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Trial In Progress: Phase 1b Study of AMG 757, a Half-Life Extended Bispecific T Cell Engager (HLE BiTE®) Immuno-Oncology Therapy, Combined With AMG 404, an Anti-PD-1 Antibody, in Patients With Small Cell Lung Cancer (SCLC)

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BACKGROUND

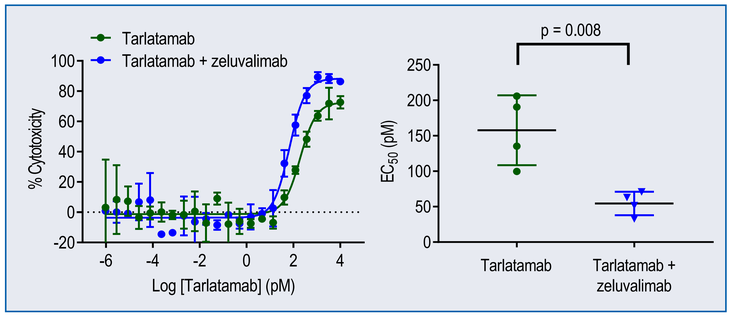
- Delta-like ligand 3 (DLL3) is a promising therapeutic target because it is highly expressed in small cell lung cancer (SCLC) and minimally expressed in normal tissues[1]
- AMG 757 (tarlatamab) is a half-life extended bispecific T cell engager (HLE BiTE®) therapy that binds DLL3 on cancer cells and CD3 on T cells to redirect T cell-dependent killing of tumor cells[2,3]
- In a phase 1 study in SCLC, tarlatamab given every 2 weeks was safe, with encouraging efficacy up to 100 mg[4,5]
- In early trials, programmed cell death-1 (PD-1) receptor or ligand (PD-L1) antibodies were well tolerated and also provided efficacy in relapsed/refractory (RR) SCLC[6,7]

RATIONALE FOR TARLATAMAB AND AMG 404 (ZELUVALIMAB*) COMBINATION

- Upregulation of PD-1 in the tumor microenvironment has been shown to blunt effectiveness of BiTE molecules[8,9]
- Combining an anti-PD-1 antibody with a BiTE molecule could increase T cell activity and antitumor response
- Zeluvalimab is a monoclonal antibody targeting PD-1
  - At doses evaluated to date, zeluvalimab was tolerable with no dose limiting toxicities reported[10]
- Preclinical data showed that tarlatamab treatment upregulates PD-1/PD-L1 and the combination with zeluvalimab increased T cell mediated lysis of tumor cells compared with tarlatamab alone (**Figure 1**)[11]
- **Based on these preclinical findings, the purpose of this study is to evaluate the safety and efficacy of tarlatamab in combination with zeluvalimab in patients with SCLC**

*Pending International Nonproprietary Name; application for United States Approved Name still pending.

Figure 1. Tarlatamab With Zeluvalimab Increases Cytotoxicity In Vitro



EC_{50}, half maximum effective concentration.

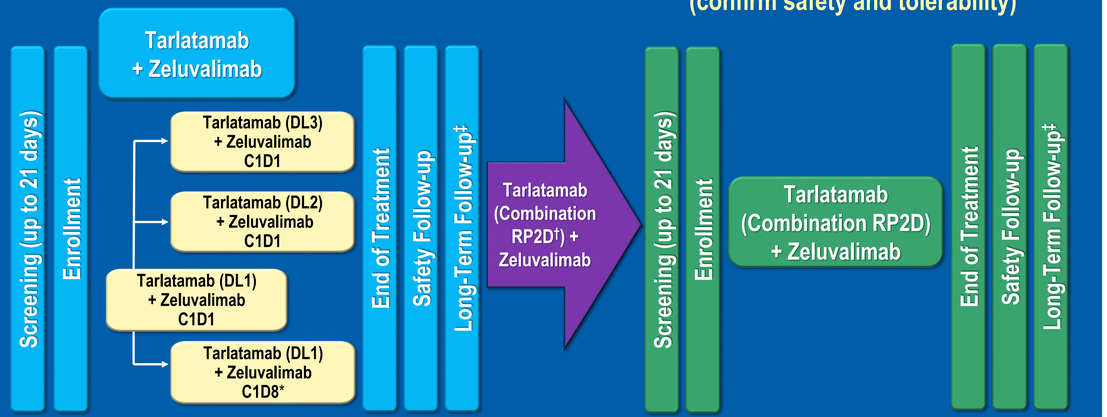
Key Eligibility Criteria

- Adults ≥18 years of age
- Informed consent provided before the initiation of any study activities or procedures
- Confirmed RR SCLC whose disease progressed/recurred after ≥1 platinum-based chemotherapy regimen; no untreated or symptomatic brain metastases
- Measureable lesions per modified RECIST 1.1 criteria
- Eastern Cooperative Oncology Group performance status of 0–1
- Prior therapy, including anti-PD-1 or PD-L1 therapy, is permitted ≥28 days before the first dose of tarlatamab

PD-1, programmed cell death-1 receptor; PD-L1, programmed cell death-1 ligand; RECIST, Response Evaluation Criteria in Solid Tumors; RR SCLC, relapsed/refractory small cell lung cancer.

Study Overview

- **Multicenter, open-label, phase 1b study evaluating tarlatamab with zeluvalimab**



*Zeluvalimab administered on cycle 1 day 8 if combination is not tolerated (based on target dose limiting toxicity rate > 30%). †MTD/RP2D estimated using a modified toxicity probability interval. ‡Every 3 months up to 1 year from the first dose of tarlatamab for all patients who have not withdrawn consent.
C1D1, cycle 1 day 1; C1D8, cycle 1 day 8; DL, dose level; MTD, maximum tolerated dose; RP2D, recommended phase 2 dose for combination therapy.

Key Messages

- **The combination of tarlatamab, an HLE BiTE therapy, and zeluvalimab, an anti-PD-1 antibody, may be well tolerated and have the potential to further increase antitumor activity compared with tarlatamab alone**
- **We are conducting a phase 1b study to evaluate tarlatamab in combination with zeluvalimab in patients with SCLC**
  - **ClinicalTrials.gov identifier: NCT04885998**
  - **The study is currently open and recruiting patients**
- **For more information, please contact Amgen Medical Information: medinfo@amgen.com**

ENDPOINTS

Primary Endpoints

- Dose-limiting toxicities (see box)
- Treatment-emergent and -related adverse events (AEs)
- Clinically significant changes in
  - Vital signs
  - Electrocardiograms
  - Clinical laboratory tests
- RP2D of the tarlatamab and zeluvalimab combination

Primary Endpoint: Dose-Limiting Toxicities

- Any AE with an onset within the first 28 days following the first dose of tarlatamab with any of the following criteria
  - Grade 3 AE lasting > 3 days*
  - ≥ Grade 4 AE regardless of duration†
  - Recurrent ≥ grade 2 pneumonitis
  - Toxicity requiring permanent discontinuation of zeluvalimab

*Exceptions include fatigue and endocrinopathies, if manageable with replacement therapy.
†Does not include laboratory parameters of grade 4, not considered clinically relevant, and improved to grade ≤ 2 within 72 hours.

Secondary Endpoints

- Antitumor activity
- Pharmacokinetics of tarlatamab in combination with zeluvalimab

DISCLOSURES

Afshin Dowlati: Advisory Role to Takeda, Abbvie, Seattle Genetics, AstraZeneca, and BMS; speakers' bureau for Loxo, Bayer, Incuron, Takeda, Regeneron, Tesaro, Seattle Genetics, Symphogen, Abbvie, and Ispen.

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