#674 A phase 1 dose-escalation and expansion study of CUE-101, given as monotherapy and in combination with pembrolizumab in recurrent/metastatic HPV16+ head and neck cancer patients

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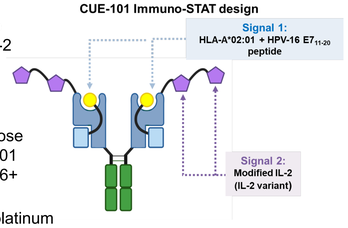
Background and Study Design

- CUE-101 is a modular T cell engager, comprised of an HLA-A*0201 complex, a peptide epitope derived from the HPV16 E7 protein, and 4 molecules of reduced affinity IL-2 that is designed to deliver attenuated interleukin-2 (IL-2) selectively to HPV16-specific CD8+ T cells for treatment of HPV16+ cancers.
- CUE-101-01 (NCT03978689) is a Phase 1, open label, dose escalation and expansion study of CUE-101 in HLA-A*0201 positive patients with HPV16+ recurrent/metastatic HPV16+ head and neck cancer (R/M HNSCC).
  - Patients with R/M HNSCC that progressed following platinum or checkpoint inhibitor-based therapies are eligible for CUE-101 monotherapy given every 3 weeks.
  - Newly diagnosed R/M HNSCC patients are eligible for treatment with CUE-101 plus pembrolizumab 200 mg every 3 three weeks.
  - Trial eligibility includes HLA-A*0201 genotype and HPV16+ HNSCC, determined by P16 IHC and HPV16 mRNA in-situ hybridization. Pembrolizumab combination patients are also required to have a CPS ≥ 1.
- Enrollment in both the monotherapy and combination therapy arms of the study is now complete. Here we report the updated results of the CUE-101 recommended phase 2 dose (RP2D) of 4 mg/kg in both monotherapy and in combination with pembrolizumab, 200 mg Q3W.

CUE-101 Immuno-STAT design

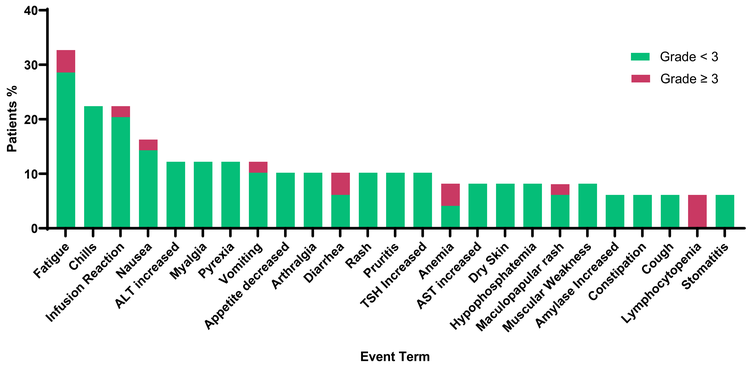


Patient Demographics & Prior Therapies

		Monotherapy	Combination with Pembro
Patients		N = 49	N = 27
Age (years)	Mean (range)	63.7 (48-82)	64.2 (43-77)
Sex	Male	47 (95.9%)	26 (96.3%)
	Female	2 (4.1%)	1 (3.7%)
Race	White	45 (91.8%)	25 (92.6%)
	Black / African American	1 (2.0%)	0 (0.0%)
	Other / Not Reported	3 (6.1%)	2 (7.4%)
ECOG	0	23 (46.9%)	15 (55.6%)
	1	26 (53.1%)	12 (44.4%)
CPS SCORE	≥ 1 to < 20	---	16 (59.3%)
	≥ 20	---	11 (40.7%)
Prior Lines of Therapy*	No prior lines of therapy	0 (0.0%)	6 (24.0%)
	Median (range)	3 (1-10)	1 (0-2)
	- Platinum Based	45 (91.8%)	17 (68.0%)
	- Checkpoint Inhibitor	49 (100.0%)	3 (12.0%)
	- PD-1	46 (93.9%)	2 (8.0%)
	- PD-L1	6 (12.2%)	1 (4.0%)
	- CTLA-4	1 (2.0%)	0 (0.0%)
	- EGFR Inhibitor	35 (71.4%)	2 (8.0%)
	- Other	43 (87.8%)	4 (16.0%)

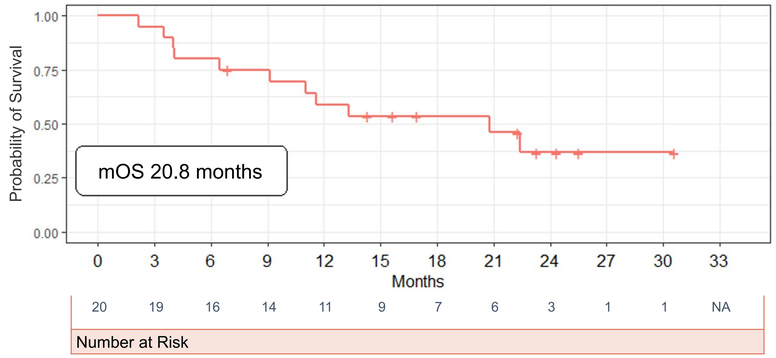
*Patients with > 1 prior line of therapy are counted once/category and may be counted in > 1 category. Combination patients with initial presentation of metastatic disease have no prior therapy. Data extracted from EDC 01-Oct-2023 (N = 28 combo patients: 27 & 25, respectively have EDC data for Demographics & Prior Therapy).

Treatment Related Adverse Events in Monotherapy Patients



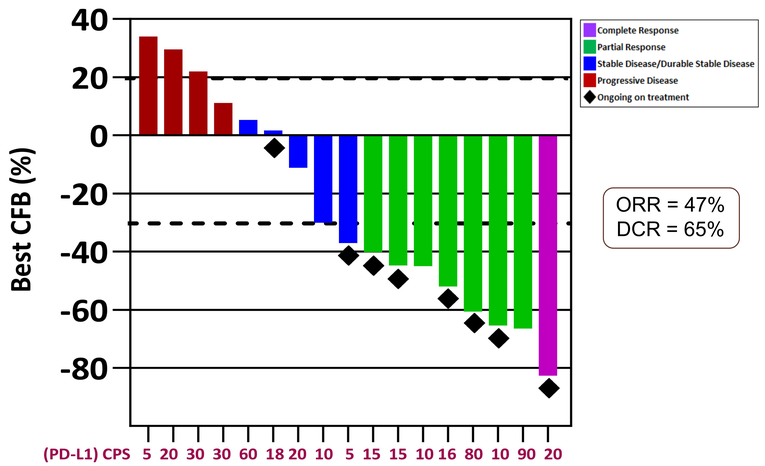
Treatment Related Adverse Events (TRAEs) occurring at ≥ 5% frequency in all monotherapy patients treated with ≥1 dose of CUE-101 as of 07-Sep-2023 (N=49). AEs coded using MedDRA V21.0 and NCI-CTCAE v5.0. Causality determination made by investigator or medical monitor. At each level of summation patients reporting >1 occurrence of the same AE are counted once at highest toxicity.

Prolonged Survival in 2L+ Patients Treated with CUE-101



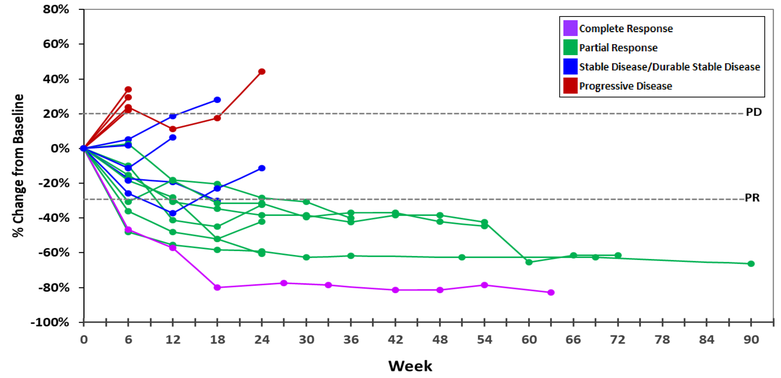
Overall survival (months) in the 20 patients treated with CUE-101 monotherapy (4 mg/kg), from time of first dose of drug as of 07-Sep-2023. Kaplan-Meier estimate of median OS 20.8 months [95% CI; 11.0, NA]. Landmark 12-month OS is 0.5893 (0.4060, 0.8554) with 11 patients reaching the 12-month landmark.

Best Overall Response in 1L Patients Treated with Combination



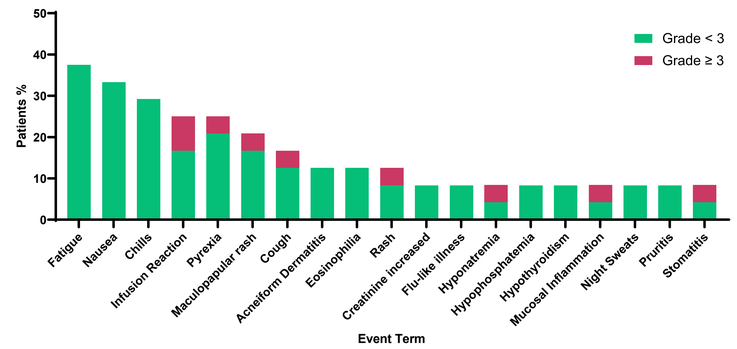
Waterfall plot illustrates best change from baseline in the sum of diameters of target lesions with best overall response as measured by RECIST 1.1. Seventeen patients treated with 4 mg/kg CUE-101 and pembrolizumab with ≥ 1 post-dose scan as of 27-Sep-2023 are included. All responses are confirmed. Overall Response Rate (ORR) 47%, Disease Control Rate (DCR) 65%.

Temporal Changes in Tumor Burden in 1L Patients Treated with Combination



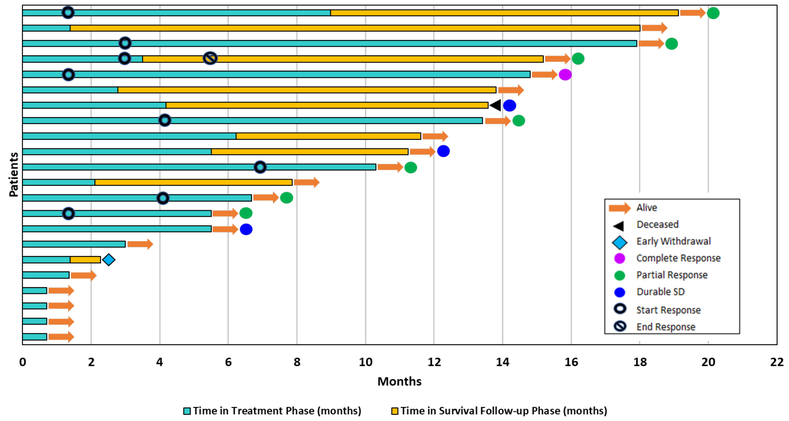
Spider plot shows change from baseline over time in the sum of diameters of target lesions as measured by RECIST 1.1. Seventeen patients treated with 4 mg/kg CUE-101 and pembrolizumab with ≥ 1 post-dose scan as of 27-Sep-2023 are included. Scans are obtained at baseline and Q6 weeks thereafter.

Treatment Related Adverse Events in Combination Patients



TRAEs occurring at ≥ 5% frequency in all patients treated with ≥1 dose of CUE-101 + pembrolizumab (N=20) as of 07-Sep-2023. AEs coded using MedDRA V21.0 and NCI-CTCAE v5.0. Attribution determined by investigator or medical monitor. At each level of summation patients reporting >1 occurrence of the same AE are counted once at highest toxicity.

Survival in 1L Patients Treated with Combination



Overall survival (months from 1st dose) in patients treated with 4 mg/kg CUE-101 and pembrolizumab (N=22) at 27-Sep-2023. Durable stable disease (SD) requires RECIST 1.1 SD on ≥ 2 consecutive scans. Response duration is indicated on the plot. Kaplan-Meier estimate of median PFS 5.8 months [95% CI; 2.6, NA].

Summary

- Enrollment in the monotherapy and combination arms of protocol CUE-101-01 is complete.
- Median overall survival of 20.8 months observed in 2L+ patients treated with CUE-101 monotherapy (Kaplan-Meier estimate, [95% CI; 11.0, NA]). Landmark 12-month OS is 59%.
- Objective response rate of 47% (1 CR, 7 PR) observed in newly diagnosed R/M patients treated with CUE-101 in combination with pembrolizumab. Complete Response and 5 out of 7 Partial Responses occurring in tumors with CPS of 20 or less and a DCR of 65%.
- Twenty of the 22 patients who have received the combination of CUE-101 and pembrolizumab remain alive at time of data cut-off, including 8 patients for ≥ 12 months. Thirteen remain on treatment.
- Adverse events are consistent with the CUE-101 mechanism of action, known profile of pembrolizumab and underlying disease. The risk of ≥Grade 3 TRAEs was low, most TRAEs were ≤Grade 2, reversible, and easily managed with appropriate medical care.

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