2024 ASCO® ANNUAL MEETING

A Phase 1 Dose-escalation and Expansion Study of CUE-101, Given as Monotherapy and in Combination with Pembrolizumab, in Patients with HPV16+ Recurrent/ Metastatic Head and Neck Squamous Cell Cancer (R/M HNSCC)

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Disclosures

- **Employer:** Washington University in St Louis.
- **Consultant or Scientific Advisory Board:** Adlai Nortye USA, Boehringer Ingelheim, Cue Biopharma, Calliditas, Eisai, EMD Serono, GenMab, GSK, Immunitas, Inhibrx, Jazz Pharmaceuticals, Kura Oncology, Merck, Merck KGaA, Merus, Natco Pharma, Purple Biotech, Regeneron, Seagen, and TargImmune Therapeutics.
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- **I do not have any vested interest, but I do intend to discuss off-label and/or investigational use of pharmaceuticals or devices.**

Key Results

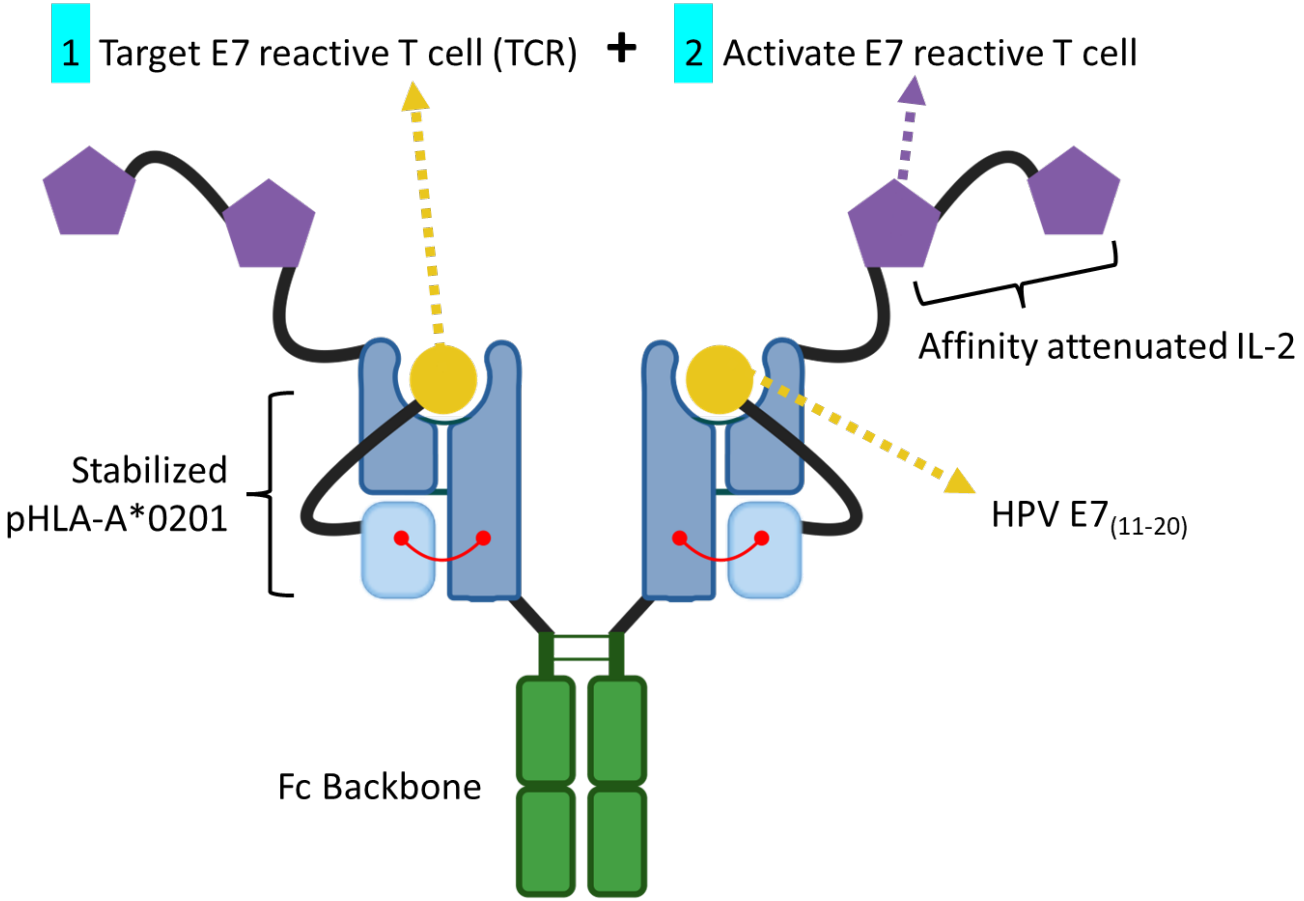
- CUE-101 given as monotherapy or with pembrolizumab was safe and tolerable.

- Second-Line treatment with CUE-101 monotherapy resulted in an ORR of 5%; however, the median OS was 20.8 months.

- First-Line treatment with CUE-101 + pembrolizumab resulted in an ORR of 46%. The 12-month OS was 95.5%.

CUE-101: Mechanism of Action

"Selective Engager of Tumor-specific T Cells"



Components:

- 2 HPV-16 E7 epitopes that are presented to the T cell by HLA-A02:01
- 4 Affinity-attenuated IL-2 molecules

Properties:

- Selective activation and expansion of HPV16-specific T cells
- Limited non-selective T cell effects to decrease IL-2-related toxicity

Objectives/Endpoints

- **Dose Escalation**
  - Determine RP2D of CUE-101.
  - Determine RP2D of CUE-101 plus pembrolizumab.
  - Endpoints: Adverse events, DLTs (cycle 1), & markers of biologic activity.

- **Dose Expansion**
  - Determine ORR with CUE-101 given as 2L treatment of CPI- and/or platinum-pretreated disease.
  - Determine ORR with CUE-101 + pembrolizumab given as 1L treatment of R/M disease.
  - Endpoint: tumor response, RECIST1.1 (investigator-assessed).

Hypotheses/Statistics

- **Hypotheses**
  - CUE-101 monotherapy or with pembrolizumab would be tolerable.
  - The ORR with 2L CUE-101 would be at least 20%.
  - The ORR with 1L CUE-101 + pembrolizumab would be at least 35%.
- **Statistical Analysis Plan**
  - RP2D was determined using a Bayesian Logistic Regression Model, and a composite analysis of the maximum tolerated dose, overall safety, and markers of biologic activity.
  - The sample sizes for the dose expansion cohorts were calculated using the 95% confidence interval around the hypothetical ORR based on the Clopper-Pearson method.

Study Design

Dose Escalation

CUE-101
- 7 dose cohorts (n=3-9 pts)
- Dose levels: 0.06-8.0 mg/kg Q3W

CUE-101 + Pembrolizumab
- 3 dose cohorts (n=3 pts)
- Dose levels: 1.0-4.0 mg/kg Q3W
- Pembrolizumab 200 mg Q3W

Dose Expansion

CUE-101
- CUE-101 (RP2D)
- ~20 patients

CUE-101 + Pembrolizumab
- CUE-101 (RP2D) + Pembrolizumab Q3W
- Maximum 35 cycles
- ~20 patients

Eligibility

- **All patients**
  - R/M HNSCC
  - Tumor HPV16+ by mRNA ISH and p16+ by IHC (centrally confirmed)
  - HLA-A*0201 genotype (centrally confirmed)
  - ECOG Performance Status 0 or 1
  - Adequate organ function

- **CUE-101**
  - Prior CPI and/or platinum agent

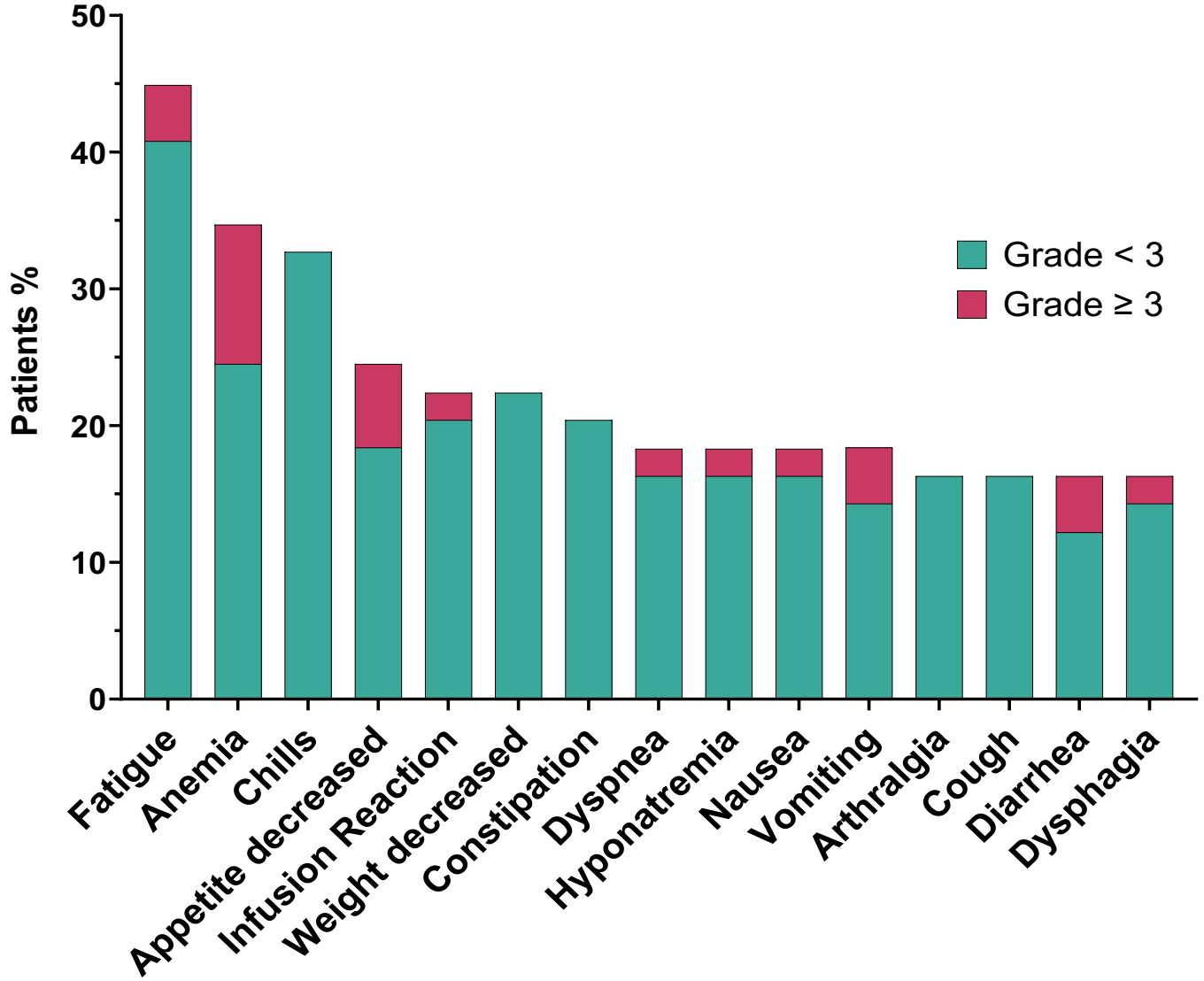
- **CUE-101 + Pembrolizumab**
  - No prior therapy for R/M HNSCC
  - PD-L1 CPS ≥1

Baseline Characteristics

Treatment Arm		Monotherapy (N=49)	Combination (N=31)
Age (years)	Mean (range)	64 (48-82)	65 (43-79)
Sex	Male Female	47 (95.9%) 2 (4.1%)	30 (96.8%) 1 (3.2%)
PD-L1 CPS	< 20 ≥ 20	– –	18 (**58.1%**) 13 (**41.9%**)
Lines of Therapy for R/M HNSCC§	Median (range) • CPI • Platinum-based	3 (1-10) 49 (**100%**) 45 (**91.8%**)	**0** – –

§ Patients with >1 prior line of therapy are counted once per category and may be included in >1 category

Adverse Events with CUE-101 (All Patients)



DLT

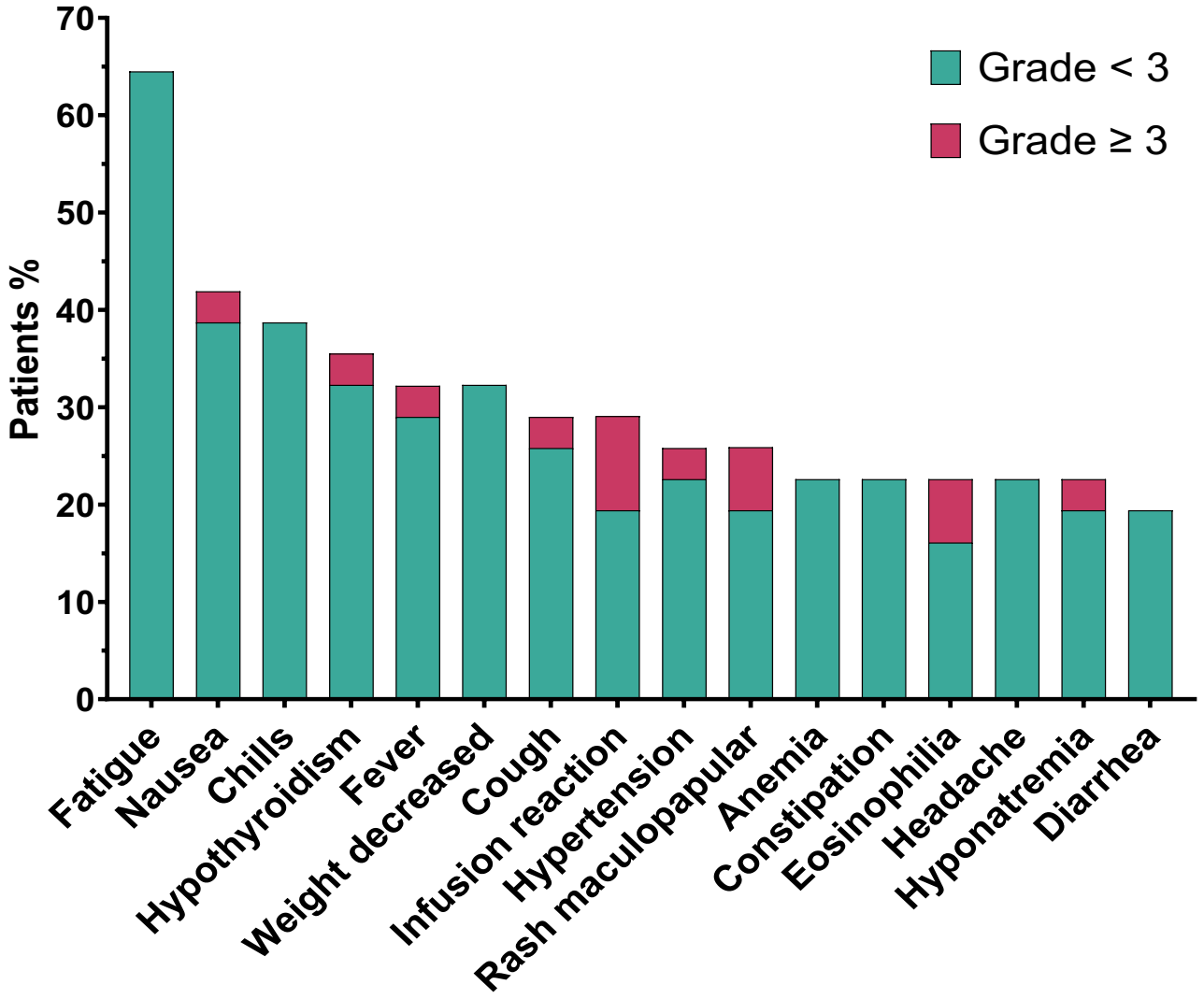
- 1 patient (anemia)
- Occurred at 1 mg/kg

RP2D

- 4 mg/kg IV Q3W

Data Extract: 17-Apr-2024.

Adverse Events CUE-101 + Pembrolizumab (All Patients)



DLT

- No events

RP2D of CUE-101

- 4 mg/kg IV Q3W

Data Extract: 17-Apr-2024.

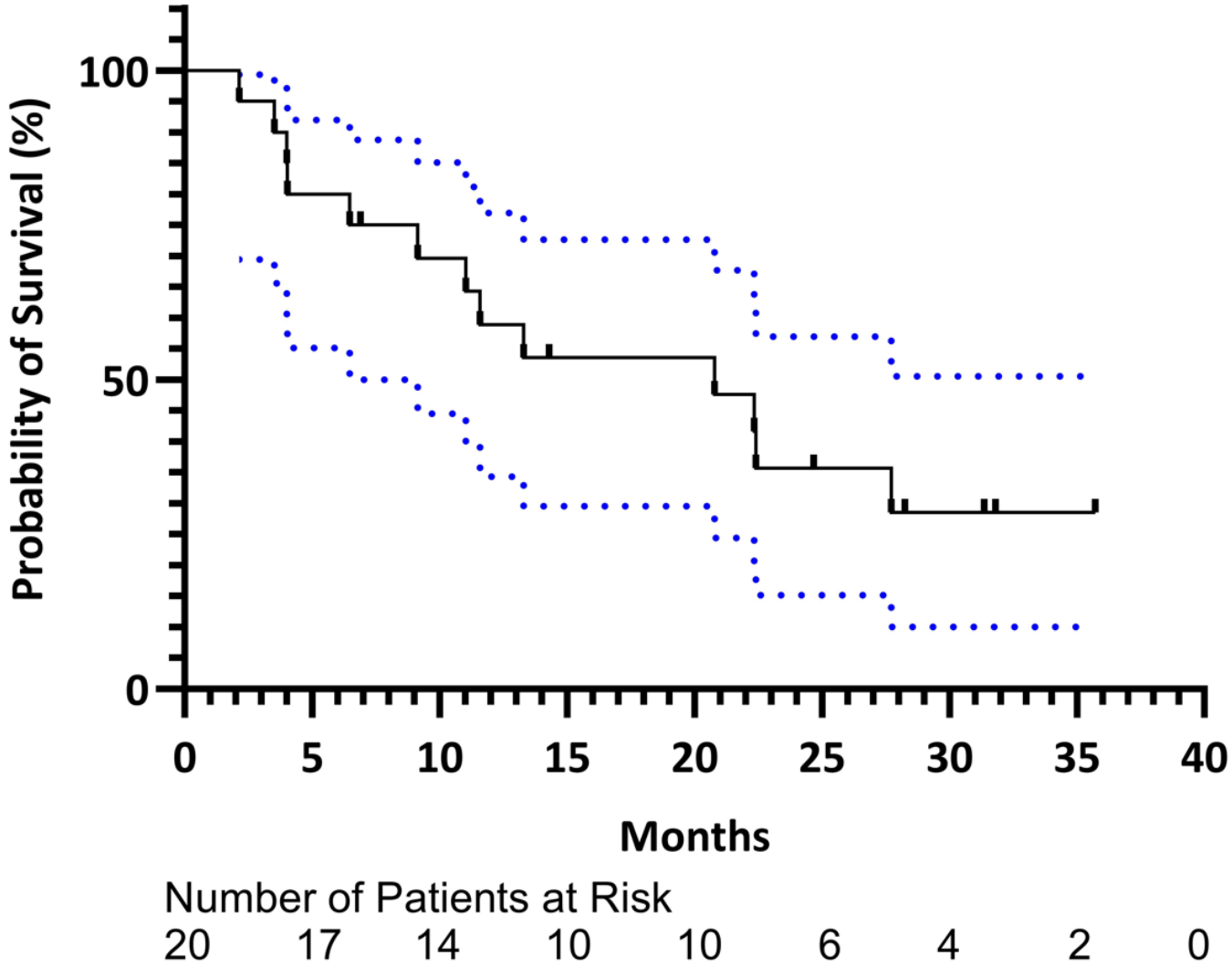
2L CUE-101 (4 mg/kg)

ORR 5%

- 1 PR (n=20)
- DoR: 9.7 mos

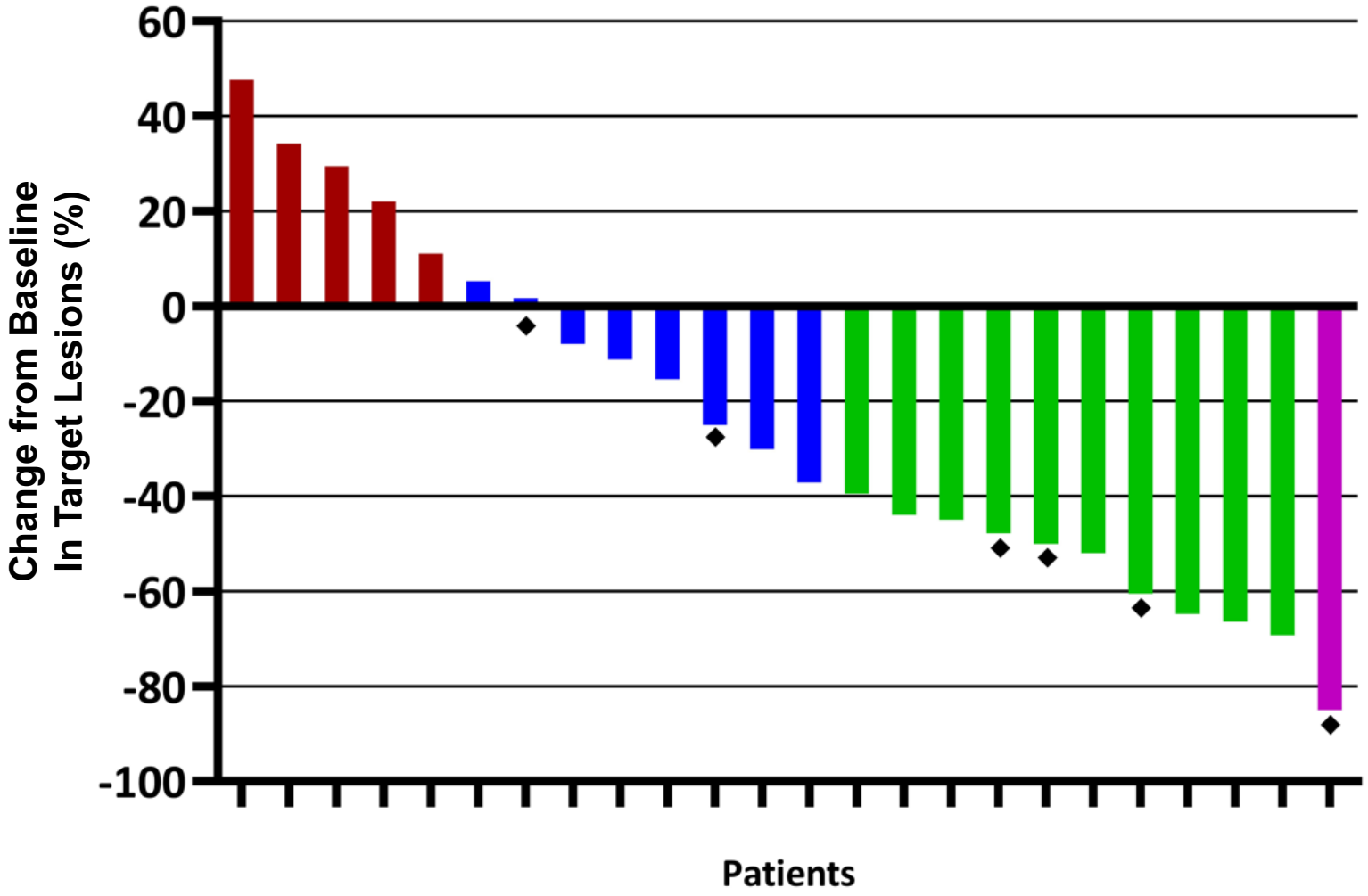
Median OS 20.8 months

(95% CI 10.0, NA)



Data Extract: 01-May-2024.

1L CUE-101 (4 mg/kg) + Pembrolizumab (n=24)



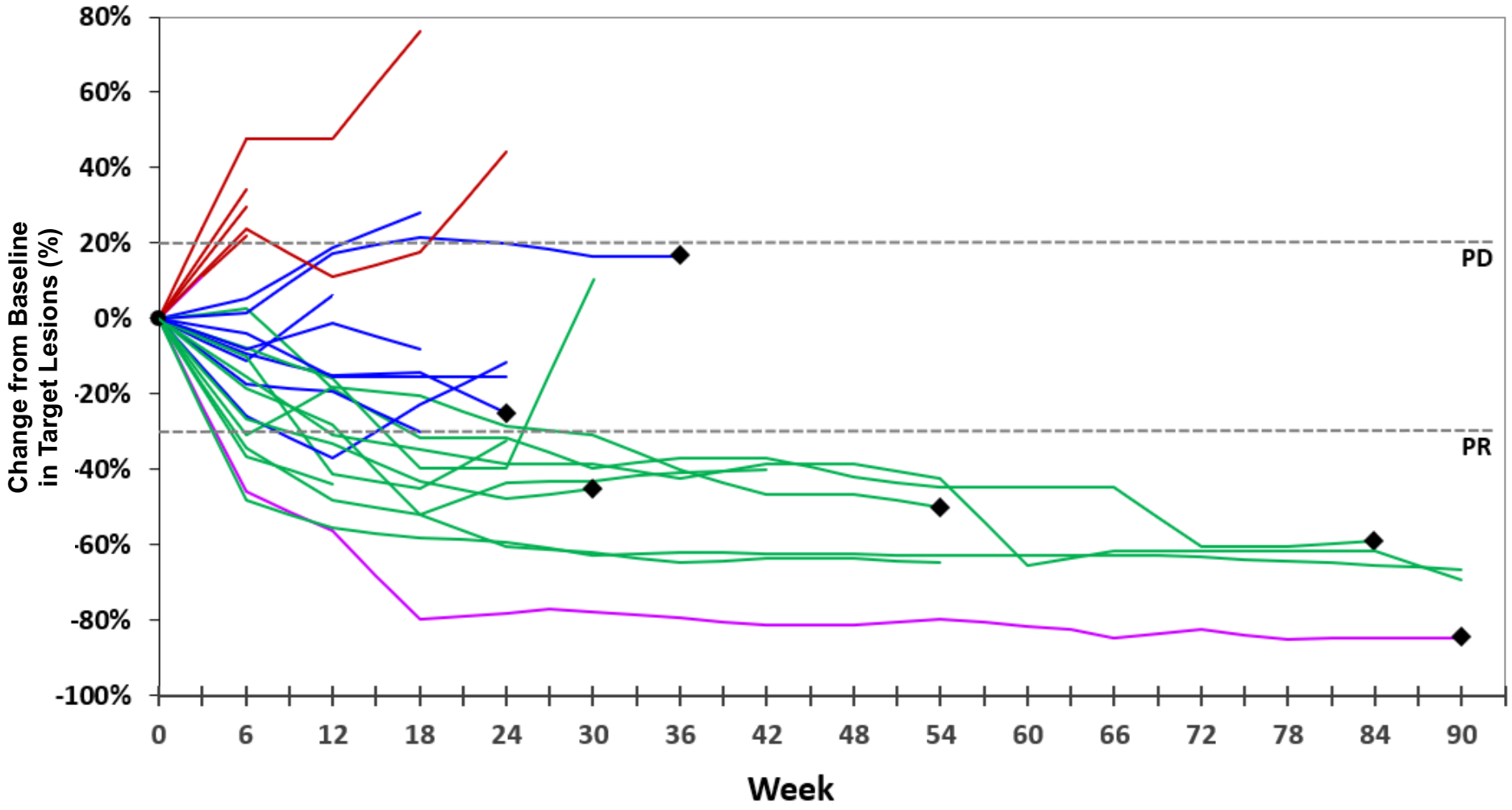
ORR: 46%

- 95% CI 25.6, 67.2
- 1 CR, 10 PR

Complete Response
Partial Response
Stable Disease/Durable Stable Disease
Progressive Disease
Ongoing Treatment Phase

Data Extract: 01-May-2024.

1L CUE-101 (4 mg/kg) + Pembrolizumab



Complete Response
Partial Response
Stable Disease/Durable Stable Disease
Progressive Disease
Ongoing Treatment Phase

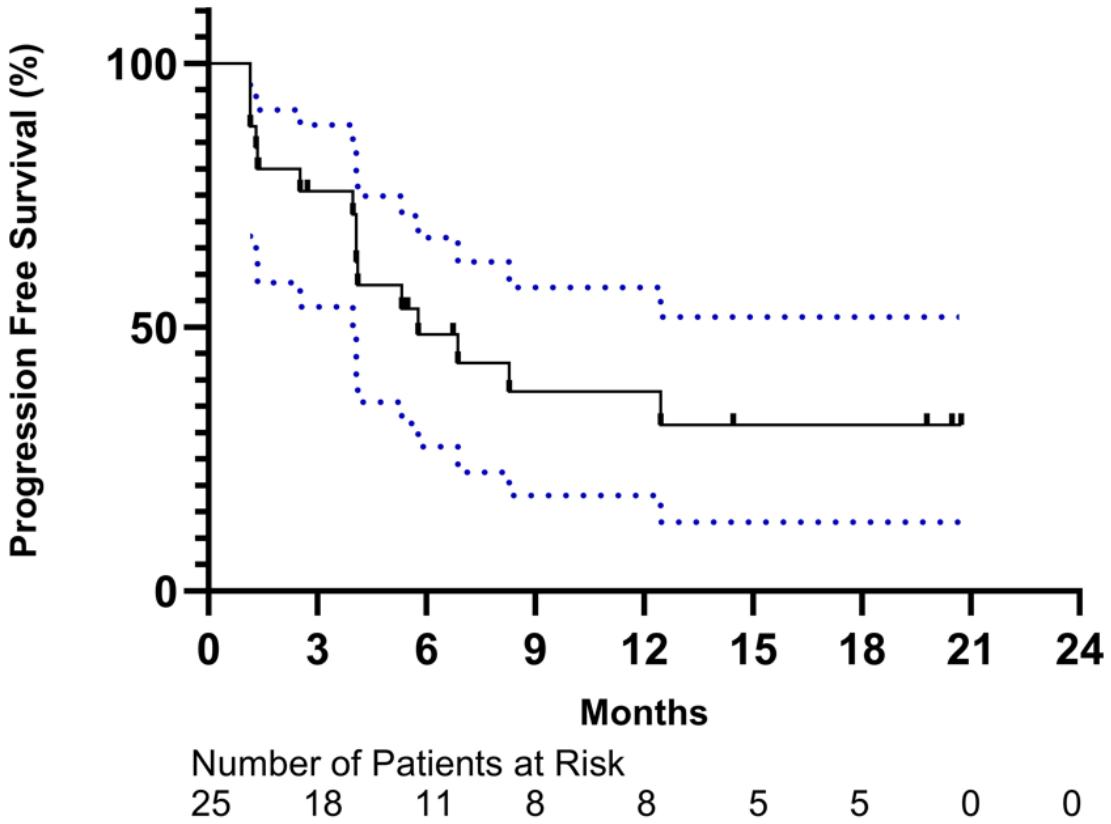
mDOR not reached

Data Extract: 01-May-2024.

1L CUE-101 (4 mg/kg) + Pembrolizumab

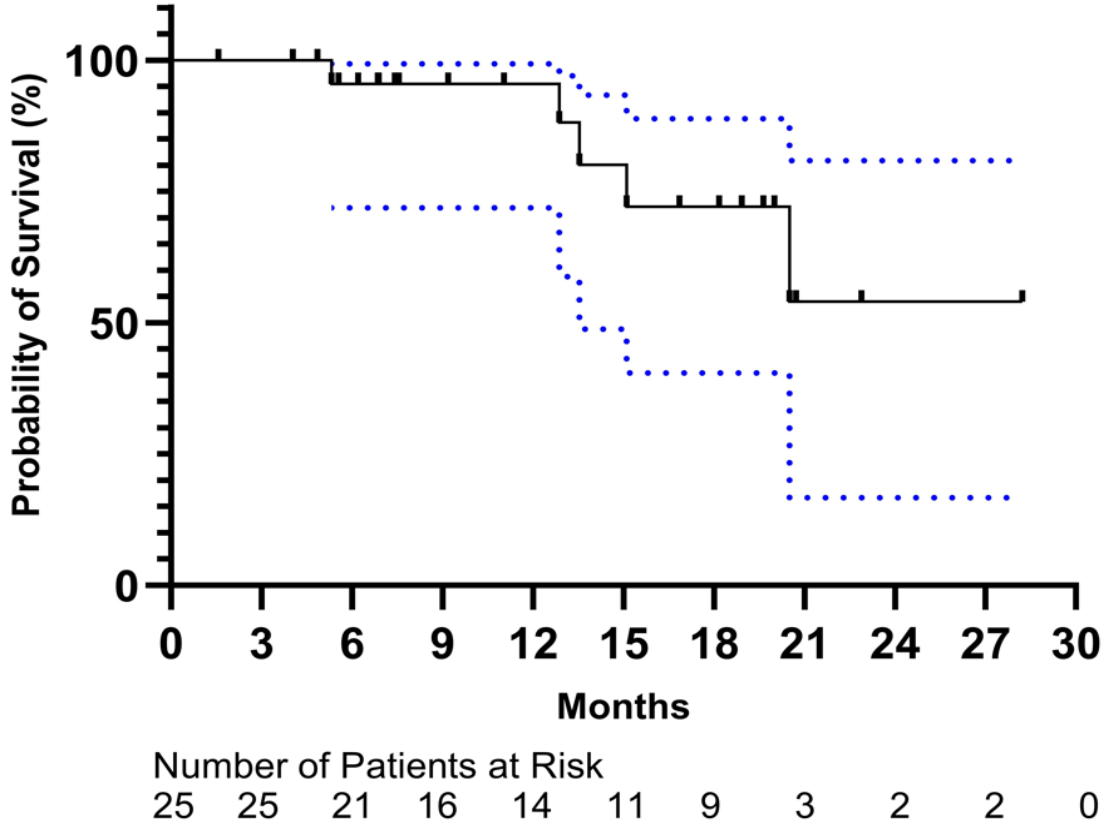
Progression-Free Survival

Median: 5.8 mos



Overall Survival

12-Month OS: 95.5%



Data Extract: 01-May-2024.

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