

Five-Year Survival Outcomes of Patients With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia Treated With Brexucabtagene Autoleucel in ZUMA-3

Olalekan O. Oluwole, MD, MBBS, MPH¹; Armin Ghobadi, MD²; Ryan D. Cassaday, MD³; Jae H. Park, MD⁴; Roch Houot, MD, PhD⁵; Aaron C. Logan, MD, PhD⁶; Nicolas Boissel, MD, PhD⁷; Thibaut Leguay, MD⁸; Michael R. Bishop, MD⁹; Max S. Topp, MD¹⁰; Kristen M. O'Dwyer, MD¹¹; Maria R. Baer, MD¹²; Gary J. Schiller, MD¹³; Mehrdad Abedi, MD¹⁴; Monique C. Minnema, MD, PhD¹⁵; Patrick Stiff, MD¹⁶; Lang Zhou, PhD¹⁷; Rita Damico Khalid, DO¹⁷; and Bijal D. Shah, MD¹⁸

¹Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; ²Washington University School of Medicine, St Louis, MO, USA; ³University of Washington School of Medicine and Fred Hutchinson Cancer Center, Seattle, WA, USA; ⁴Memorial Sloan Kettering Cancer Center, New York, NY, USA; ⁵CHU Rennes, Univ Rennes, Inserm & EFS, Rennes, France; ⁶UCSF Medical Center, San Francisco, CA, USA; ⁷Hôpital Saint-Louis, Paris, France; ⁸Service d'hématologie clinique et thérapie cellulaire Hôpital du Haut-Leveque CHU de Bordeaux, Bordeaux, France; ⁹The University of Chicago Medicine, Chicago, IL, USA; ¹⁰Medizinische Klinik und Poliklinik II, Universitätsklinikum Würzburg, Würzburg, Germany; ¹¹University of Rochester Medical Center, Rochester, NY, USA; ¹²University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, MD, USA; ¹³David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; ¹⁴University of California Davis Comprehensive Cancer Center, Sacramento, CA, USA; ¹⁵UMC Utrecht Cancer Center, MS Hematologie, University Medical Center Utrecht, Utrecht, The Netherlands, on behalf of HOVONLLPC; ¹⁶Loyola University Chicago Stritch School of Medicine, Maywood, IL, USA; ¹⁷Kite, a Gilead Company, Santa Monica, CA, USA; and ¹⁸Moffitt Cancer Center, Tampa, FL, USA

BACKGROUND

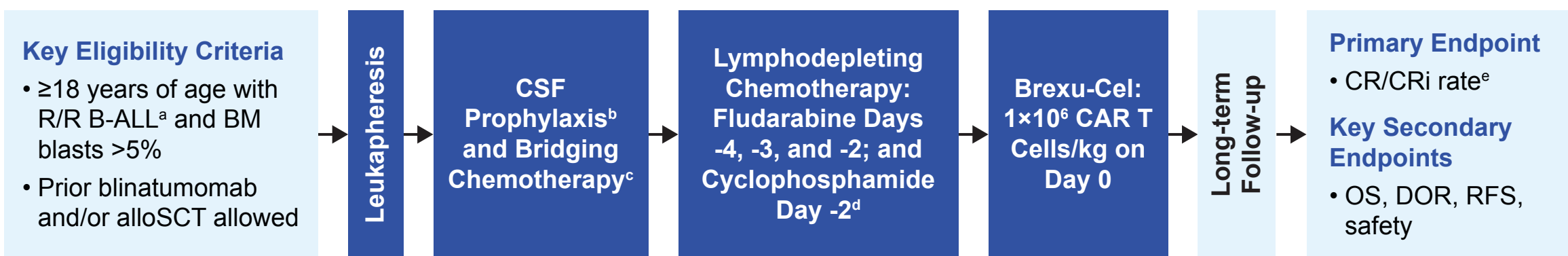
- Brexucabtagene autoleucel (brexu-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved for patients with relapsed or refractory B-cell acute lymphocytic leukemia (R/R B-ALL) who are ≥18 years of age in the United States (US) and ≥26 years of age in the European Union (EU) based on the pivotal Phase 2 ZUMA-3 study^{1,2}
 - The primary analysis of ZUMA-3 demonstrated a complete remission (CR)/CR with incomplete hematologic recovery (CRI) rate of 71% and CR rate of 56% (N=55) per independent radiologic review committee (IRRC) after 1 infusion of brexu-cel³
- After 4 years in ZUMA-3, the median overall survival (OS) was 25.6 months (95% CI, 16.2-60.4; 47.0 months [95% CI, 23.2-not evaluable (NE)] in responders) in pooled Phase 1 and 2 patients who received the pivotal dose of brexu-cel (1×10⁶ CAR T cells/kg; N=78); the 4-year OS rate was 40% (95% CI, 28-52), with survival benefits observed across key subgroups⁴
- Considering the ongoing need for therapies that can induce durable remissions and long-term survival in R/R B-ALL, and the curative potential of brexu-cel in this setting, we continue to update long-term outcomes in ZUMA-3

OBJECTIVE

- To assess the updated survival, safety, and causes of mortality in ZUMA-3, including outcomes in key subgroups, after 5 years of median follow-up

METHODS

Figure 1. ZUMA-3 Study Design³



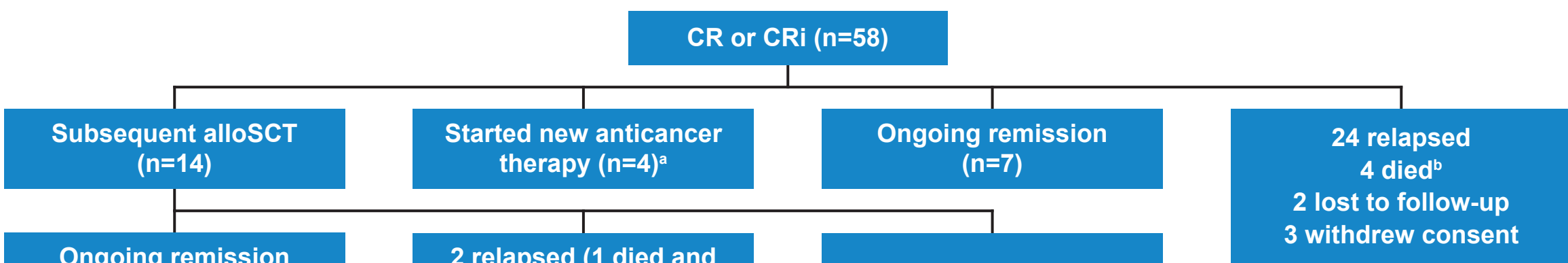
^a R/R disease was defined as primary refractory, first relapse within 12 months, R/R after ≥2 prior lines of systemic therapy or relapsed after alloSCT. ^b All patients received CSF prophylaxis consisting of an intrathecal regimen according to institutional or national guidelines. ^c Bridging chemotherapy was recommended for all patients, particularly those with >25% marrow blasts or >1000 blasts/μL of peripheral blood at screening, per physician's discretion. ^d Fludarabine 25 mg/m² IV on Days -4, -3, -2 and cyclophosphamide 900 mg/m² IV on Day -2. ^e Disease assessment was performed per IRRC through the Month 24 visit or until disease progression. Disease assessment after the Month 24 visit for patients whose disease had not progressed was performed per standard of care via investigator assessment.

- ZUMA-3 is a multicenter, single-arm, Phase 1 and 2 study evaluating safety and efficacy of brexu-cel (NCT02614066); methods have been previously reported (Figure 1)³
- Updated endpoints were assessed in pooled Phase 1 and 2 patients treated at the pivotal dose of brexu-cel (N=78), and for patients aged ≥26 years (n=63) based on the EU approval
- Response data reported here are per investigator assessment
- The Kaplan-Meier method was used to analyze time-to-event outcomes; post hoc subgroup analyses were exploratory in nature and descriptive statistics are reported herein
- Consolidative subsequent allogeneic stem cell transplantation (alloSCT) was allowed per physician's discretion

RESULTS

- As of July 23, 2024 (the OS data cutoff date), the median follow-up time for all Phase 1 and 2 patients (N=78) was 65.7 months (range, 56.7-94.3); for patients aged ≥26 years (n=63), median follow-up was 65.6 months (range, 56.7-94.3)
 - The data cutoff date for response assessment was November 7, 2023
- ZUMA-3 demographic and baseline characteristics, including for key subgroups, were previously reported^{4,6}
 - Briefly, baseline characteristics were generally similar to the overall population, with some notable differences in key subgroups
 - Patients with ≥2 prior therapies (n=63) had a higher proportion of patients aged ≥65 years⁸
 - Patients with prior blinatumomab (n=38) or prior inotuzumab (n=17) had a higher number of median prior therapies and higher percentage of baseline bone marrow blasts⁸
 - Patients with prior alloSCT (n=29) had a higher median number of prior therapies⁸
 - Baseline characteristics were similar between responders (per central assessment) with (n=14) and without (n=43) subsequent alloSCT; differences included 57% vs 70% of patients with ECOG PS of 1, 14% vs 28% with Philadelphia chromosome–positive disease, 37% vs 60% median baseline bone marrow blasts, 2 vs 3 median prior lines of therapy, 7% vs 21% prior inotuzumab, and 7% vs 49% prior alloSCT, respectively⁶

Figure 2. Response Status by Investigator Assessment in ZUMA-3 (n=58)

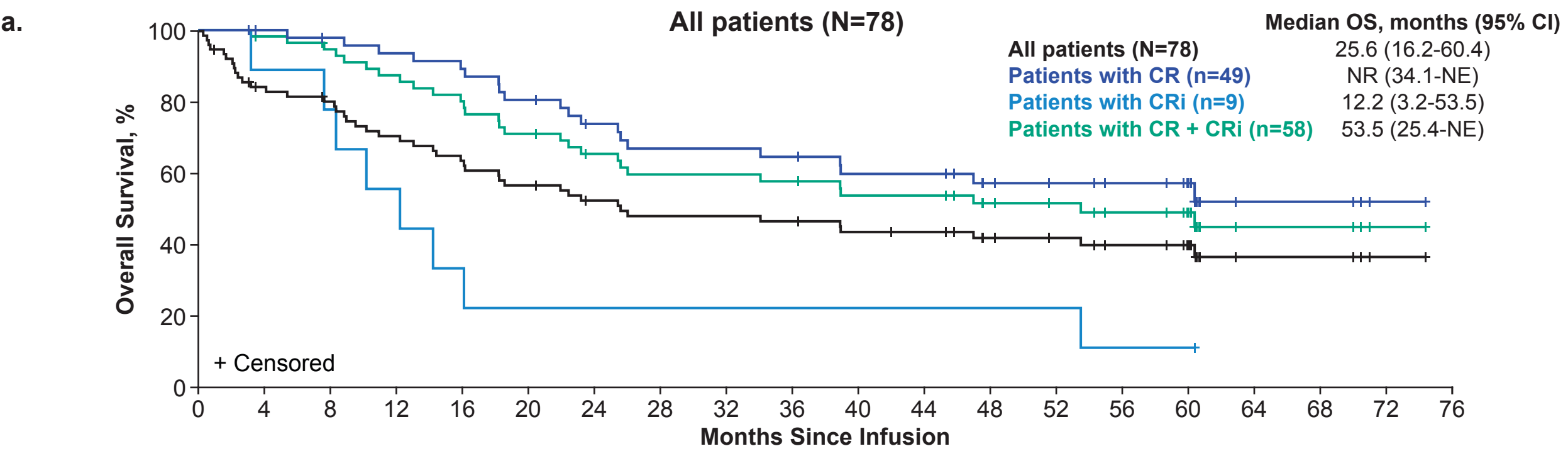


Data cutoff date: November 7, 2023. ^a Reason for starting new anticancer therapy: MPO+ (n=2) and relapse according to bone marrow biopsy by investigator (n=2). ^b Deaths were due to COVID-19 (n=1), PD (n=1), AE of GVHD (n=1), and metastatic carcinoma of unknown primary origin that was unrelated to brexu-cel (n=1). ^c AE, adverse event; alloSCT, allogeneic stem cell transplantation; brexu-cel, brexucabtagene autoleucel; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; GVHD, graft-versus-host disease; PD, progressive disease.

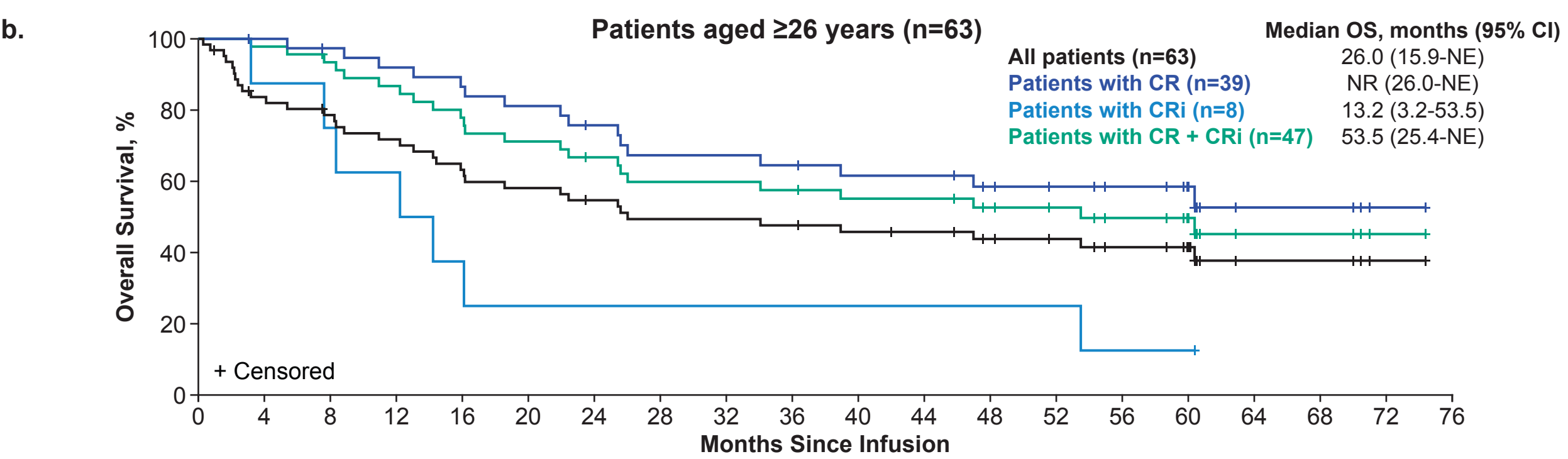
- As of the response data cutoff, among 58 patients with CR/CRi, per investigator review, 24 relapsed, 14 proceeded to subsequent alloSCT (6 in ongoing remission), 7 were in ongoing remission without subsequent therapy or alloSCT, 4 started new anticancer therapy, 4 died, 3 withdrew consent, and 2 were lost to follow-up (Figure 2)
- Among the 24 patients who relapsed prior to subsequent anticancer therapy or alloSCT, 15 received subsequent therapy (9 died and 6 were alive at last follow-up, 2 of whom received alloSCT following subsequent therapy), 5 died without subsequent therapy or alloSCT, 2 received a second infusion of brexu-cel (both with no response; 1 patient died and 1 was lost to follow-up), and 2 patients were lost to follow-up

RESULTS (Continued)

Figure 3. Overall Survival Update in ZUMA-3



All patients at risk: 78 70 62 60 58 53 51 49 46 44 41 39 36 34 33 33 33 32 31 29 28 26 25 24 23 21 20 18 16 15 5 4 4 4 4 1 1 0
CR at risk: 49 48 46 45 44 42 41 40 37 35 32 30 29 28 27 25 25 23 20 19 18 16 16 13 5 4 4 4 4 1 1 0
CRi at risk: 9 9 8 8 7 6 5 4 3 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 1 1 1 1 0 0 0 0 0 0 0 0
CR + CRi at risk: 58 58 55 54 52 50 48 46 44 42 39 37 34 32 31 31 31 31 30 29 27 27 25 22 21 20 19 17 17 14 5 4 4 4 4 1 1 0

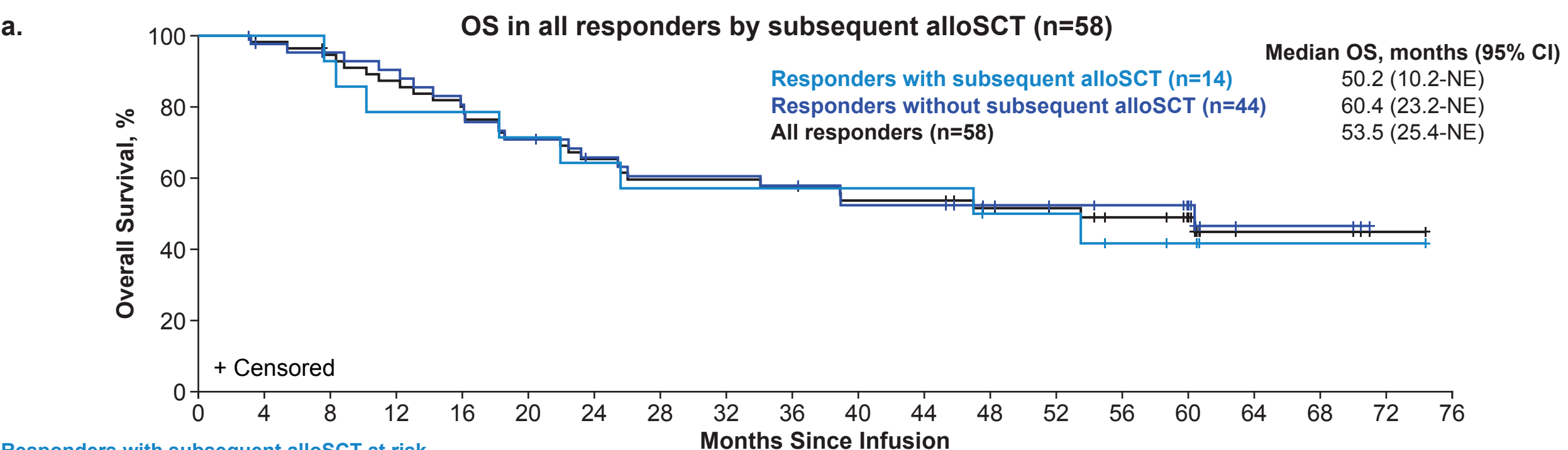


All patients at risk: 63 57 50 48 46 43 42 40 37 35 34 33 31 29 28 28 28 27 26 25 24 23 21 20 19 18 16 16 13 5 4 4 4 4 1 1 0
CR at risk: 39 39 38 37 36 35 34 33 32 31 30 29 27 25 24 24 24 23 22 21 21 21 18 17 16 16 14 11 5 4 4 4 4 1 1 0
CRi at risk: 8 8 7 7 6 5 4 3 2 2 2 2 2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 0 0 0 0 0 0 0 0
CR + CRi at risk: 47 47 45 44 42 40 39 37 35 33 32 31 29 27 26 26 26 25 24 23 23 22 20 19 18 17 15 12 5 4 4 4 4 1 1 0

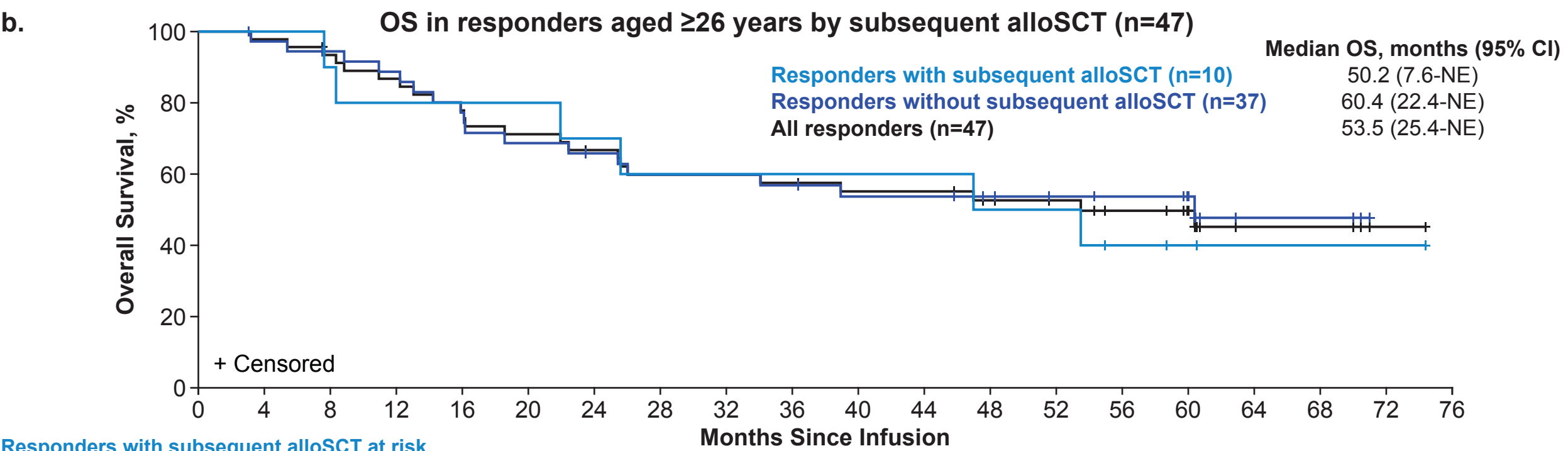
Data cutoff date: July 23, 2024. Response status was assessed by investigator review. CR, complete remission; CRi, complete remission with incomplete hematologic recovery; NE, not estimable; NR, not reached.

- The median OS was 25.6 months (95% CI, 16.2-60.4) for Phase 1 and 2 treated patients (N=78), which was unchanged since the 4-year analysis, and the 5-year OS rate was 40% (95% CI, 28.4-51.3; Figure 3a)⁴
- Per investigator review, responders (CR/CRi; n=58) reached a median OS of 53.5 months (95% CI, 25.4-not estimable [NE]) and those with a CR (n=49) had not reached a median OS (95% CI, 34.1-NE)
- For patients aged ≥26 years (n=63), the median OS remained the same since the 4-year analysis at 26.0 months (95% CI, 15.9-NE), with a 5-year OS rate of 42% (95% CI, 28.6-53.9; Figure 3b)⁴
 - Among responders aged ≥26 years (n=47), the median OS was 53.5 months (95% CI, 25.4-NE)

Figure 4. Overall Survival Update in ZUMA-3 by Subsequent AlloSCT



Responders with subsequent alloSCT at risk: 14 14 14 14 13 12 11 11 11 11 10 9 9 8 8 8 8 8 8 8 8 7 6 6 6 6 6 6 5 5 4 3 3 3 3 3 3 3 0
Responders without subsequent alloSCT at risk: 44 44 41 40 39 38 37 35 33 31 29 28 25 24 23 23 23 22 21 19 19 19 17 16 15 14 13 12 11 4 4 3 3 3 0 0 0
All responders at risk: 58 58 55 54 52 50 48 46 44 42 39 37 34 32 31 31 31 30 29 27 27 25 22 21 20 19 17 17 14 5 4 4 4 4 1 1 0

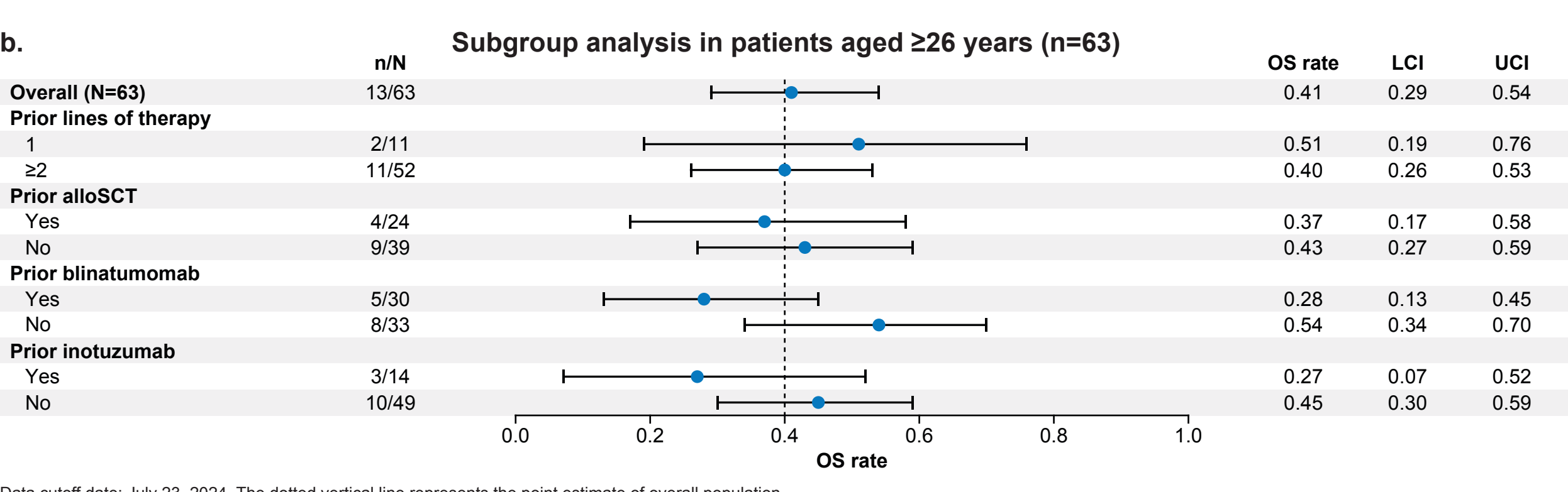
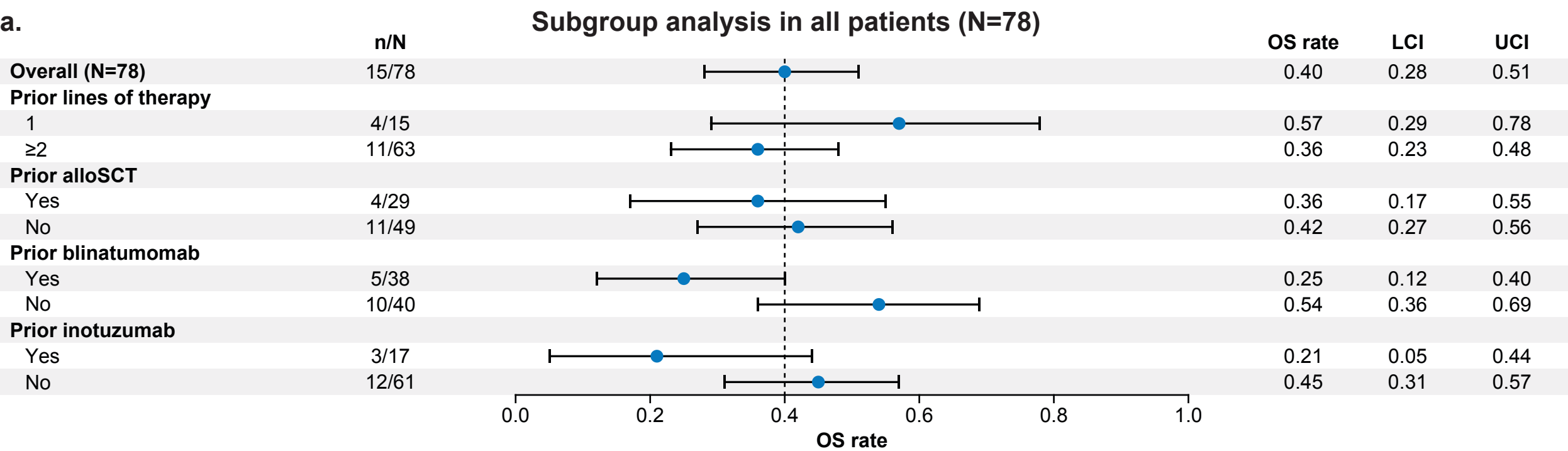


Responders with subsequent alloSCT at risk: 10 10 10 10 9 8 8 8 8 7 6 6 6 6 6 6 6 6 5 5 5 4 3 3 2 1 1 1 1 1 1 0
Responders without subsequent alloSCT at risk: 37 37 35 34 33 32 31 29 27 25 24 24 22 21 20 20 20 19 18 17 17 16 15 14 13 12 11 4 4 3 3 3 0 0 0
All responders at risk: 47 47 45 44 42 40 39 37 35 33 32 31 29 27 26 26 26 25 24 23 23 22 20 19 18 17 15 12 5 4 4 4 4 1 1 0

Data cutoff date: July 23, 2024. Response status was assessed by investigator review. NE, not estimable; OS, overall survival.

- Median OS was 50.2 months (95% CI, 10.2-NE) in all responders (per investigator review, n=58) who received subsequent alloSCT (n=14) and 60.4 months (95% CI, 23.2-NE) in responders who did not receive subsequent alloSCT (n=44; Figure 4a); the 5-year OS rates were 42% (95% CI, 16.4-65.4) and 52% (95% CI, 35.8-66.5), respectively
- Among responders aged ≥26 years (n=47), the median OS was 50.2 months (95% CI, 7.6-NE) with subsequent alloSCT (n=10) and 60.4 months (95% CI, 22.4-NE) without subsequent alloSCT (n=37; Figure 4b); the 5-year OS rates were 40% (95% CI, 12.3-67.0) and 54% (95% CI, 35.8-68.6), respectively

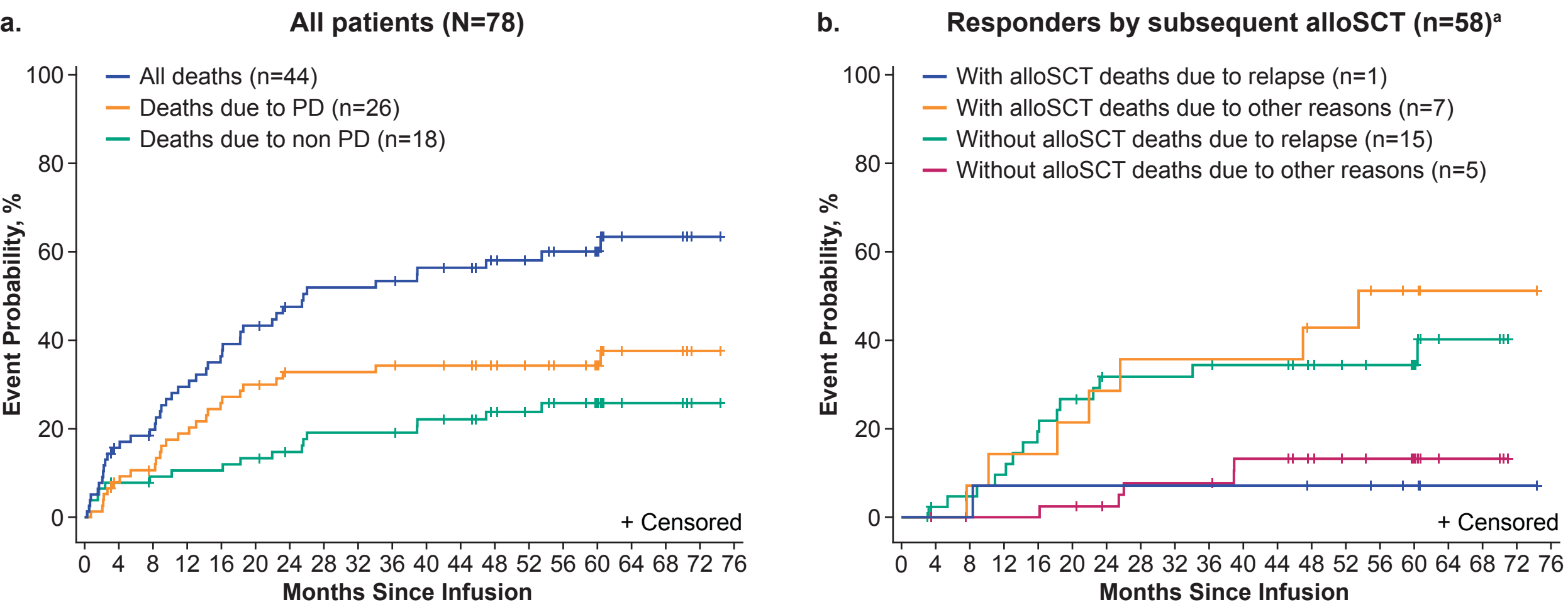
Figure 5. Overall Survival Rates at 5 Years in ZUMA-3 by Key Subgroups (N=78)



Data cutoff date: July 23, 2024. The dotted vertical line represents the point estimate of overall population. alloSCT, allogeneic stem cell transplantation; LCI, lower confidence interval; OS, overall survival; UCI, upper confidence interval.

- In the subgroup analysis of all treated patients, the 5-year OS rates were (Figure 5a):
 - 57% for patients with 1 prior therapy (n=15) and 36% for patients with ≥2 prior therapies (n=63)
 - 36% for patients with prior alloSCT (n=29) and 42% for patients without prior alloSCT (n=49)
 - 25% for patients with prior blinatumomab (n=38) and 54% for patients without (n=40) prior blinatumomab
 - 21% for patients with prior inotuzumab (n=17) and 45% for patients without prior inotuzumab (n=61)
- Among patients aged ≥26 years, the 5-year OS rates were (Figure 5b):
 - 51% for patients with 1 prior therapy (n=11) and 40% for patients with ≥2 prior therapies (n=52)
 - 37% for patients with prior alloSCT (n=24) and 43% for patients without prior alloSCT (n=39)
 - 28% for patients with prior blinatumomab (n=30) and 54% for patients without (n=33) prior blinatumomab
 - 27% for patients with prior inotuzumab (n=14) and 45% without prior inotuzumab (n=49)

Figure 6. 5-Year Cumulative Incidence of Cause-Specific Mortality in All Patients and by Subsequent AlloSCT in Responders per Investigator Assessment



* There was high censorship in patient subgroups due to high survival rate. Response status was assessed by investigator review. alloSCT, allogeneic stem cell transplant; brexu-cel, brexucabtagene autoleucel; CIF, cumulative incidence function; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; NE, not estimable; PD, progressive disease.

- As of the OS data cutoff, 44 of 78 patients (56%) had died, 20 patients (26%) were alive, and 14 patients were lost to follow-up or withdrew consent
- The estimated 60-month cumulative incidence of death due to progressive disease (PD) and other causes were 34% (95% CI, 23.5-45.2) and 26% (95% CI, 16.0-36.7), respectively, for all patients (N=78; Figure 6a)
 - Prior reasons for non-PD–related mortality were reported in the 4-year follow-up analysis⁴
- Of the 14 responders who received subsequent alloSCT, 8 had died by OS data cutoff, 1 (7%) due to relapse and 7 (50%) due to non-relapse–related reasons (Figure 6b)
 - The estimated 60-month cumulative incidence of relapse-related mortality and non-relapse–related mortality in responders with subsequent alloSCT were 7% (0.4-28.6) and 51% (21.4-74.8), respectively
 - Whereas the estimated 60-month cumulative incidence of relapse-related mortality and non-relapse–related mortality in responders without subsequent alloSCT were 34% (20.2-49.1) and 13% (4.7-26.2), respectively
 - Since the 4-year analysis, 1 new adverse event and death were reported, both in the same patient who had previously received post-brexu-cel alloSCT, cervical cancer and death due to pulmonary failure (both deemed unrelated to brexu-cel)
- No secondary T-cell malignancies were reported in ZUMA-3 at any time

CONCLUSIONS

- The 5-year analysis of ZUMA-3 represents the longest follow-up of a CAR T-cell therapy approved for adults with B-ALL, to our knowledge
- Brexu-cel continued to demonstrate long-term benefits to patients, with a 40% OS rate at 5 years
 - Responders had the greatest benefit with a median OS of >5 years for patients with CR/CRi per investigator review (n=58), and not reached for those with CR (n=49)
- Patients benefited from brexu-cel regardless of age, prior therapy, or subsequent alloSCT status, though benefits were less apparent in patients with prior blinatumomab or prior inotuzumab
- Responders with subsequent alloSCT had numerically lower median OS and a numerically higher rate of non-relapse–related mortality than responders without subsequent alloSCT
- Small sample sizes and/or unbalanced patient characteristics limit interpretation of post hoc subgroup and subsequent alloSCT analyses
- The long-term safety was favorable, with no new safety signals observed
- Further studies are needed to fully understand how prior therapies and subsequent alloSCT may impact long-term outcomes in patients with R/R B-ALL treated with brexu-cel

PLAIN LANGUAGE SUMMARY

- Brexucabtagene autoleucel (brexu-cel)** is a type of anticancer treatment that is made from a person's own immune cells called **chimeric antigen receptor T-cell therapy**
- Brexu-cel is approved in the United States and Europe for **commercial** use to treat people with a blood cancer called **relapsed or refractory (R/R) B-cell acute lymphoblastic leukemia (B-ALL)**
- The ZUMA-3 **clinical trial** followed people for over 5 years to see how safe and well brexu-cel worked in people with R/R B-ALL long term
- This study showed that after 5 years, 40% of people who were treated with brexu-cel were still alive. Brexu-cel did not work as well in people who had certain anticancer treatments before brexu-cel
- More people in the trial died due to **progressive disease** than for reasons unrelated to cancer
- These results showed that brexu-cel can provide long-term benefit to people with R/R B-ALL

Words in **bold text** are defined in the glossary that is accessible through the QR code

REFERENCES

- TECARTUS® (brexucabtagene autoleucel) [Prescribing information]. Kite Pharma, Inc; 2024.
- TECARTUS® (brexucabtagene autoleucel) [summary of product characteristics]. Amsterdam, The Netherlands: Kite Pharma EU B.V.; 2024.
- Shah BD, et al. *Lancet*. 2021;398:491-502.
- Oluwole OO, et al. *J Clin Oncol*. 2024;42(Suppl 16):6531.
- Shah BD, et al. *J Immunother Cancer*. 2023;11:e007118.
- Shah BD, et al. *Leukemia*. 2025. doi:10.1038/s41375-025-02532-7.

ACKNOWLEDGMENTS

- The patients, families, friends, and caregivers
- The study investigators, coordinators, and health care staff at each study site
- Medical writing support was provided by Ashley Pavlovsky, PhD, CMPP, and Rohina Rubicz, PhD, CMPP, of Nexus Global Group Science, funded by Kite, a Gilead Company
- This study was funded by Kite, a Gilead Company

DISCLOSURES

- OOO**: honoraria from Gilead Sciences and Pfizer; consulting/advisory role for AbbVie, ADC Therapeutics, Cargo, Caribio Biosciences, Epizyme, Gilead Sciences, Kite, a Gilead Company, Nektar, Novartis, Pfizer, and TGR; speakers' bureau participation for ADC Therapeutics; and research funding from Allogene, Daiichi Sankyo, Kite, and Pfizer.
- Full author disclosures are available through the Quick Response (QR) code

Copies of this presentation obtained through QR code are for personal use only and may not be reproduced without permission from the author of this poster.



FULL AUTHOR DISCLOSURES

OOO: honoraria from Gilead Sciences and Pfizer; consulting/advisory role for AbbVie, ADC Therapeutics, Cargo, Caribou Biosciences, Epizyme, Gilead Sciences, Kite, a Gilead Company, Nektar, Novartis, Pfizer, and TGR; speakers' bureau participation for ADC Therapeutics; and research funding from Allogene, Daiichi Sankyo, Kite, and Pfizer. **AG:** honoraria from Kite, a Gilead Company; consulting/advisory role for Amgen, Atara, Bristol Myers Squibb, CRISPR Therapeutics, Kite, and Wugen Inc.; research funding from Amgen, Genentech, and Kite. **RDC:** employment with and stock or other ownership in Seagen (immediate family member); honoraria from Amgen, Jazz, Kite, a Gilead Company, and Pfizer; consultancy/advisory role for Amgen, Autolus, and Kite; research funding from Amgen, Incyte, Kite, Merck, Pfizer, Servier, and Vanda; travel support from Kite; and other relationship with Autolus (independent review committee), and PeproMene Bio (DSMB). **JHP:** consulting/advisory role for AstraZeneca, Kite, a Gilead Company, and Novartis; and research funding from Amgen, Genentech, and Juno. **RH:** honoraria from ADC Therapeutics, Bristol Myers Squibb, Celgene, Gilead Sciences, Janssen, Kite, a Gilead Company, MSD, and Novartis; and consulting/advisory role for Kite and Gilead Sciences. **ACL:** consulting/advisory role for AbbVie, Actinium, Bristol Myers Squibb, Pfizer, and Takeda; research funding from Amgen, Astellas, Autolus, Kadmon, Kite, a Gilead Company, Pharmacyclics, and Talaris; and other relationship with **DSMB:** Servier. **NB:** honoraria and consulting/advisory role for Amgen, Kite, a Gilead Company, and Novartis; and research funding and expert testimony for Amgen. **TL:** honoraria from Amgen, Incyte, Kite, a Gilead Company, and Servier; and consulting/advisory role for Amgen, Incyte, and Servier. **MRB:** honoraria from ADC Therapeutics, Bristol Myers Squibb, Incyte, and Sanofi; consulting/advisory role for Bristol Myers Squibb, Kite, a Gilead Company, Novartis, and Sana Bio; and speakers' bureau participation for ADC Therapeutics, Bristol Myers Squibb, Incyte, and Sanofi. **MST:** consulting/advisory role for AstraZeneca, Bristol Myers Squibb, Genmab, Kite, a Gilead Company, and Roche; research funding from Kite, Regeneron, Roche, and Takeda; and travel support from Janssen and Kite. **KMO:** no relevant financial relationships to disclose. **MRB:** research funding from AbbVie, Ascentage, Kite, a Gilead Company, Kura, and Takeda. **GJS:** honoraria and research funding from and speakers' bureau participation for Kite, a Gilead Company. **MA:** honoraria from and consulting/advisory role for Celgene; speakers' bureau participation for AbbVie, Bristol Myers Squibb, Celgene, and Kite, a Gilead Company. **MCM:** consulting or advisory role for CDR-life, GSK, and Janssen/Cilag (institution); speakers' bureau participation for BMS, Jansen/Cilag, Pfizer, and Siemens; research funding from BeiGene (institution); and travel, accommodations, and expenses from Bristol Myers Squibb. **PS:** honoraria from and consulting or advisory role for MorphoSys and CRISPR Therapeutics; and research funding from Amgen, Gamida Cell, Pfizer, Karyopharm, Gilead Sciences, Incyte, Seagen, and Cellectar. **LZ:** employment with Kite, a Gilead Company; and stock or other ownership in AbbVie RSU. **RS:** employment with Amgen and Kite, a Gilead Company; stock or other ownership in Amgen and Gilead Sciences; and travel support from Kite/Gilead Sciences. **RDK:** employment with, stock or other ownership in, and travel support from Kite, a Gilead Company. **BDS:** consulting/advisory role for Adaptive Biotechnologies, Amgen, Autolus, BeiGene, Bristol Myers Squibb, Century Therapeutics, Deciphera, Jazz, Kite, a Gilead Company, Lilly, Novartis, Precision Biosciences, Pfizer, and Takeda; research funding from Jazz Pharmaceuticals, Kite, and Servier; and other relationship with PeproMene Bio.