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Abstract #: 359

AMG 757, a half-life extended bispecific T-cell engager (BiTE®) immune therapy against DLL3 in SCLC: phase 1 interim results

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Disclosure information

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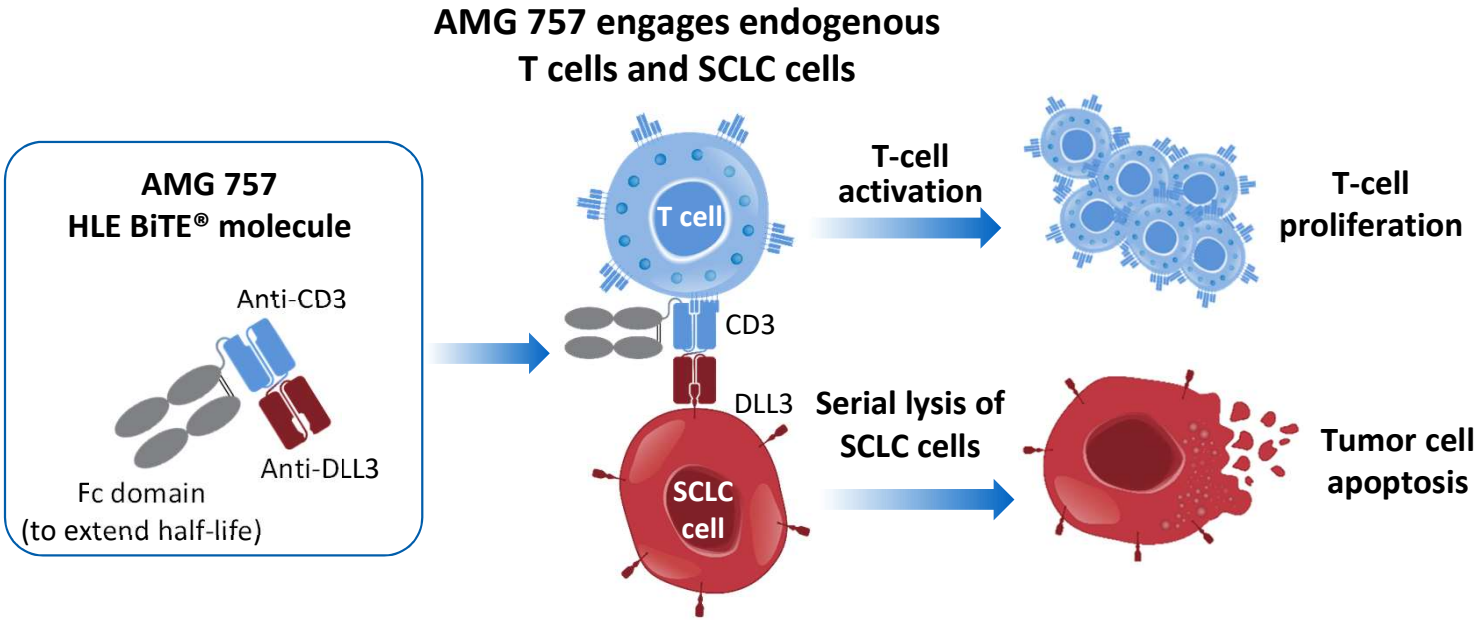
Unmet Medical Need for Small Cell Lung Cancer (SCLC)

- SCLC is an aggressive tumor with poor prognosis and few treatment options[1]
- Immune therapies assessed to date have limited benefit in patients with SCLC[2]
  - Overall survival in clinical trials of immune therapies is around 1 year or less[3]
- Delta-like ligand 3 (DLL3) is an inhibitory Notch ligand and is a promising therapeutic target in SCLC with high tumor and low normal tissue expression[4]
- We report the first safety and efficacy data of a half-life extended clinical bispecific T-cell engager (BiTE®) immune therapy, AMG 757, in patients with relapsed and/or refractory SCLC

1. van Meerbeeck JP, et al. *Lancet*. 2011;378:1741-1755.
2. Taniguchi H, et al. Front Oncol. 2020;10:741.
3. Rossi A. European Medical Journal. 2019;4(2):45-53.
4. Leonetti A, et al. Cell Oncol (Dordr). 2019;42:261-273.

AMG 757: A Half-life Extended Bispecific T-cell Engager (BiTE®) Targeting DLL3 for SCLC

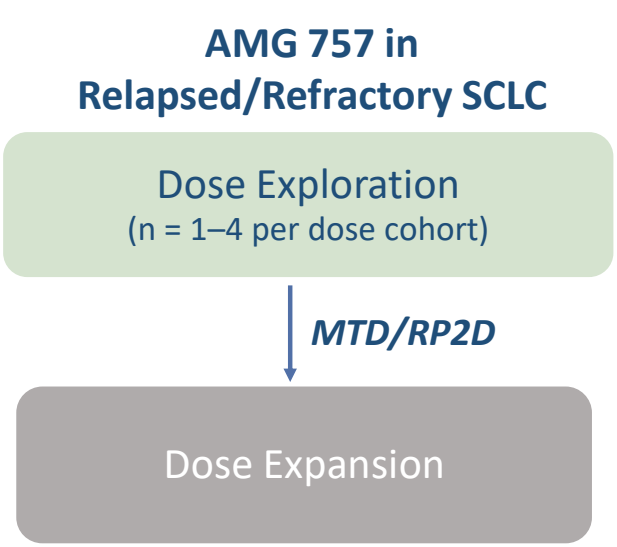


CD, cluster of differentiation; DLL3, delta-like ligand 3; Fc, fragment crystallizable domain; HLE BiTE®, half-life extended bispecific T-cell engager; SCLC, small cell lung cancer.

- BiTE molecules engage a patient's own T cells to attack and eradicate cancer cells[1,2]

1. Stieglmaier J, et al. *Expert Opin Biol Ther*. 2015;15:1093-1099
2. Einsele H, et al. *Cancer*. 2020;126:3192-3201

First-In Human Dose Exploration Study of AMG 757



Primary Objectives
- Evaluate safety and tolerability in SCLC
- Determine MTD or RP2D

Secondary Objectives
- Characterize PK
- Evaluate preliminary antitumor activity

Exploratory Objectives
- Evaluate immunogenicity, biomarkers, and target protein & outcomes

- **Study design** – NCT03319940: open-label, multi-center study of AMG 757 (target dose: 0.003–10.0 mg), administered by IV infusion every 2 weeks, with/without step dose
- **Disease assessment** – Antitumor activity assessed using modified RECIST 1.1

IV, intravenous; MTD, maximum tolerated dose; PK, pharmacokinetics; RP2D, recommended phase 2 dose; RR, relapsed or refractory; SCLC, small-cell lung cancer.

Key Eligibility Criteria & Demographics

Inclusion Criteria

- Histologically/cytologically confirmed SCLC
  - Received ≥ 1 line systemic therapy
  - Progressed/recurred following ≥ 1 platinum-based chemotherapy
- ECOG performance status: 0–2
- ≥ 1 measurable lesion(s)
- Adequate organ function

Exclusion Criteria

- Untreated or symptomatic brain metastases
- Prior anti-cancer therapy within 28 days
- Immunodeficiency or systemic steroid use
- Interstitial lung disease

	All Patients (N = 40)*
Median (range) age, years	64 (44–80)
Current/former smoking n (%)	6 (15) / 27 (68)
ECOG performance status: 0–1, n (%)	39 (98)
Prior lines of therapy	
1–2, n (%)	28 (70)
≥ 3, n (%)	12 (30)
Median (range)	2 (1–6)
Prior PD-1 or PD-L1 treatment, n (%)	17 (43)
Extensive stage disease, n (%)	39 (98)
Brain / liver metastases, n (%)	12 (30) / 18 (45)

*Data cutoff: 7 August 2020.

ECOG, Eastern Cooperative Oncology Group; PD-1, programmed death-1; PD-L1, programmed death-ligand 1.

Treatment Duration and Adverse Events (AEs) Summary

- Median treatment duration of 6.1 (range: 0.1–59.4) weeks
- Treatment-emergent AEs occurred in 39/40 (98%) patients
  - Grade ≥ 3 occurred in 21 (53%) patients
  - Grade 5 (pneumonitis) occurred in 1 (3%) patient
- Treatment-related AEs occurred in 32 (80%) patients, resulting in discontinuation in 1 (3%) patient
  - Grade 5 (pneumonitis)

Treatment-related AEs	Patients (N = 40)	
	All Grades, n (%)	Grade ≥3, n (%)*
Any treatment-related AE	32 (80)	7 (18)
Treatment-related AEs in > 10% of patients		
CRS	**17 (43)**	**0**
Pyrexia	7 (18)	0
Fatigue	6 (15)	0
Nausea	5 (13)	0
Anemia	5 (13)	1 (3)

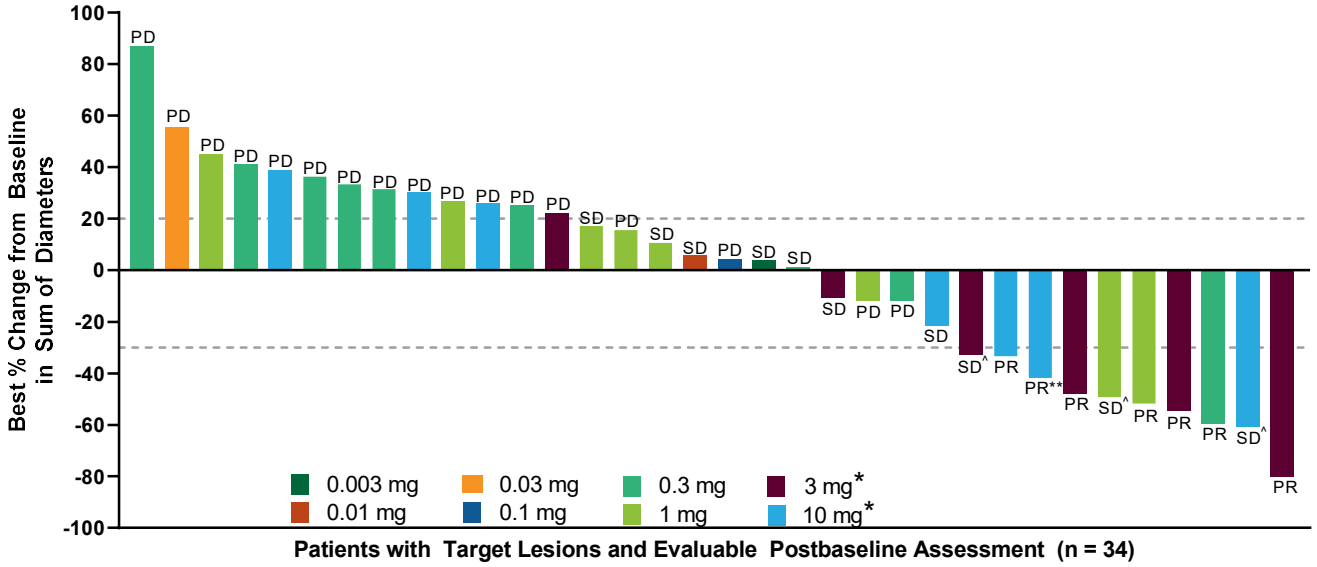
*Includes one patient with grade 5 pneumonitis.

AE, adverse event; CRS, cytokine release syndrome.

Characteristics of Cytokine Release Syndrome (CRS)

- CRS was reversible, manageable, and most commonly associated with fever ± hypotension, tachycardia and nausea (Lee 2014 grading)
  - No grade ≥ 3 CRS events (ie, no O_2 requirement ≥ 40%, no need for high-dose or multiple vasopressors for hypotension, no grade 4 elevated aminotransferases)
  - No CRS events that led to treatment interruptions or discontinuations
  - 5 (13%) patients had grade 2 CRS as worst grade
- CRS typically occurred in cycle 1 and did not recur in subsequent cycles
  - CRS was managed with supportive care and prophylactic corticosteroids
- Additional information regarding CRS is included in our poster (#359) being presented during this conference

AMG 757 Demonstrates Preliminary Anti-Tumor Activity in Patients with SCLC

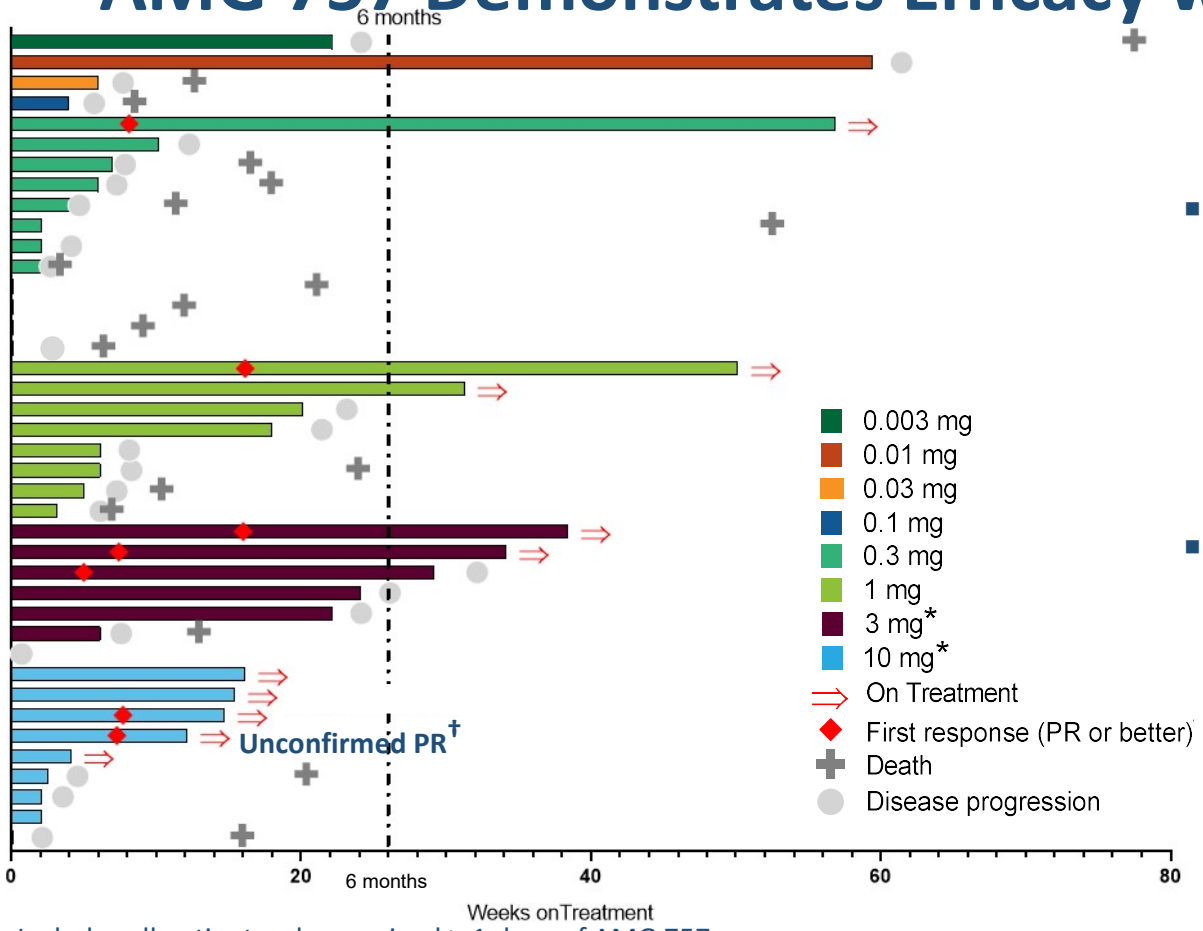


Modified RECIST 1.1 Responses

- **6/38 (16%) patients had confirmed partial response**
  - 1/12 (8%) for 0.3 mg target dose
  - 1/8 (13%) for 1 mg target dose
  - 3/7 (43%) for 3 mg target dose
  - 1/7 (14%) for 10 mg target dose
- **1 (3%) patient had unconfirmed partial response**
- **11 (29%) patients had stable disease**
- **The 4-week disease control rate was 45%**

PR** indicates the PR is unconfirmed.
SD^ indicates patients who had an initial PR, but did not have confirmation of PR on the subsequent scan.
* Step dosing.
PD, progressive disease; PR, partial response; SCLC, small cell lung cancer; SD, stable disease.

AMG 757 Demonstrates Efficacy with Durable Responses



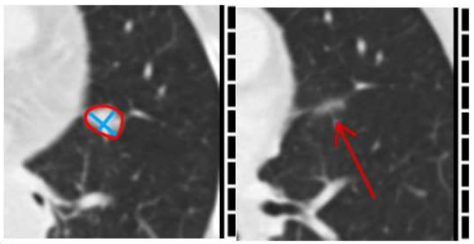
- **7/40 (18%) patients have completed ≥ 6 months (≥ 24 weeks) of treatment**
  - With a median follow-up of 8.8 mo, 5/6 patients who had partial responses are still receiving therapy and have on-going response
- **The median time to response was 1.8 months**

Includes all patients who received ≥ 1 dose of AMG 757.
*Step dosing; †Need additional scan to confirm response status. PR, partial response.

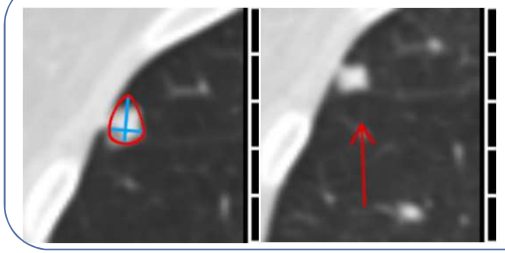
Patient with Partial Response at First Follow-up Scan

Patient	66 year old woman; first dose of AMG 757 on 12 May 2020
Prior Rx	6 lines of prior treatment: cisplatin + etoposide, topotecan, gemcitabine + irinotecan, cyclophosphamide + doxorubicin + vincristine, paclitaxel, lurbinectedin
Dose	10 mg with cycle 1 step dosing; received 3 complete cycles; treatment ongoing at data cutoff
Outcomes	Partial response at time of data cutoff Follow-up time: 2.9 months

Baseline **Day 55**

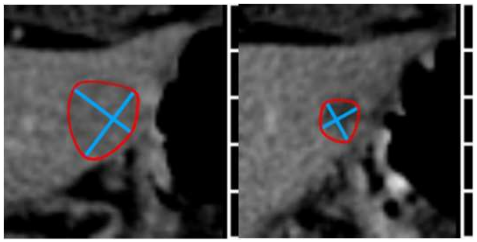


Lung upper lobe left
66.7% decrease vs baseline

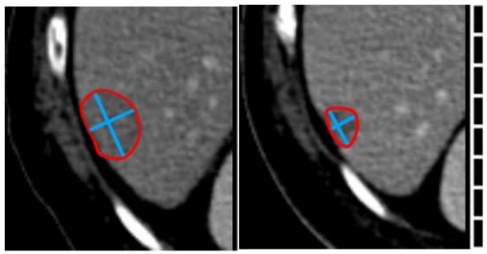


Lung upper lobe right
51.3% decrease vs baseline

Baseline **Day 55**



T04 liver segment II
45.7% decrease vs baseline



T05 liver segment VI
41.8% decrease vs baseline

Conclusions

- AMG 757 is the first half-life extended BiTE immune therapy to show an acceptable safety profile and encouraging clinical activity in patients with relapsed/refractory SCLC
  - Treatment-related CRS events occurred in 43% of patients, all of which were grade 1 or 2 and reversible and manageable
  - Encouraging preliminary efficacy was observed with 16% confirmed PR, 29% SD, and a 4-week disease control rate of 45%
- The maximum tolerated dose for AMG 757 has not been reached; dosing optimization for monotherapy is ongoing
- Additional information included in our poster (#359) being presented during this conference

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Questions?

Backup Slides

Treatment-Emergent Adverse Events (AEs)

Treatment-emergent AEs	All Grades, n (%)	Grade ≥3, n (%)
Any treatment-emergent AE	39 (97.5)	21 (52.5)
TEAEs in > 10% of patients		
CRS	**18 (45.0)**	**0 (0.0)**
Constipation	12 (30.0)	0 (0.0)
Nausea	10 (25.0)	1 (2.5)
Anemia	8 (20.0)	3 (7.5)
Fatigue	8 (20.0)	1 (2.5)
Pyrexia	8 (20.0)	0 (0.0)
Dyspnea	7 (17.5)	2 (5.0)
Back pain	7 (17.5)	0 (0.0)
Headache	7 (17.5)	0 (0.0)
Hypokalemia	5 (12.5)	1 (2.5)
Decreased appetite	5 (12.5)	0 (0.0)
Cough	5 (12.5)	0 (0.0)

AE, adverse events; CRS, cytokine release syndrome.