 11–17 subjects (figure 1). Subjects will be pooled from Part A and Part B to a total of 23 subjects treated at the recommended dose for expansion. The patient population is adult subjects with histologically/cytologically confirmed unresectable small cell lung carcinoma (SCLC), large cell neuroendocrine lung carcinoma (LCNEC), combined SCLC, or combined LCNEC as per WHO 2021 criteria. Patients enrolled have received at least one prior line of standard treatment with progression or insufficient response, and for whom standard treatment is intolerable, unlikely to confer significant clinical benefit, is no longer effective, or the subject declines further standard treatment. Other key criteria include ECOG PS 0 or 1; life expectancy > 4 months per investigator judgment; available archival or fresh biopsy tissue, presence of ≥ 1 radiologically measurable lesion per RECIST 1.1, and adequate organ function per protocol. No prior DLL3 targeted therapy is allowed. LB2102 will be manufactured from autologous T cells collected from peripheral mononuclear blood cell apheresis. Subjects may receive optional bridging therapy followed by lymphodepletion chemotherapy with fludarabine and cyclophosphamide for 3 days. The subject will then receive one infusion of LB2102 and will be followed post-infusion for safety and disease assessments. The objectives of the study include characterization of safety and tolerability, evaluation of the recommended phase 2 dose, and assessment of preliminary antitumor activity. US sites will begin enrollment in fall 2023.

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Trial Registration

Registered on Clinicaltrial.gov (NCT05680922).

REFERENCES


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