Poster #: 155TiP

Phase 2 Study of Tarlatamab, a Half-Life Extended Bispecific T-cell Engager (HLE BiTE®) Immuno-oncology Therapy Targeting DLL3, in Third-line or Later Small Cell Lung Cancer (DeLLphi-301 Study)

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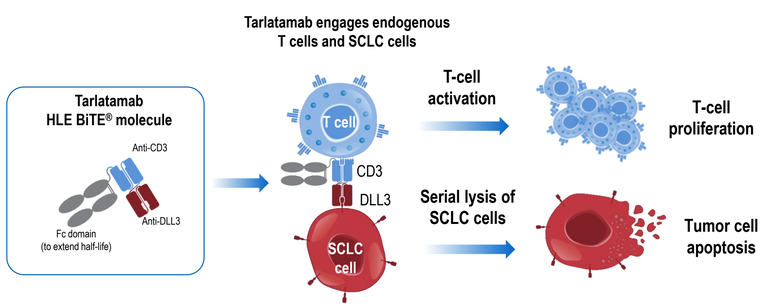
BACKGROUND

- SCLC is an aggressive disease with limited treatment options beyond first-line chemo-immune therapy and no approved third-line therapy[1,2]
- Delta-like ligand 3 (DLL3) is a Notch ligand that is upregulated and aberrantly expressed on the cell surface in most SCLC, making it a compelling therapeutic target[3,4]
- Tarlatamab (formerly AMG 757) is a DLL3-targeting HLE BiTE® designed to bind DLL3 on target cancer cells and CD3 on T cells, forming a cytolytic synapse and resulting in T cell activation & expansion and T cell-dependent killing of tumor cells (**Figure 1**)[5]
- Interim results of an ongoing first-in-human study of tarlatamab in patients with relapsed/refractory SCLC (NCT03319940) show promising and durable efficacy with an acceptable safety profile[6,7]
- These findings support further study of tarlatamab in SCLC

Figure 1. Tarlatamab: A HLE BiTE® Therapy Targeting DLL3



ABBREVIATIONS

BICR, blinded independent central review; CD, cluster of differentiation; DCR, disease control rate; DLL3, delta-like ligand 3; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; Fc, fragment crystallizable domain; FIH, first-in-human; HLE BiTE, half-life extended bispecific T cell engager; ORR, objective response rate; OS, overall survival; PK, pharmacokinetics; PFS, progression-free survival; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SCLC, small cell lung cancer

DISCLOSURES

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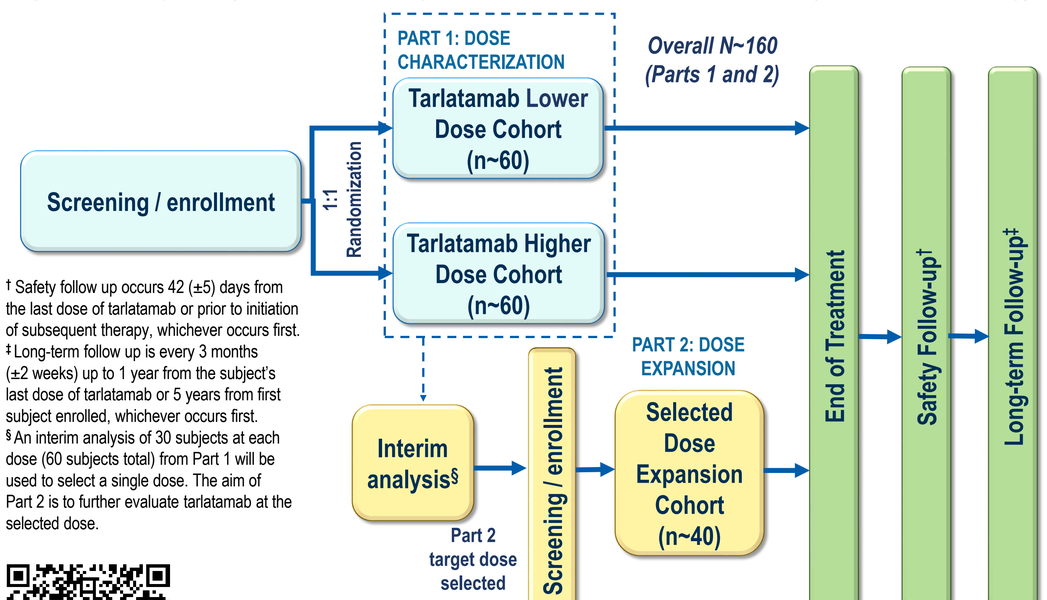
KEY TAKEAWAYS

- **Phase 1 FIH (NCT03319940) data shows tarlatamab has an overall manageable and reversible AE profile and delivers promising and durable efficacy in relapsed/refractory SCLC**
- **Based on promising outcomes from the phase 1 study, a phase 2 study (NCT05060016) is being conducted to evaluate the efficacy, safety, tolerability, and PK of tarlatamab in third line and later SCLC patients**
  - **Two different doses of tarlatamab will be evaluated in Part 1 (Dose Characterization)**
  - **In Part 2 (Dose Expansion) enrollment will continue at the selected target dose based on Part 1 results**
  - **Enrollment is ongoing**

Figure 2. Study Design - Phase 2 Study of Tarlatamab in 3L or Later SCLC (DeLLphi-301 Study)



† Safety follow up occurs 42 (±5) days from the last dose of tarlatamab or prior to initiation of subsequent therapy, whichever occurs first.
‡ Long-term follow up is every 3 months (±2 weeks) up to 1 year from the subject's last dose of tarlatamab or 5 years from first subject enrolled, whichever occurs first.
§ An interim analysis of 30 subjects at each dose (60 subjects total) from Part 1 will be used to select a single dose. The aim of Part 2 is to further evaluate tarlatamab at the selected dose.

STUDY OVERVIEW

DeLLphi-301 (NCT05060016) is a phase 2, open-label, registrational study in subjects with relapsed/refractory SCLC (**Figure 2**)

OBJECTIVES AND ENDPOINTS

PART 1 ONLY

Primary Objective: To evaluate safety and efficacy (per RECIST 1.1 by investigator) of 2 dose levels of tarlatamab

ALL PARTS

Primary Objective: Evaluate anti-tumor activity of tarlatamab as determined by ORR per RECIST 1.1 by BICR

Secondary Objectives: Evaluate anti-tumor activity of tarlatamab as determined by other measures per RECIST 1.1 (DOR, DCR, PFS, OS); safety and tolerability; pharmacokinetics; immunogenicity

KEY ELIGIBILITY CRITERIA

- Adults with histologically or cytologically confirmed SCLC
- Progressed/recurred after two or more lines of prior treatment including at least 1 platinum-based chemotherapy regimen (including a PD-L1 inhibitor, if standard of care, with certain exceptions per protocol)
- ECOG performance status ≤1
- Treated brain metastases permitted provided defined criteria are met

REFERENCES

1. Sabari JK, et al. *Nat Rev Clin Oncol*. 2017;14:549-561.
2. Mathieu L, et al. *Oncologist*. 2021;26:433-438.
3. Leonetti A, et al. *Cell Oncol (Dordr)*. 2019;42:261-273.
4. Saunders LR, et al. *Sci Transl Med*. 2015;7:302ra136.
5. Giffin MJ, et al. *Clin Cancer Res*. 2021;27:1526-1537.
6. Owonikoko TK, et al. Abstract 8510. Presented at: ASCO Annual Meeting, June 4–8, 2021; Virtual.
7. Amgen Inc. (2022, February 8). Amgen outlines growth strategy through 2030 at virtual business review [press release]. Retrieved from www.amgen.com/newsroom/press-releases/2022/02/amgen-outlines-growth-strategy-through-2030-at-virtual-business-review

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