

INTRODUCTION

Background

- Time-of-day (ToD) of immune checkpoint inhibitor administration may affect outcomes, with early infusions hypothesized to enhance T-cell activation and antitumor immunity.
- Tarlatamab, a bispecific T-cell engager (BiTE) approved for relapsed/refractory small cell lung cancer (SCLC), drives both efficacy and toxicity (CRS, ICANS) through T-cell activation, making an effect of infusion timing biologically plausible.
- ToD has not been studied for bispecific agents.

Hypothesis

- Early ToD tarlatamab infusion during cycle 1 improves clinical outcomes in SCLC.

METHODS

- Multicenter, retrospective cohort: 58 adults with biopsy-proven SCLC, ≥1 tarlatamab dose at Duke and UNC (06/12/2024–10/20/2025) with follow-up imaging.
- Groups by ToD of C1D1/C1D8 (early =infusion start 0800–1500:
 - 0-dose early (n=14): neither C1D1 nor C1D8 early
 - 1-dose early (n=24): C1D1 or C1D8 (not both) early
 - 2-dose early (n=20): both C1D1 and C1D8 early
- All patients received C1D15 during early ToD.
- Primary outcome was objective response rate (ORR; confirmed complete + partial response).
- Secondary outcomes were progression-free survival (PFS), overall survival (OS), and any-grade CRS and ICANS.
- Treating physicians assessed responses by reviewing follow-up imaging (radiology reports and images).
- Categorical outcomes were compared with the χ^2 or Fisher exact test

DISCUSSION AND CONCLUSION

Summary of Outcomes by Time-of-Day Group

Outcome	0-Dose Early (n=14)	1-Dose Early (n=24)	2-Dose Early (n=20)
Objective response, %	43	29	20
Disease control, %	64	54	40
Median PFS, months	8.8	3.4	2.1
Median OS, months	NR	14.7	8.5
CRS, any grade, %	21	58	30
ICANS, any grade, %	21	21	35

Actionable Take-Away Message

- Early cycle-1 ToD did **not** improve ORR, PFS, or OS
- Trended toward worse survival with more early doses.
- No reduction in CRS or ICANS with early ToD.
- Signal opposite to checkpoint inhibitors; BiTE timing biology may differ and warrants prospective study.

Future Direction for Research

- Prospective, adequately powered trials needed to define optimal BiTE infusion timing and whether ToD influences CRS/ICANS risk.

Limitations

- Retrospective, non-randomized, small N
- Baseline groups were imbalanced, so survival trends may reflect confounding rather than a timing effect

REFERENCES & ACKNOWLEDGEMENTS

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- Inoue S, et al. JAMA Netw Open. 2026;9(5)
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- We gratefully acknowledge the patients, families, and caregivers whose care and clinical data made this analysis possible.

RESULTS

Baseline Characteristics by Time-of-Day Dosing Group

Characteristic	0-Dose Early (n=14)	1-Dose Early (n=24)	2-Dose Early (n=20)
Age, median (IQR), y	67.5 (61–74)	69 (61–74)	63.5 (59.5–68.5)
Sex: Female, n (%)	8 (57.1)	13 (54.2)	12 (60.0)
Race: White, n (%)	8 (57.1)	17 (70.8)	14 (70.0)
Race: Black, n (%)	3 (21.4)	6 (25.0)	4 (20.0)
Current/former smoker, n (%)	13 (92.9)	24 (100)	18 (90.0)
ECOG PS 0–1, n (%)	13 (92.9)	22 (91.7)	16 (80.0)
Prior lines of therapy, median (IQR)	2 (1–2)	2 (1–2)	1 (1–2)
Liver metastases, n (%)	6 (42.9)	12 (50.0)	5 (25.0)
Brain metastases, n (%)	6 (42.9)	12 (50.0)	9 (45.0)
Sites of disease, median (IQR)	2.5 (2–3)	2 (2–4)	2 (1–3)

Figure 1a. Progression-Free Survival by ToD Dosing Group

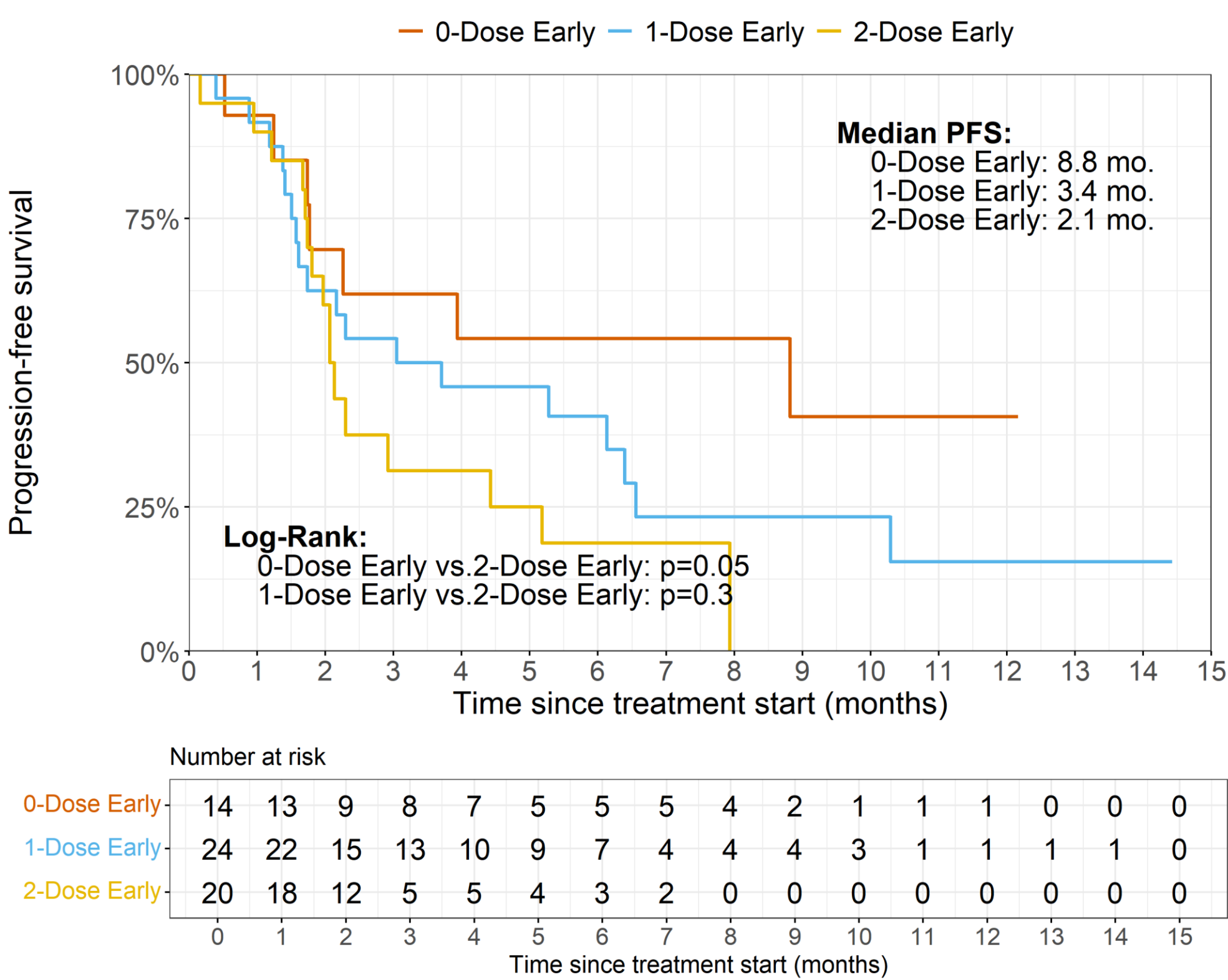


Figure 1b. Overall Survival by ToD Dosing Group

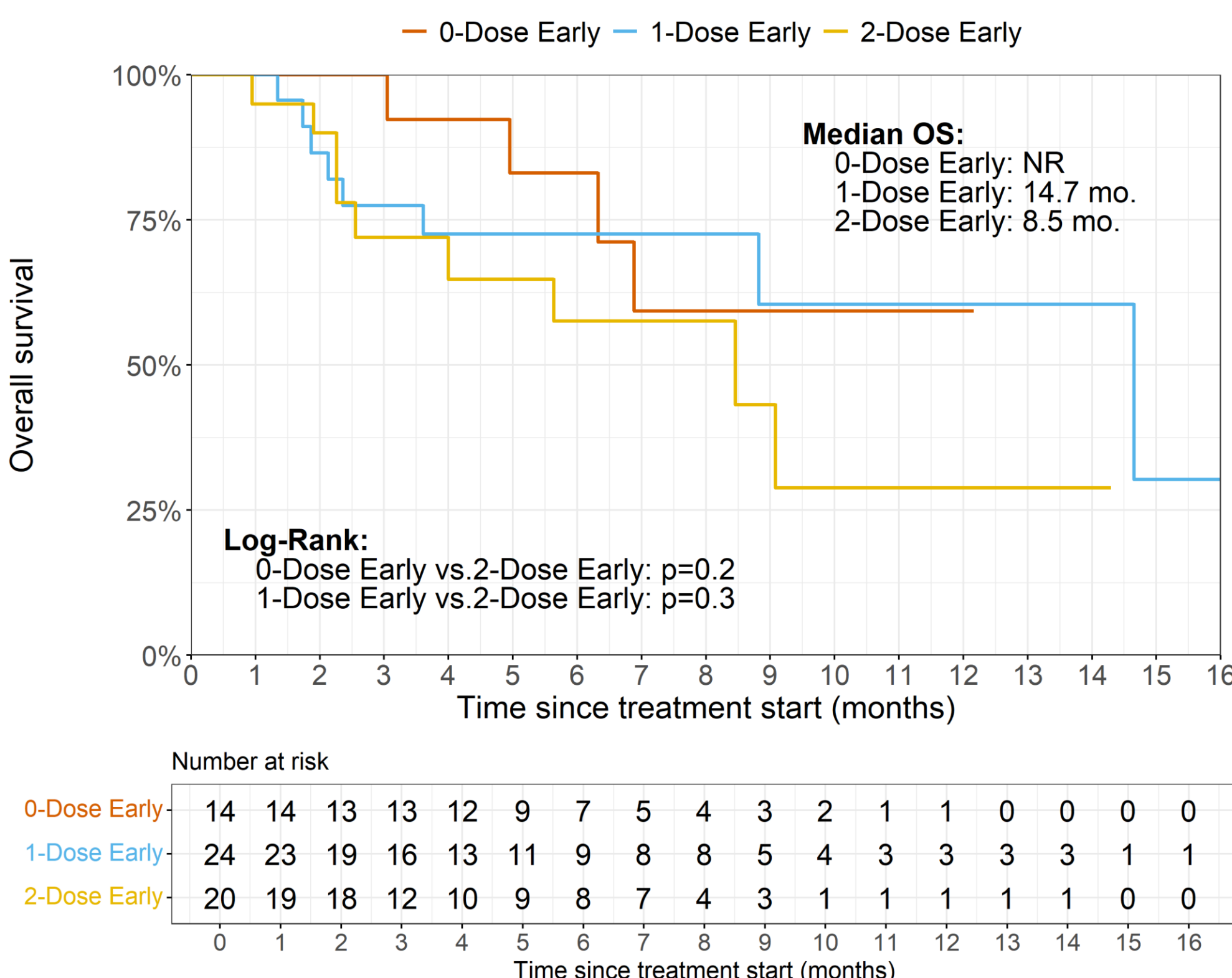


Figure 2. Best Response by ToD Dosing

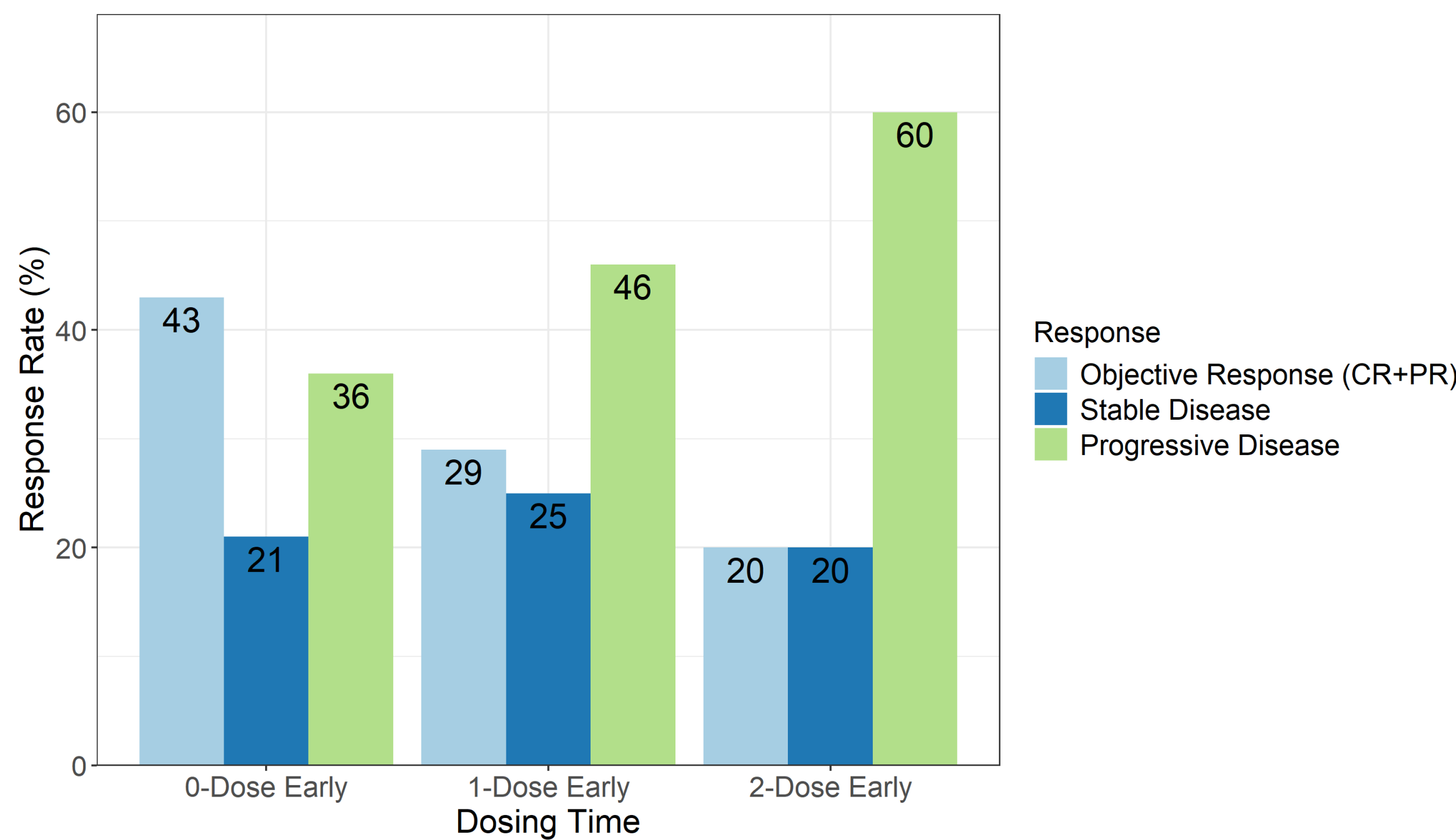


Figure 3. Any Grade CRS/ICANS by ToD Dosing

