P942

Long-Term Follow-Up From the Phase 1/2 MajesTEC-1 Trial of Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma

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Key Takeaway

With the longest follow-up of any bispecific antibody in multiple myeloma (median 30.4 months), teclistamab continues to demonstrate deep and durable responses, including in patients who transition to less frequent dosing

Conclusions

- Teclistamab ORR was 63.0%, with 46.1% of patients achieving ≥CR
- Of MRD-evaluable patients, 85.7% were MRD-negative at any point, sustained for ≥6 months in 56.1% and ≥12 months in 38.9%
- Teclistamab mDOR increased to 24 months overall, and was NR for patients in ≥CR (30-month DOR rate, 60.8%)
- Teclistamab offers an effective treatment for patients with TCE RRMM, with a manageable safety profile and no new safety signals

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Poster

Supplementary material

https://www.congresshub.com/Oncology/EHA2024/Teclistamab/Oriol

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Acknowledgments
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Disclosures
AO has served in a consulting or advisory role for Amgen, BMS/Celgene, GSK, Janssen, and Sanofi; and served on speakers' bureaus for Amgen, BMS/Celgene, GSK, Janssen, and Sanofi.

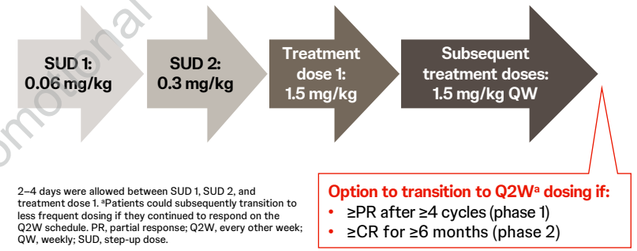
Introduction

- Teclistamab is the first approved B-cell maturation antigen (BCMA) × CD3 bispecific antibody for the treatment of triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM), with weight-based dosing[1-3]
- At 22.8-month median follow-up (mFU) in the MajesTEC-1 study, rapid, deep, and durable responses were observed in patients treated with teclistamab[4]
  - Overall response rate (ORR), 63.0%; complete response (CR) or better rate, 45.5%
  - Median duration of response (DOR), 21.6 months; median progression-free survival (PFS), 11.3 months; median overall survival (OS), 21.9 months
- Here, we present longer-term results from MajesTEC-1 at 30.4-month mFU

Methods

- The MajesTEC-1 study design has been previously described (NCT03145181, NCT04557098)[3]
  - Eligible patients had TCE RRMM with no prior BCMA-directed therapy
  - Primary endpoint: ORR
  - Patients received teclistamab at the recommended phase 2 dose (RP2D), with the option to transition to less frequent dosing (**Figure 1**)

Figure 1: Teclistamab dosing schedule



2–4 days were allowed between SUD 1, SUD 2, and treatment dose 1. [a]Patients could subsequently transition to less frequent dosing if they continued to respond on the Q2W schedule. PR, partial response; Q2W, every other week; QW, weekly; SUD, step-up dose.

Results

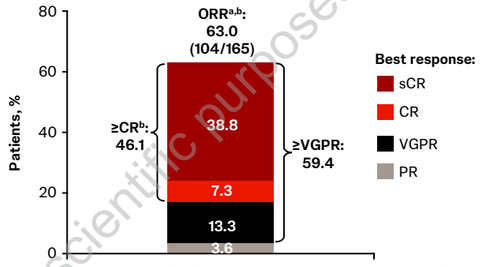
Study population

- At 30.4-month mFU (data cut-off: Aug 22, 2023), 165 patients had received teclistamab at the RP2D
  - Baseline characteristics have been previously presented[3,4]
  - 65 patients had transitioned to less frequent dosing (eg, Q2W)
- 38 patients remain on treatment (37 on a less frequent dosing schedule)

Efficacy

- ORR was 63.0% (≥CR, 46.1%); responses continued to deepen and remained durable (**Figures 2** and **3**)
- 85.7% (48/56) of minimal residual disease (MRD)-evaluable patients achieved MRD negativity (10^{-5} threshold), sustained for ≥6 months in 56.1% (23/41) and for ≥12 months in 38.9% (14/36); 30-month DOR, PFS and OS rates were ≥80% for patients with sustained MRD negativity for ≥6 months (**Table 1** and **Supplemental Figure 2**)
- DOR, PFS, and OS were further improved for patients who achieved very good partial response (VGPR) or better, ≥CR, or MRD negativity, and for those with ≤3 vs >3 prior lines of therapy (LOT) (**Figure 4** and **Table 1**)
  - No notable differences in baseline characteristics were observed between patients with ≤3 vs >3 prior LOT

Figure 2: ORR



[a]Response assessed by independent review committee. [b]At 30-month mFU of the phase 2 efficacy population (patients enrolled in cohort A on or before March 18, 2021; n=110 patients supporting the USPI[c]): ORR, 61.8%; ≥CR, 46.4% (n=51). sCR, stringent complete response; USPI, United States prescribing information.

Table 1: DOR, PFS, and OS in patient subgroups

	mDOR, mo (95% CI)	mPFS, mo (95% CI)	mOS, mo (95% CI)
All RP2D (N=165)[a]	24.0 (17.0–NE)	11.4 (8.8–16.4)	22.2 (15.1–29.9)
≥CR (n=76)[a]	NR (26.7–NE)	NR (26.9–NE)	NR (35.5–NE)
≥VGPR (n=98)[a]	25.6 (18.1–NE)	26.7 (19.4–NE)	NR (31.0–NE)
MRD-neg (n=48)[b]	NR (19.2–NE)	NR (21.0–NE)	NR (29.9–NE)
≤3 pLOT (n=43)	24.0 (14.0–NE)	21.7 (13.8–NE)	NR (18.3–NE)
>3 pLOT (n=122)	22.4 (14.9–NE)	9.7 (6.4–13.1)	17.7 (12.2–29.7)
Phase 2 efficacy (USPI) (n=110)[c]	22.4 (14.9–NE)	10.8 (7.4–16.4)	21.7 (12.7–29.9)
≥CR (n=51)[c]	NR (21.6–NE)	NR (22.8–NE)	NR (NE–NE)

[a]**Supplemental Figure 1**. [b]**Supplemental Figure 2**. [c]**Supplemental Figure 3**.
mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; MRD-neg, MRD-negative; NE, not estimable; NR, not reached; pLOT, prior line of therapy.

Figure 3: DOR

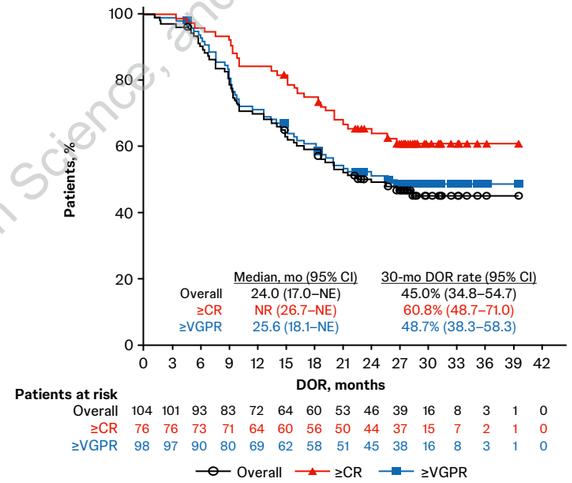
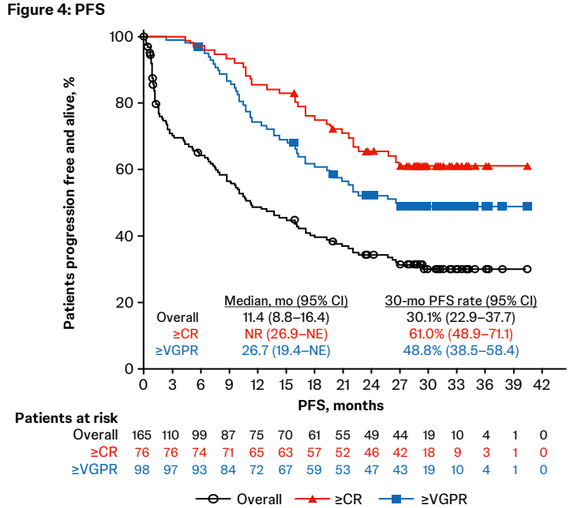


Figure 4: PFS



Safety

- The most common treatment-emergent adverse event (TEAEs) remained cytopenias and infections (**Table 2**)
- No changes in cytokine release syndrome (CRS) or immune effector cell–associated neurotoxicity syndrome at 30.4-month mFU
- Infections occurred in 78.8% of patients (grade 3/4, 55.2%)
  - Of grade 5 infections, 18/22 were due to COVID-19
    - No new grade 5 COVID-19 TEAEs at 30.4-month mFU
  - Onset of new grade ≥3 infections continued to generally decline over time
    - Factors such as transitioning to Q2W dosing and increasing use of immunoglobulin replacement may contribute to this trend
- TEAEs leading to dose reduction (n=1 [0.6%]) or discontinuation (n=8 [4.8%]; 5 due to infection) were infrequent
- No new safety signals were reported

Table 2: TEAEs occurring in ≥20% of patients in MajesTEC-1

TEAEs, n (%)	N=165	
	Any Grade	Grade 3/4
Any TEAE	**165 (100)**	**156 (94.5)**
Hematologic		
Neutropenia	118 (71.5)	108 (65.5)
Anemia	91 (55.2)	62 (37.6)
Thrombocytopenia	69 (41.8)	38 (23.0)
Lymphopenia	60 (36.4)	57 (34.5)
Leukopenia	33 (20.0)	15 (9.1)
Nonhematologic		
Infections	130 (78.8)	91 (55.2)
COVID-19	48 (29.1)	35 (21.2)
CRS	119 (72.1)	1 (0.6)
Diarrhea	57 (34.5)	6 (3.6)
Pyrexia	51 (30.9)	1 (0.6)
Fatigue	50 (30.3)	4 (2.4)
Cough	46 (27.9)	0
Nausea	45 (27.3)	1 (0.6)
Injection site erythema	44 (26.7)	0
Arthralgia	42 (25.5)	2 (1.2)
Headache	40 (24.2)	1 (0.6)
Constipation	37 (22.4)	0
Hypogammaglobulinemia	36 (21.8)	3 (1.8)
Back pain	33 (20.0)	4 (2.4)

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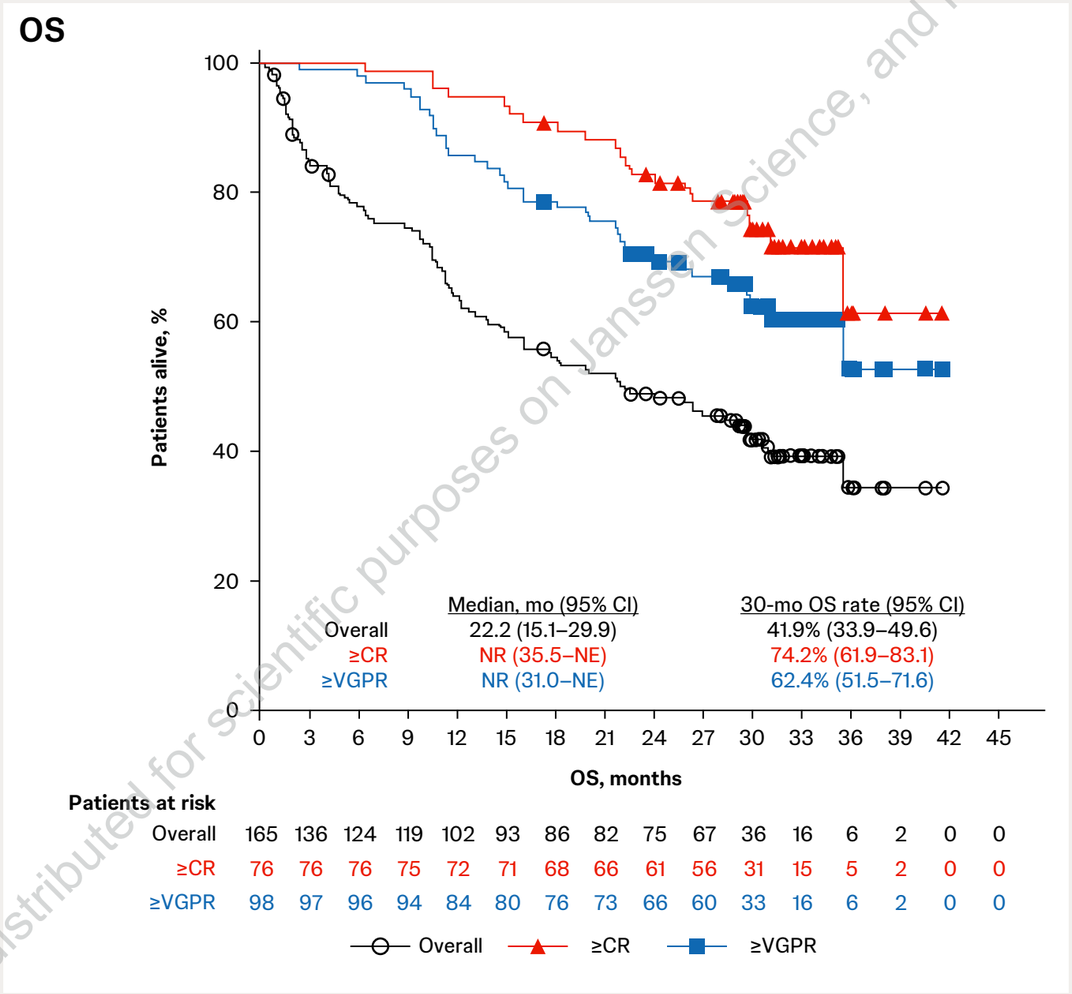
1. TECVAYLI (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2022. 2. TECVAYLI (teclistamab). Summary of product characteristics. Leiden, Netherlands: Janssen Biologics BV; 2022. 3. Moreau P, et al. *N Eng J Med* 2022;387:495-505. 4. van de Donk NWCJ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. Poster #8011.

Multiple Myeloma

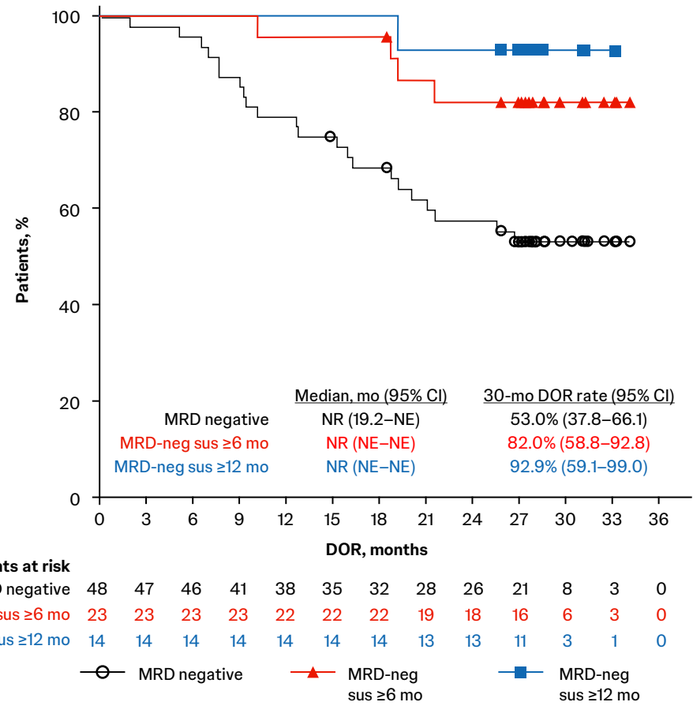
Supplemental Figure 1: OS



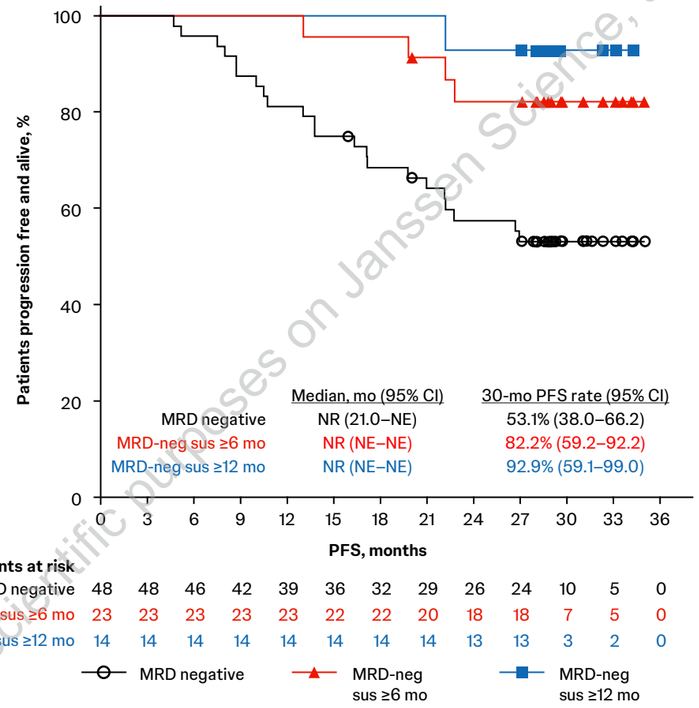
CR, complete response; NE, not estimable; NR, not reached; OS, overall survival; VGPR, very good partial response.

Supplemental Figure 2:
DOR, PFS, and OS in MRD-Negative Patients

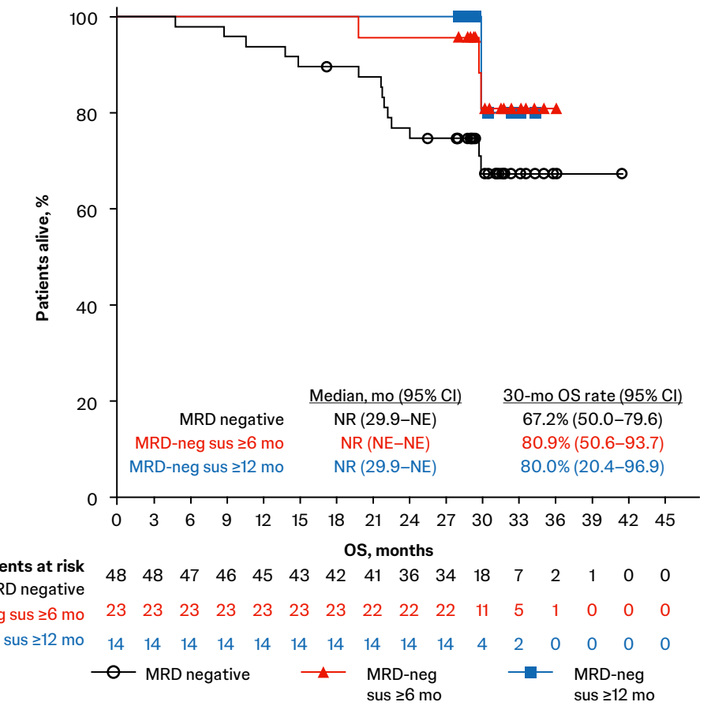
DOR



PFS

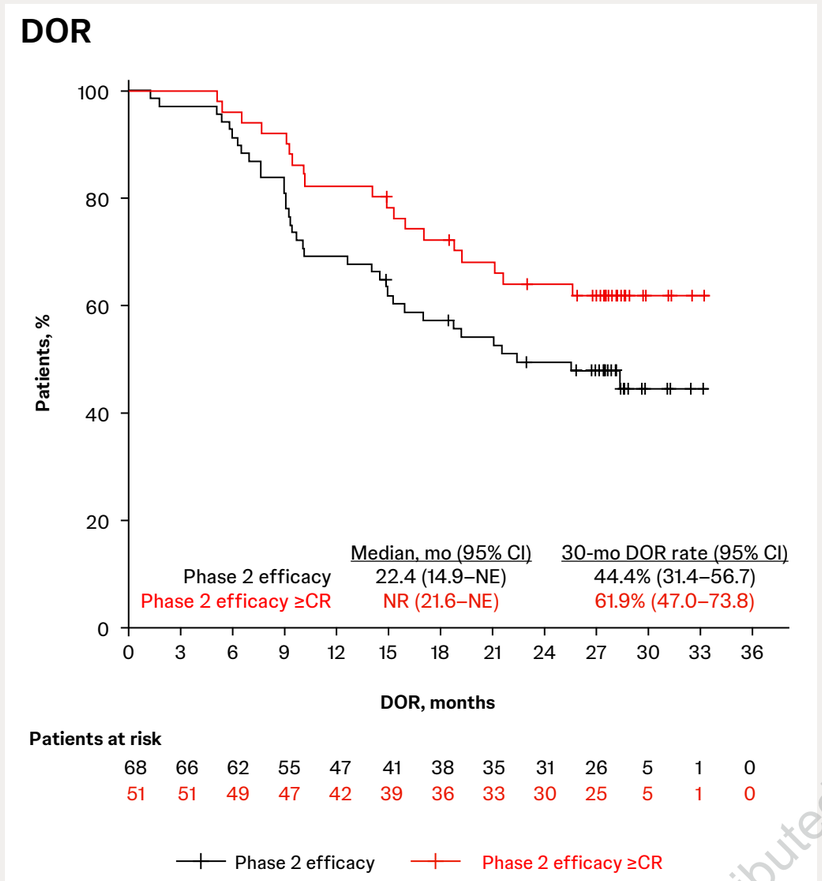


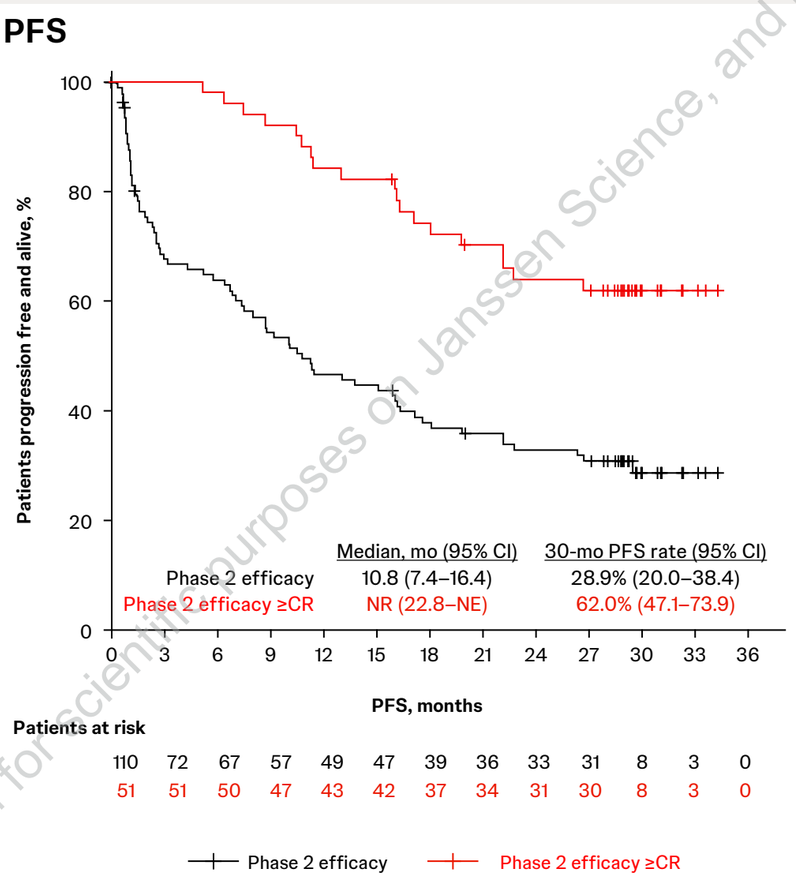
OS

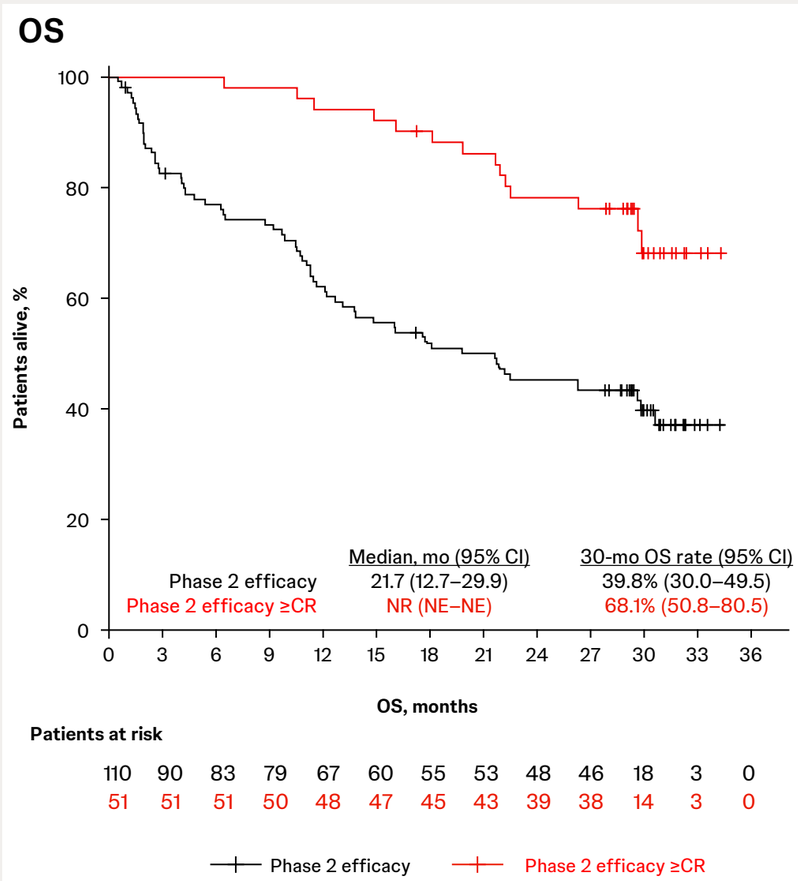


CR, complete response; DOR, duration of response; MRD, minimal residual disease; MRD-neg, MRD negative; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; sus, sustained.

Supplemental Figure 3:
DOR, PFS, and OS in the Phase 2 Efficacy Population (USPI)[a]







[a]Includes patients enrolled in cohort A on or before March 18, 2021; these data reflect 30-month median follow-up of the n=110 patients that supported the USPI.[1]
CR, complete response; DOR, duration of response; MRD, minimal residual disease; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; USPI, United States prescribing information.
1. TECVAYLI® (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2022.