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A Phase 1 Dose Escalation and Expansion Study of CUE-101 as Monotherapy and in Combination with pembrolizumab in Patients with Recurrent/Metastatic HPV16+ Head and Neck Squamous Cell Cancer

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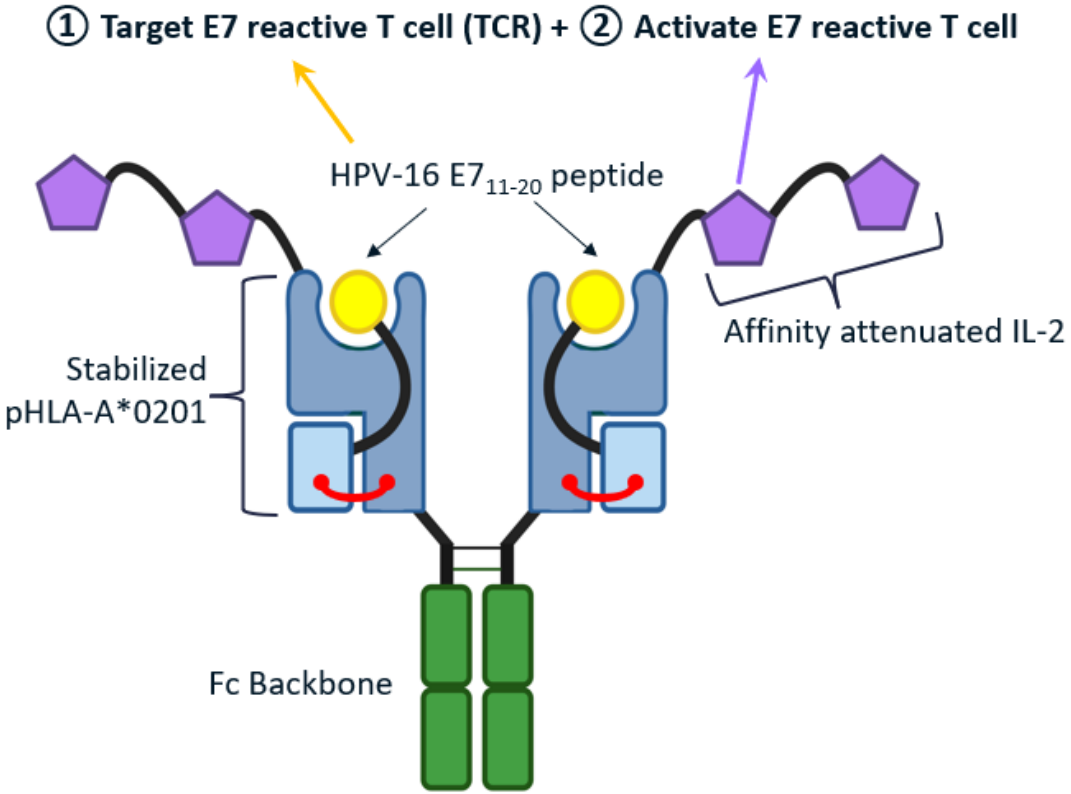
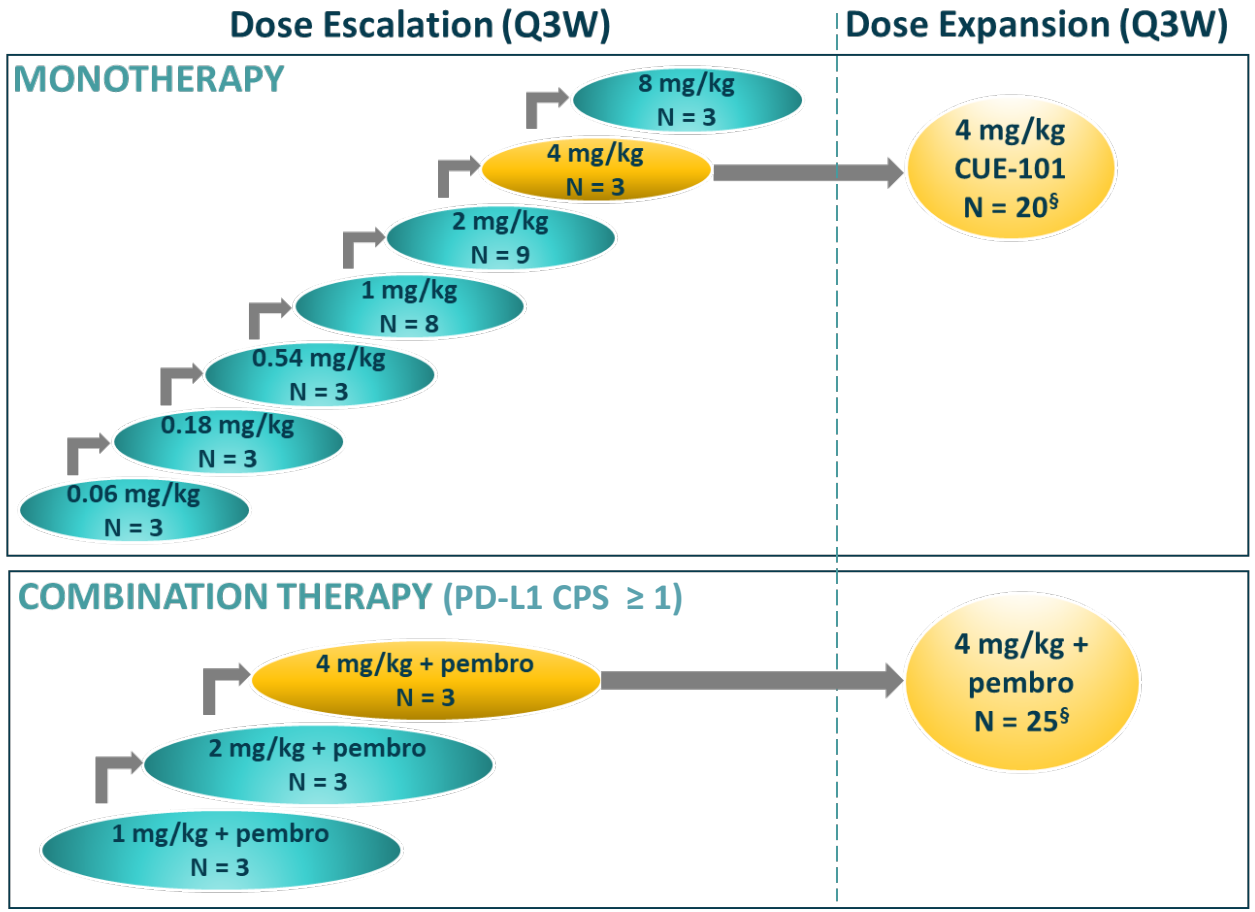
CUE-101 is a selective engager of HPV-16-specific T cells



- CUE-101 is a modular T cell engager comprised of:
  - An HLA-A*0201 complex
  - An immunodominant peptide epitope derived from the HPV16 E7 protein
  - 4 molecules of reduced affinity Interleukin-2 (IL-2)
- CUE-101 selectively expands and activates HPV16-specific CD8+ T cells
- Selective targeting of attenuated IL-2 to tumor-specific T cells avoids non-specific T cell activation and toxicities associated with untargeted IL-2

Study Design: CUE-101 ± 200 mg/kg pembrolizumab in HPV16+ R/M HNSCC



§ Includes all patients treated at 4 mg/kg from Dose Escalation and Dose Expansion.

Key Eligibility Criteria

- HLA-A*02:01 genotype with HPV16+ recurrent/metastatic HNSCC
- Monotherapy patients require prior platinum-based therapy and/or checkpoint inhibitor
- Combination therapy patients are treatment-naïve for R/M HNSCC

Objectives

- Primary: Safety, tolerability and PK
- Secondary: Objective response, disease control, survival, immune response, immunogenicity

Biomarkers

- Immunophenotyping and monitoring of immune cell subsets
- Serum biomarkers, cytokines, cfDNA, and TCR sequencing

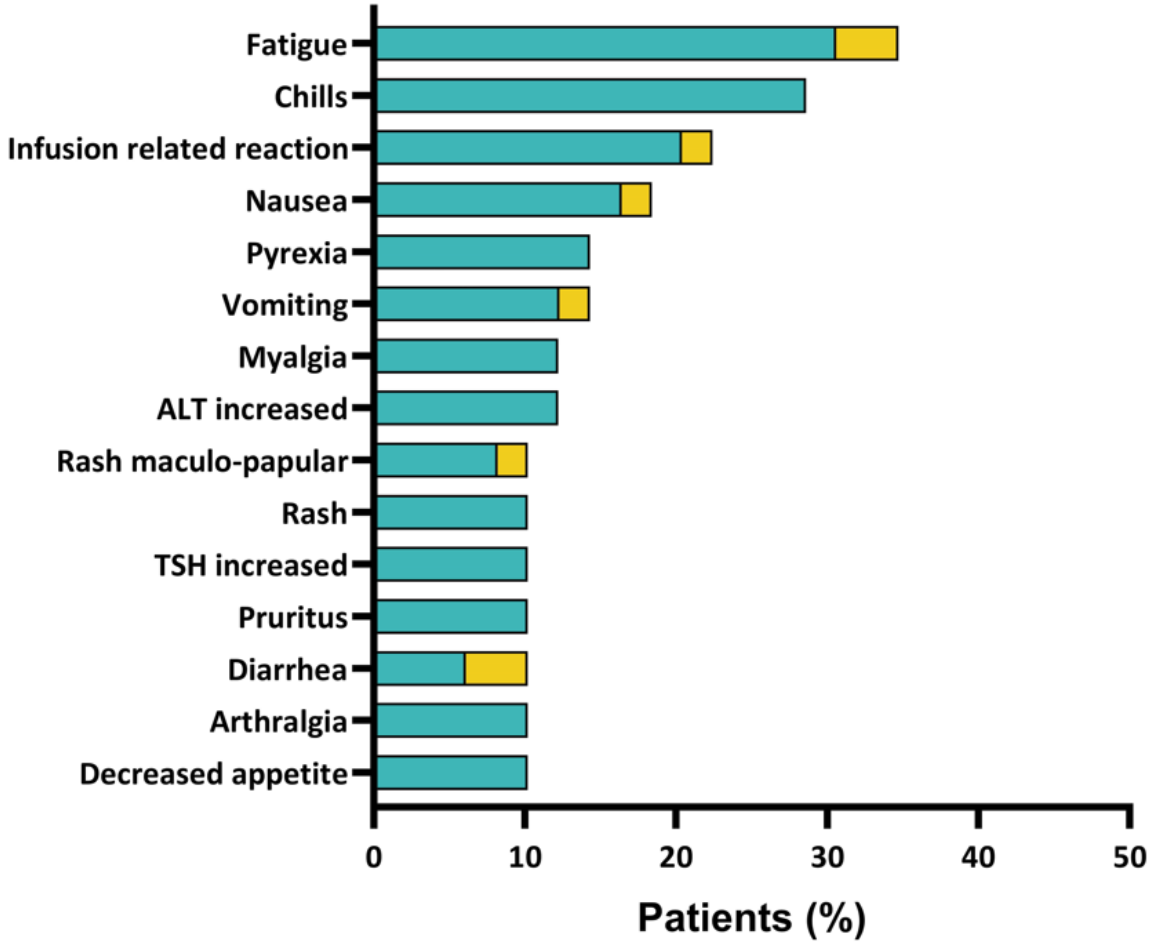
- **Enrollment is complete**
- **N=49 Monotherapy; N=31 Combination Therapy**

Patient Demographics

Treatment Arm		Monotherapy (N=49) N (%)	Combination (N=31) N (%)
Age (years)	Mean (range)	64 (48-82)	65 (43-79)
Sex	Male	47 (96%)	30 (97%)
	Female	2 (4%)	1 (3%)
PD-L1 CPS	1-19	-	18 (58%)
	≥ 20	-	13 (42%)
Lines of Therapy for R/M HNSCC[§]	Median (range)	3 (1-10)	-
	▪ Checkpoint inhibitor	49 (100%)	-
	▪ Platinum-based	45 (92%)	-

[§] Patients with > 1 prior line of therapy are counted once per category and may be included in > 1 category.
PD-L1 22C3 IHC assay used to evaluate PD-L1 expression.

CUE-101 Monotherapy is Safe and Tolerable



CUE-101 Monotherapy N = 49
(All doses)

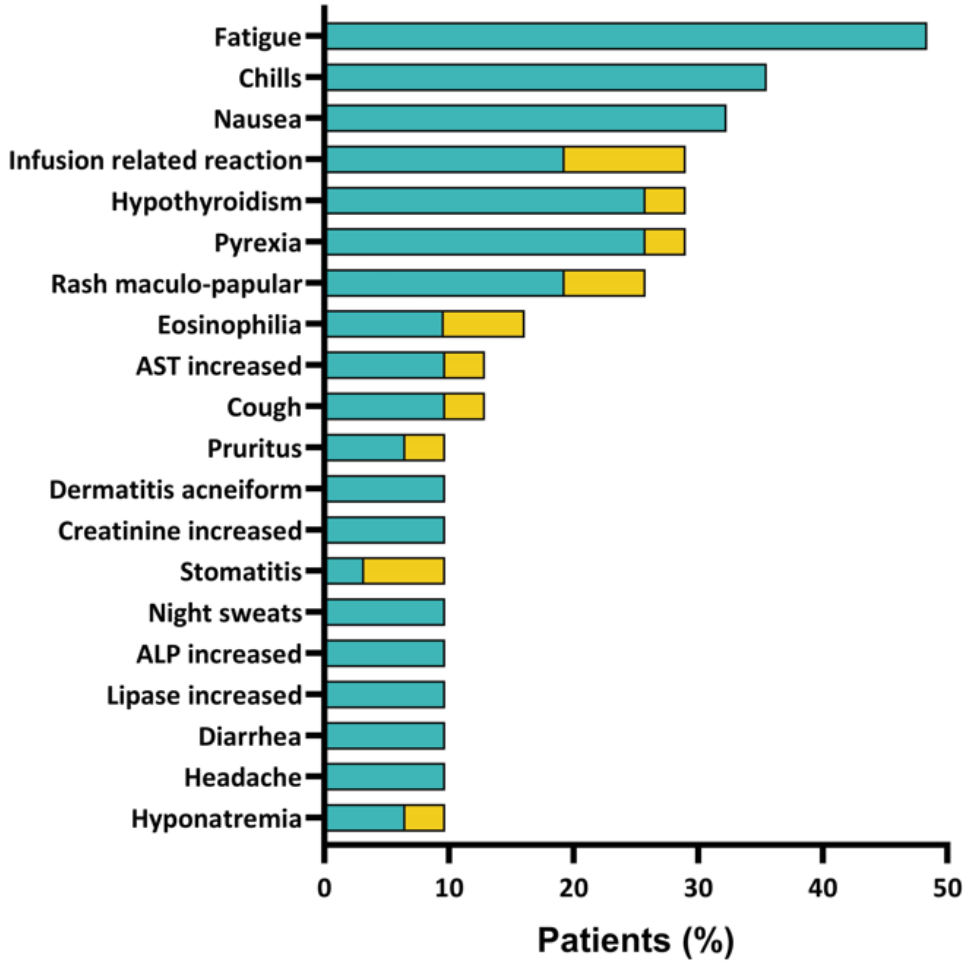
- > 90% AEs are CTCAE Grade 1-2
- No capillary leak syndrome
- No cytokine release syndrome > Grade 1
- AEs managed with standard of care treatment

Grade 1-2 Grade ≥ 3

Presents treatment related adverse events occurring in ≥ 10% patients treated with CUE-101. AEs are coded using MedDRA V21.0 and CTCAE v5.0.
At each level of summation patients reporting > 1 occurrence of the same AE are counted once at the highest toxicity.

Data analysis: 11-Sep-2024.

CUE-101 in Combination with Pembrolizumab is Safe and Tolerable



CUE-101 + Pembrolizumab N = 31
(All doses)

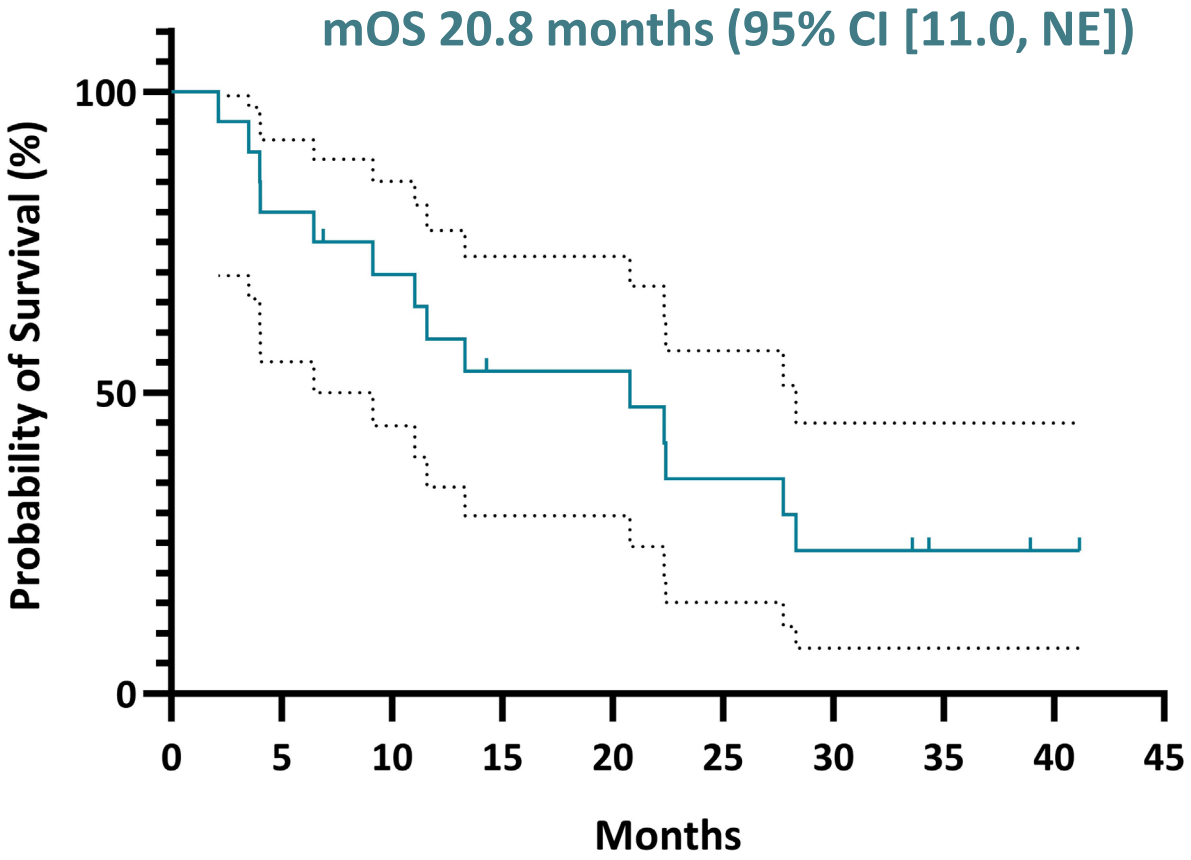
- > 90% AEs are CTCAE Grade 1-2
- No capillary leak syndrome
- No cytokine release syndrome
- AEs managed with standard of care treatment

Grade 1-2 Grade ≥ 3

Presents treatment related adverse events occurring in ≥ 10% patients treated with CUE-101 + pembrolizumab. AEs are coded using MedDRA V21.0 and CTCAE v5.0. At each level of summation patients reporting > 1 occurrence of the same AE are counted once at the highest toxicity.

Data analysis: 11-Sep-2024.

Overall Survival Following CUE-101 4 mg/kg Monotherapy



Objective Response Rate

- 5% (95% CI [0.1, 26.0])
- 1 PR

Duration of Response

- 9.7 months

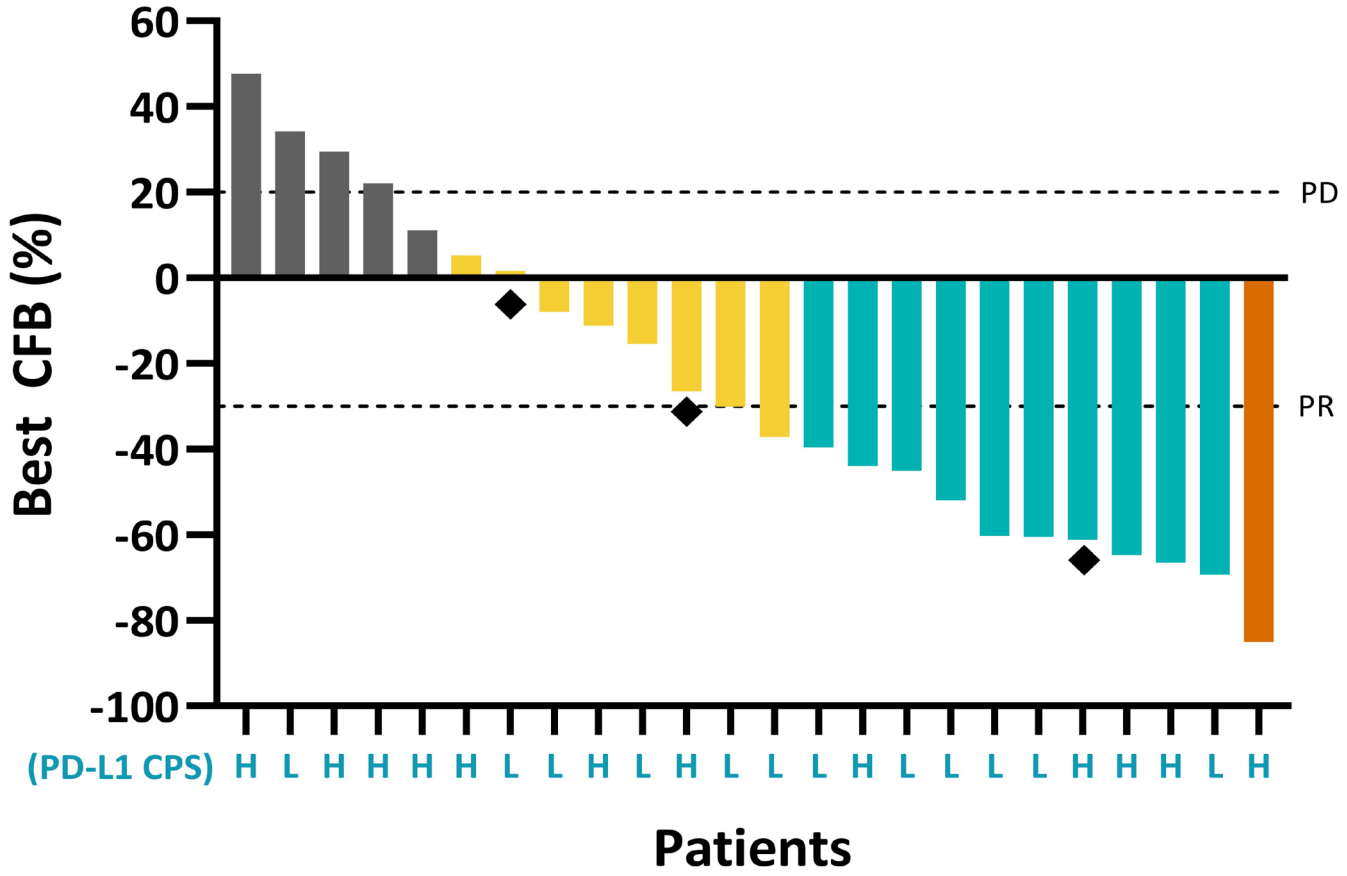
Disease Control Rate

- 37% (95% CI [16.3-61.6])
- 1 PR / 6 DSD

Includes 20/20 patients in the Safety Population and 19/20 patients in the Response Evaluable Population.
mOS = median Overall survival; DSD = Durable Stable Disease; NE = Not Estimated; PR = Partial Response
Durable Stable Disease = Requires, at a minimum, stable disease per RECIST 1.1 at the 1st and 2nd post-dose scans (through Week 12).
Disease Control Rate = Patients with CR + PR + DSD.

Data extract: 11-Sep-2024.

Favorable Response Rate Following CUE-101 + Pembrolizumab Combination Therapy



Objective Response Rate (all patients):

- 46% (95% CI [25.6-67.2])
- 1 CR / 10 PR

Disease Control Rate (all patients):

- 75% (95% CI [53.3-90.2])
- 1 CR / 10 PR / 7 DSD

PD-L1 CPS 1-19 Subpopulation:

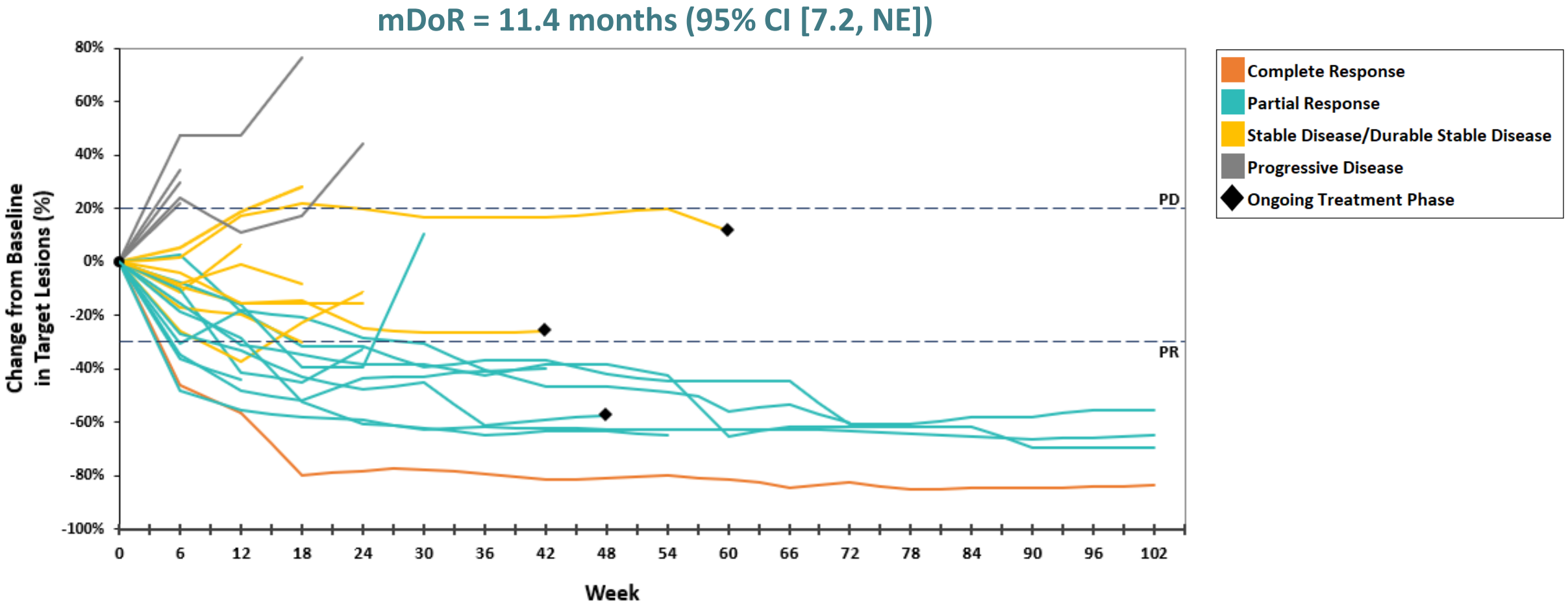
- ORR = 50% (95% CI [21.1-78.9]) 6 PR
- DCR = 92% (95% CI [61.5-99.8]) 6 PR / 5 DSD

Complete Response
Partial Response
Stable Disease/Durable Stable Disease
Progressive Disease
Ongoing Treatment Phase
L PD-L1 CPS 1-19
H PD-L1 CPS ≥ 20

Includes 24/25 patients in the Response Evaluable Population (all).
Durable Stable Disease = Requires, at a minimum, stable disease per RECIST 1.1 at the 1st and 2nd post-dose scans (through Week 12).
Disease Control Rate = Patients with CR + PR + DSD.

Data extract: 11-Sep-2024.

Durable Tumor Responses Observed Following CUE-101 + Pembrolizumab Combination Therapy

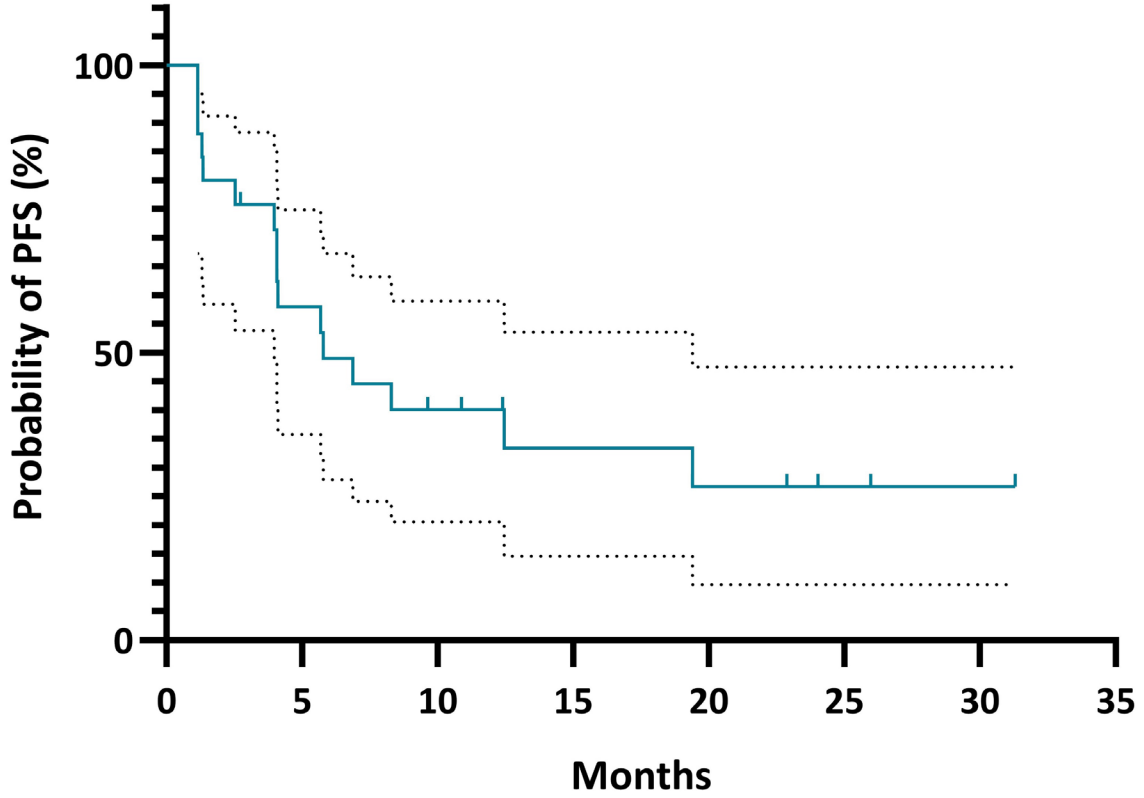


Includes 24/25 patients in the Response Evaluable Population. Change from baseline in sum of diameters of target lesions.
mDoR = median Duration of Response; NE = Not Estimated

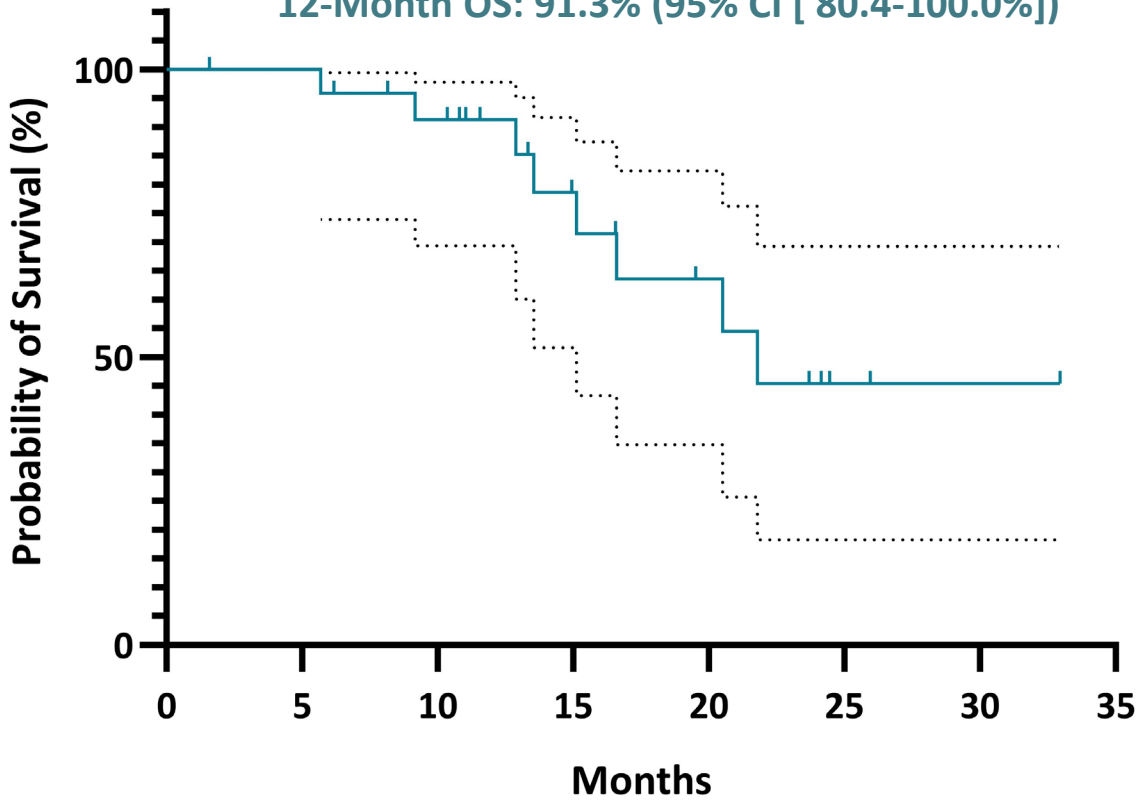
Data extract: 11-Sep-2024.

PFS and OS Data Continue to Mature for Patients Treated with CUE-101 + Pembrolizumab Combination Therapy

Progression-Free Survival
mPFS 5.8 months (95% CI [4.1-NE])



Overall Survival
mOS 21.8 months (95% CI [16.6-NE])
12-Month OS: 91.3% (95% CI [80.4-100.0%])

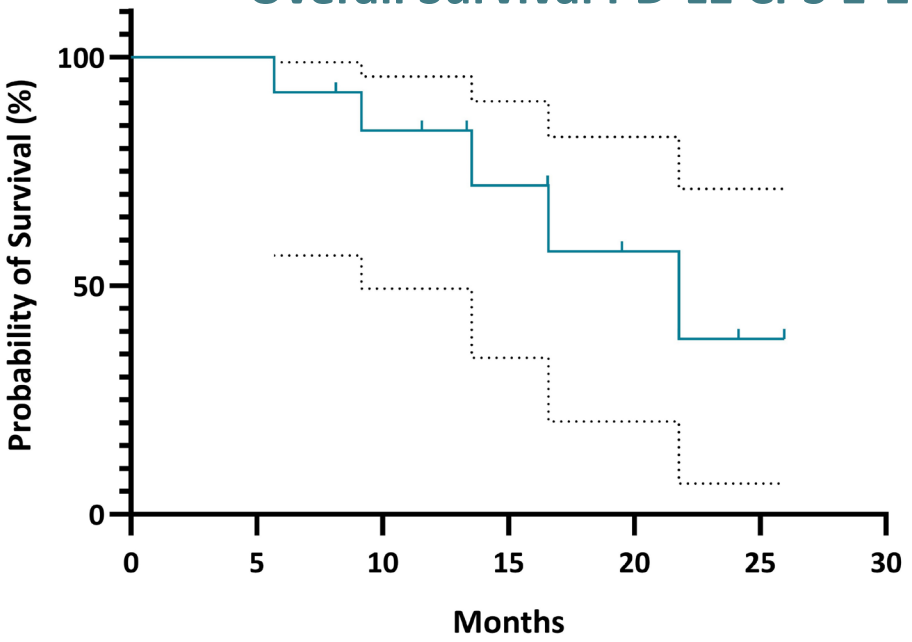


Includes 25/25 patients in the Safety Population.
NE = Not Estimated.

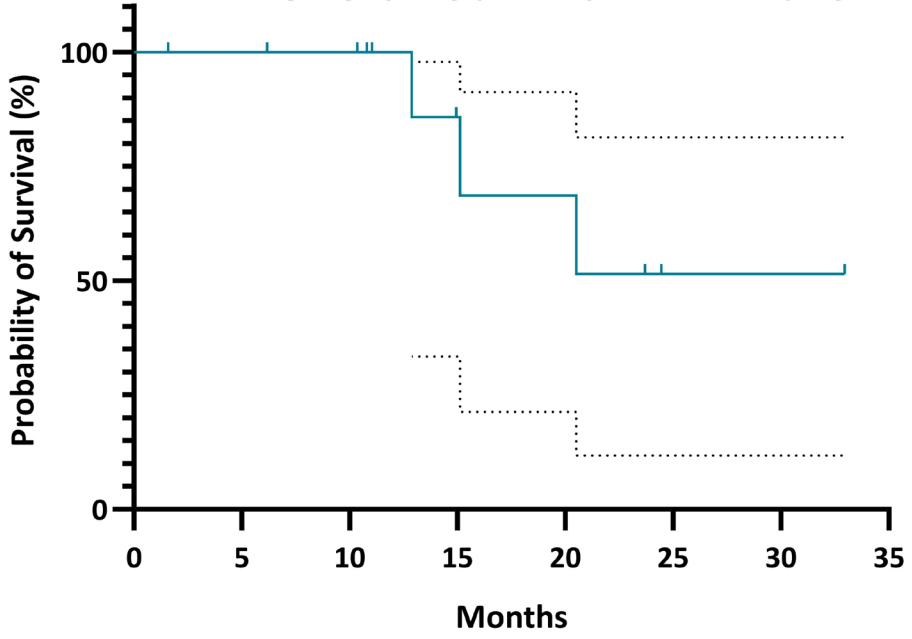
Data extract: 11-Sep-2024.

Survival in Combination Patients by Tumor PD-L1 Expression

Overall Survival PD-L1 CPS 1-19



Overall Survival PD-L1 CPS ≥ 20



	PD-L1 CPS 1-19 (N=13)	PD-L1 CPS ≥ 20 (N=12)
Median OS (months) [95% CI]	21.8 [13.5-NE]	NE [15.1-NE]
12-Month OS rate [95% CI]	83.9% [65.7-100.0%]	100.0% [100.0-100.0%]

NE = Not Estimated.

Data extract: 11-Sep-2024.

Key Results

- CUE-101 given as monotherapy or with pembrolizumab is safe and generally well tolerated
- Patients with HPV16+ R/M HNSCC refractory to platinum-based treatments and checkpoint inhibitors (2L+) receiving CUE-101 4 mg/kg monotherapy exhibit:
  - ORR of 5%
  - mOS of 20.8 months
- Patients with treatment-naïve (1L) HPV16+ R/M HNSCC receiving CUE-101 4 mg/kg + pembrolizumab combination therapy exhibit:
  - ORR of 46% with mDoR of 11.4 months
  - ORR of 50% in patients with low PD-L1 (CPS 1-19)
  - 12-month OS of 91.3% and overall mOS of 21.8 months

Acknowledgments

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