

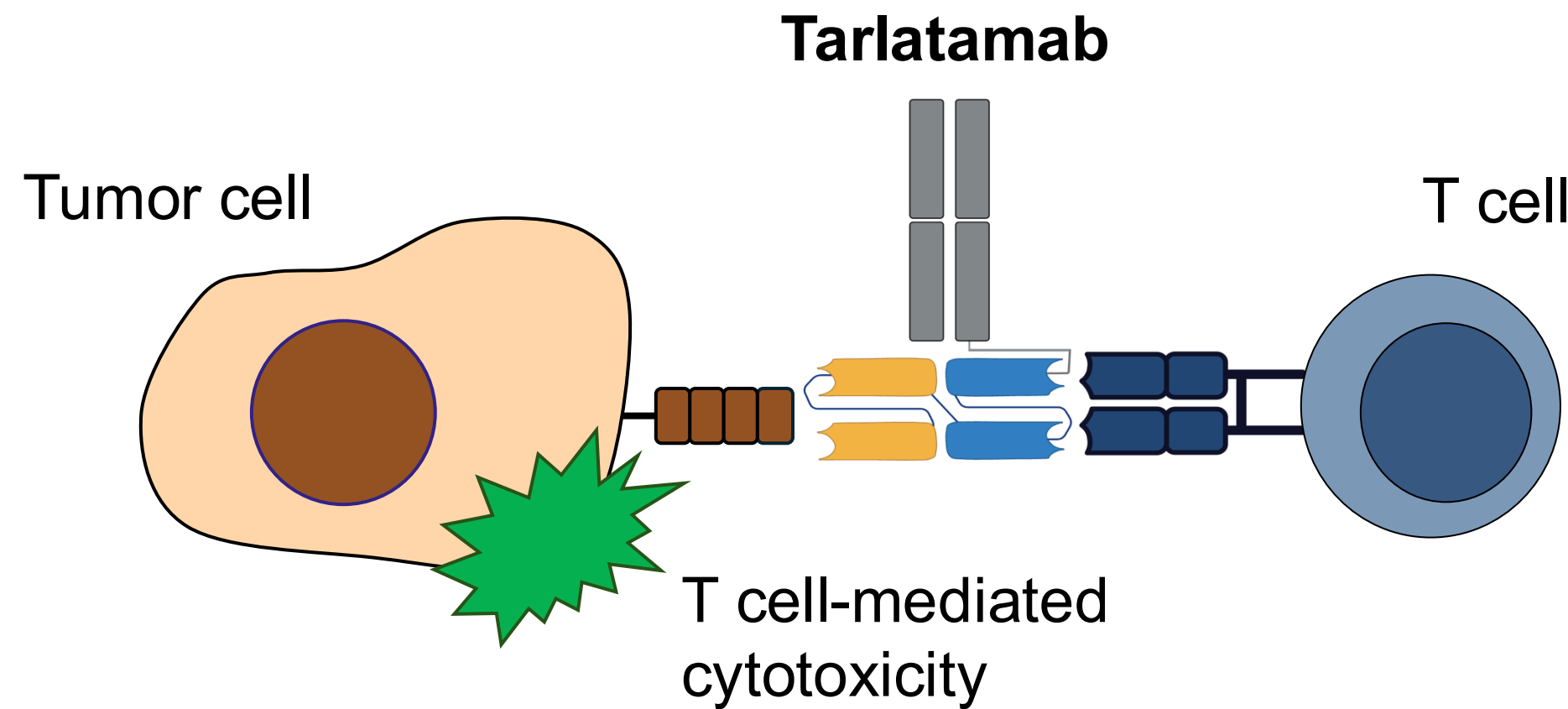
Tarlatamab in Patients with Advanced DLL3-Expressing Tumors: Updated Results From a Single Arm Phase 2 Basket Trial

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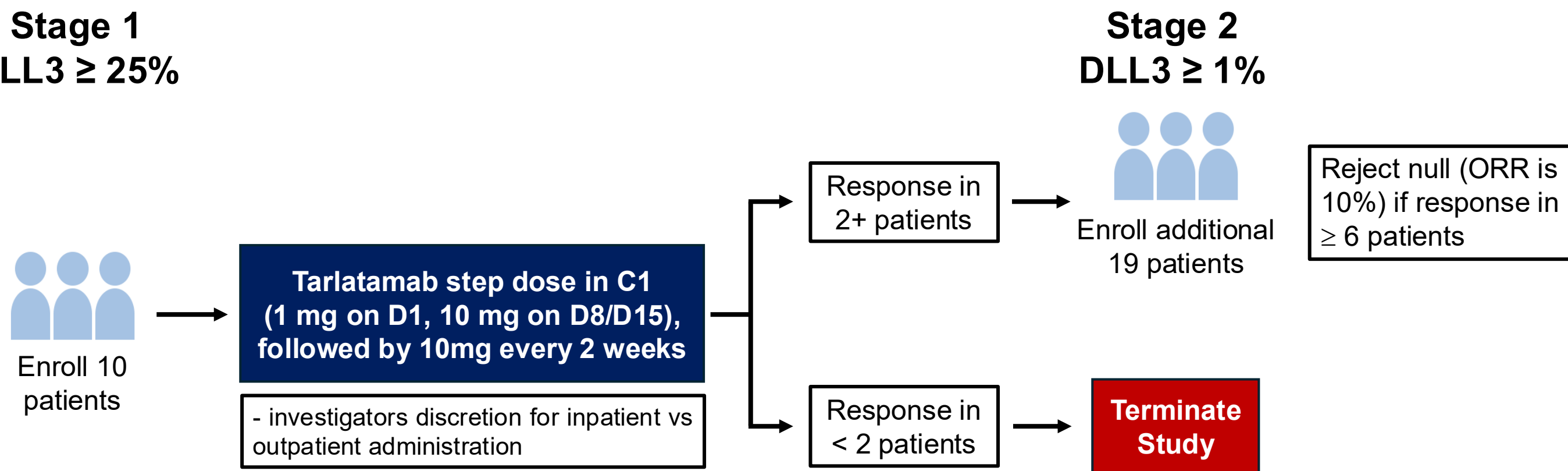
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Background

- DLL3 is an inhibitory Notch pathway ligand aberrantly expressed on tumor cells, especially those of neuroendocrine origin, and represents a targetable biomarker in small cell lung cancer (SCLC) and other neuroendocrine neoplasms (NENs).
 - Tarlatamab-dlle is a bispecific T cell engager (BiTE[®]) therapy designed to direct CD3+ T cells toward DLL3-expressing tumors, promoting cytotoxic T cell-mediated killing.
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- Prior studies of patients with previously-treated SCLC demonstrated a 35-40% objective response rate (DeLLphi-301 and DeLLphi-304), and tarlatamab is now considered standard-of-care option for second-line therapy in SCLC.
 - DLL3 expression is widespread in NENs, but therapeutic role of targeting DLL3 in tumors other than SCLC has not been well-established.

Study Design

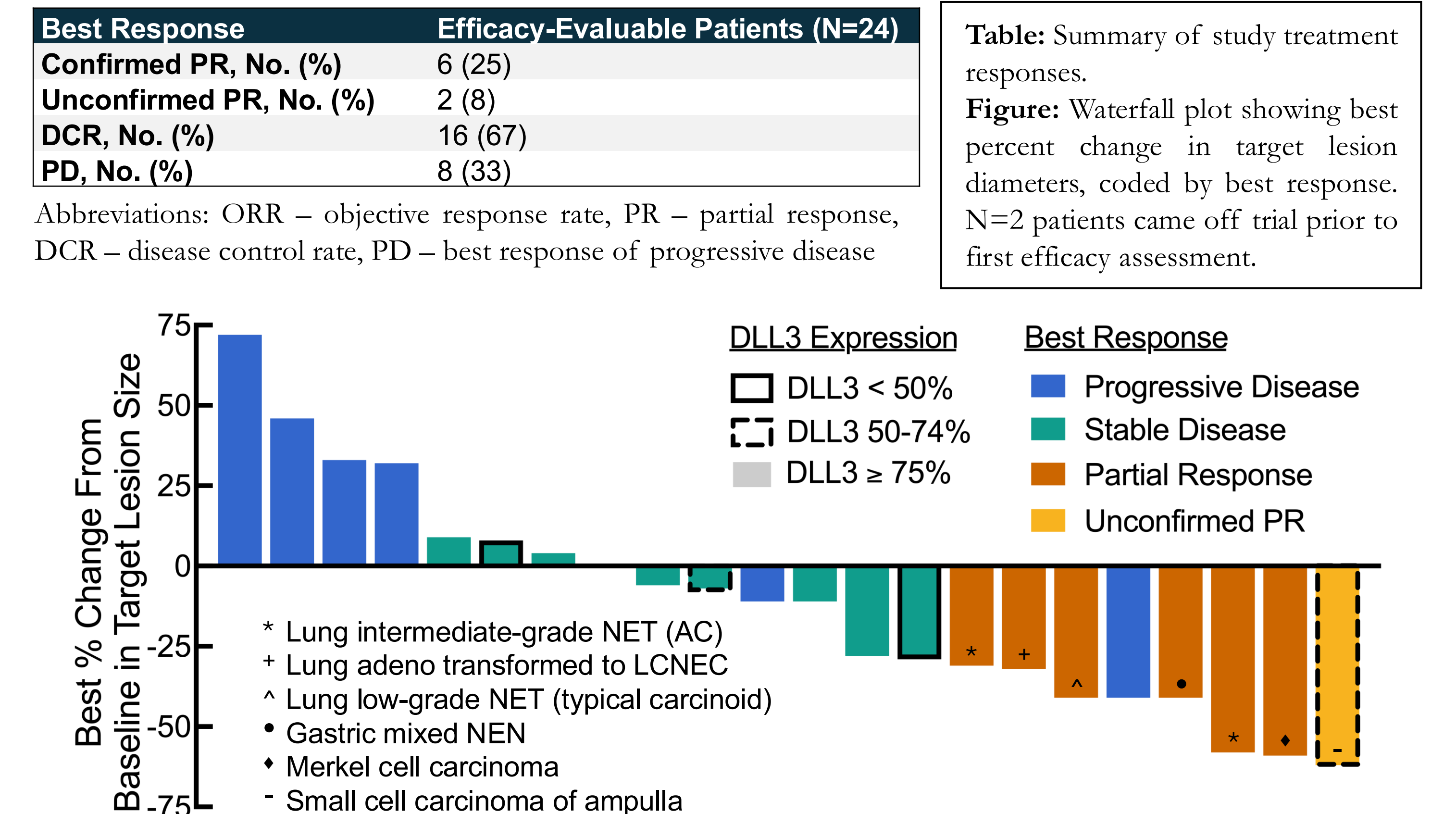
- This is a single-arm, multicenter, phase II basket study conducted through the University of California Cancer Consortium (UCCC).
 - The study utilized a Simon two-stage design as below.
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- Primary endpoints:** objective response rate (ORR)
 - Secondary endpoints:** duration of response (DOR), progression-free survival (PFS), overall survival (OS), safety data including for cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), biomarker analysis
 - Key inclusion criteria:** advanced stage malignancy other than de novo (i.e., non-transformed) SCLC or NEPC, following progression on at least one line of therapy - DLL3 expression by immunohistochemistry on tumor biopsy of at least 25% in Stage 1 and 1% for Stage 2.

Results

Baseline Demographics			
Patient Characteristic	All Patients (N=29)	Patient Characteristic	All Patients (N=29)
Age, years, median (range)	63 (34-90)	Disease type, No. (%)	
Sex, No. (%)		Lung low-grade NET (typical carcinoid)	2 (7)
Female	16 (55)	Lung intermediate-grade NET (AC)	2 (7)
Male	13 (45)	Lung adeno transformed to LCNEC	2 (7)
History of brain metastases, No. (%)		Lung adeno transformed to SCLC	1 (3)
Yes	6 (21)	Lung LCNEC	1 (3)
DLL3 tumor positivity, No. (%)		Intermediate-grade NET of thymus	2 (7)
1-49%	6 (21)	Pancreatic grade 3 NET	3 (10)
50-74%	2 (7)	GI NEC, small cell type	2 (7)
≥ 75%	21 (72)	Other GI NEC	5 (17)
Prior lines of therapy, No. (%)		Gynecologic NEC	3 (10)
1	14 (48)	Merkel cell carcinoma	2 (7)
2	7 (24)	Other well-differentiated NET	1 (3)
≥ 3	8 (28)	NEC of unknown primary	3 (10)

Abbreviations: AC – atypical carcinoid, adeno – adenocarcinoma, LCNEC – large cell neuroendocrine carcinoma, NEC – neuroendocrine carcinoma, NET – neuroendocrine tumor

- ### Efficacy
- Stage 1 completed enrollment and demonstrated an ORR of **20%**, meeting the threshold to advance to Stage 2.
 - Enrollment for Stage 2 has completed with 19 additional patients. A total of 24 patients had efficacy assessments by the 8/31/26 data cutoff and were included in preliminary analyses. Median follow-up time was 6.9 months (range 1.5-15.7).
 - PFS and OS data were not considered to be mature at data cutoff.



- ### CNS Efficacy
- Among 5 evaluable patients with pre-existing brain metastases, 4 patients (80%) achieved CNS disease control.
 - Isolated intracranial progression was observed in 2 patients, and new brain metastases were found in 2 additional patients at time of systemic progression.

Safety Outcomes		
All Evaluable Patients (N=24), No. (%)		
	Any grade	Grade 3+
AEs of any cause		
Any	23 (96)	6 (25)
Serious	5 (21)	3 (13)
Treatment-related AEs		
Any	23 (92)	0
CRS	16 (67)	0
ICANS	3 (13)	1 (4)
AEs observed in ≥ 15% of patients		
Fever	16 (67)	0
Fatigue	11 (46)	0
Dysgeusia	8 (33)	1 (4)
Myalgia	8 (33)	0
Hypotension	7 (29)	0
Constipation	7 (29)	0
Nausea	4 (17)	0
Pruritus	4 (17)	0

Note: N=22 patients were treated in outpatient setting for all infusions, including step-up doses.

- ### Summary
- The study met the prespecified Stage 1 efficacy criterion with an ORR of 20% and proceeded to Stage 2, with enrollment now complete.
 - Preliminary ORR was 25.0% as of the current data cutoff, and ORR including unconfirmed responses was 33.3% with follow up ongoing. Responses were observed across several disease types including pulmonary carcinoids.
 - The safety profile was consistent with prior experience with tarlatamab, with all low-grade CRS and only one grade ≥3 ICANS event observed to date. There were no complications related to outpatient delivery of step-up doses.

References

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Acknowledgements: This research was funded by Amgen and supported by the University of California Cancer Consortium staff.

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