A PHASE 1 STUDY OF AMG 119, A DLL3-TARGETING, CHIMERIC ANTIGEN RECEPTOR (CAR) T CELL THERAPY, IN RELAPSED/REFRACTORY SMALL CELL LUNG CANCER (SCLC)

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Background AMG 119 is a CAR-T cell therapy that targets delta-like ligand 3 (DLL3), an inhibitory Notch ligand that is expressed on the surface of most SCLC cells. In preclinical studies, AMG 119 specifically lysed DLL3-expressing SCLC cell lines and inhibited tumor growth in SCLC xenograft models.

Methods Primary objectives of this open-label, phase 1 study are to determine the safety, tolerability, and optimum cell dose of AMG 119 in adults with relapsed/refractory SCLC who progressed after ≥1 platinum-based chemotherapy regimen. Safety, efficacy, pharmacokinetics, and biomarkers were assessed.

Results At data cutoff, 5 adult subjects (median age: 59 years [range, 33-64], ECOG status: 0-1, ≥1 prior line of anticancer therapy) had received at least 1 intravenous infusion of AMG 119 as part of cohort 1 (n = 3; 3×10^5 cells/kg) or cohort 2 (n = 2; 1×10^6 cells/kg) in the dose exploration phase. One subject in cohort 1 and both subjects in cohort 2 were retreated with a second dose.

Post-infusion, a grade 1 treatment-related adverse event (TRAE) was noted in 1 subject (seizure), grade 2 TRAEs in 2 subjects (anemia and supraventricular tachycardia), and a grade 3 TRAE in 1 subject (pneumonitis; cohort 1). No dose-limiting toxicities or grade 4/5 TRAEs were observed.

Among evaluable subjects (n=4), a confirmed partial response (PR) was seen in 1 subject (cohort 2) 1.1 months after the first dose. Two subjects had stable disease, including 1 subject who experienced a 16% decrease in sum of the target lesions from baseline. One subject had progressive disease. Median progression-free survival was 3.7 months (range, 1.1-6.7) and median overall survival was 7.4 months (range, 4.6-18.9).

AMG 119 exhibited peak expansion 1-3 weeks after infusion; CAR-T cells were detectable up to 86 days in both cohorts. A preliminary dose-response relationship was observed with higher CAR-T cell expansion (~14-fold increased Cmax and AUC0-28d) in the subject with confirmed PR compared with the nonresponder (cohort 2). DLL3 expression was detected by immunohistochemistry on >85% of tumor cells in all evaluable subjects at all assessed timepoints. Changes in serum/whole blood markers were consistent with a pharmacodynamic response. The subject who achieved PR exhibited a rapid decline in total circulating tumor cell levels within 7 days of treatment initiation.

Conclusions AMG 119, the first CAR-T cell therapy for SCLC, was associated with a manageable safety profile and promising anti-tumor activity. Enrollment is currently paused but may resume.

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REFERENCE