

# Long-Term (4- and 5-Year) Overall Survival in ZUMA-1, the Pivotal Study of Axicabtagene Ciloleucel in Patients with Refractory Large B-Cell Lymphoma

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## BACKGROUND

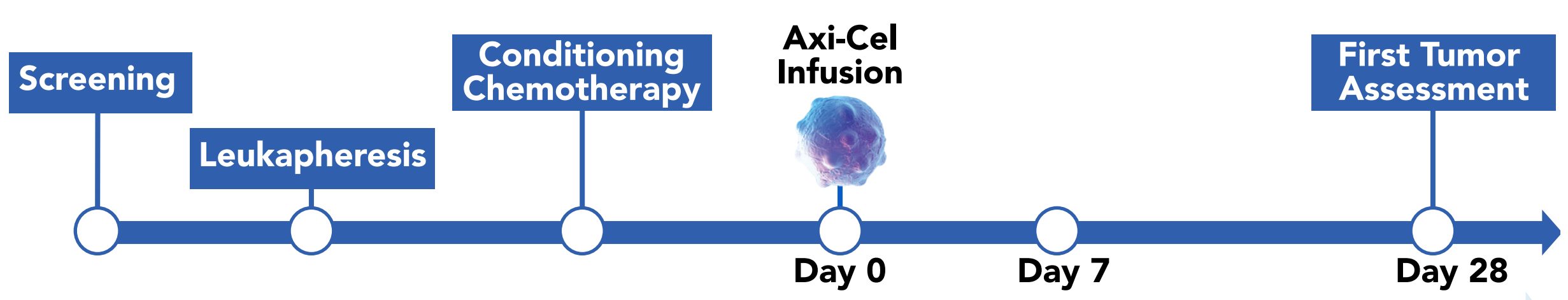
- Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved for the treatment of patients with relapsed/refractory large B-cell lymphoma (LBCL) after ≥2 prior therapies<sup>1,2</sup>
- ZUMA-1 (NCT02348216) is the multicenter, single-arm, registrational Phase 1/2 study of axi-cel in patients with refractory LBCL<sup>3,4</sup>
- In the 2-year analysis of ZUMA-1 (n=101; median follow-up from axi-cel dosing to data cutoff, 27.1 months), the objective response rate (ORR) in the pivotal Cohorts 1 and 2 was 83% (including 58% with complete response [CR]) with a 2-year overall survival (OS) rate of 50.5%<sup>4</sup>
- After ≥4 years of follow-up (median follow-up, 51.1 months), median OS was 25.8 months, with a 4-year OS rate of 44%<sup>5</sup>
- Here, we report updated survival results from Phase 2 of ZUMA-1 after 5 years of follow-up, including an exploratory analysis of OS by event-free survival (EFS) status at 12 and 24 months

## OBJECTIVE

- To present the 5-year updated analysis of Cohorts 1 and 2 from Phase 2 of ZUMA-1
- To explore the potential role of EFS at 12 and 24 months as a surrogate endpoint for OS

## METHODS

Figure 1. ZUMA-1 Treatment Schema



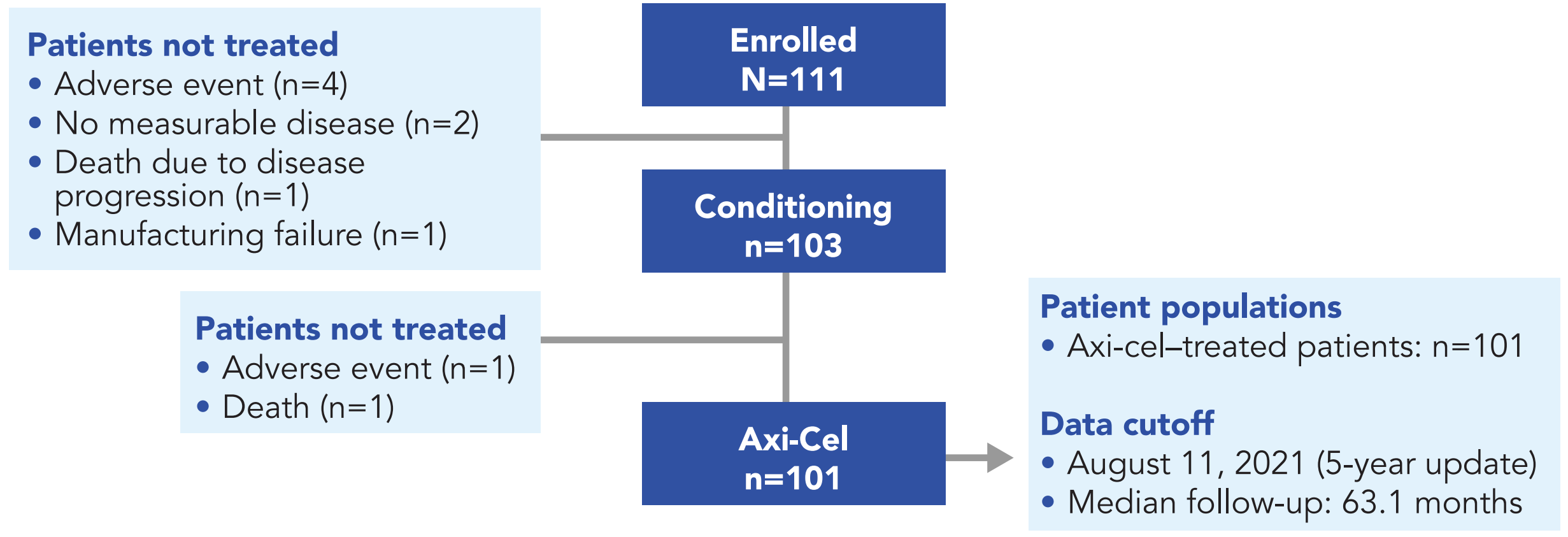
<b>Key Eligibility Criteria for ZUMA-1</b>	<b>Conditioning Regimen</b>	<b>Primary Endpoint</b>
<ul style="list-style-type: none"> <li>Refractory LBCL (DLBCL, PMBCL, TFL)</li> <li>No response to last chemotherapy or relapse ≤12 months post ASCT</li> <li>Prior anti-CD20 monoclonal antibody and anthracycline</li> </ul>	<ul style="list-style-type: none"> <li>Cyclophosphamide 500 mg/m<sup>2</sup> and fludarabine 30 mg/m<sup>2</sup> for 3 days</li> <li>Axi-Cel • 2 × 10<sup>6</sup> CAR+ cells/kg</li> </ul>	<ul style="list-style-type: none"> <li>ORR, with first response assessment 4 weeks post-infusion</li> </ul>
		<b>Key Additional Endpoints</b>
		<ul style="list-style-type: none"> <li>OS, safety, and translational evaluations</li> </ul>

ASCT, autologous stem cell transplantation; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; LBCL, large B-cell lymphoma; ORR, objective response rate; OS, overall survival; PMBCL, primary mediastinal B-cell lymphoma; TFL, transformed follicular lymphoma.

- Median OS, 5-year survival rates, and time to next therapy were estimated using Kaplan-Meier methodology
- Time to next therapy was defined as time from axi-cel infusion to initiation of new anticancer therapy, including CAR T-cell retreatment and excluding stem cell transplantation (SCT), or death from any cause
- Blood levels of CAR T cells were quantified using a validated polymerase chain reaction assay
- Exploratory analysis of OS by EFS at 12 and 24 months
  - EFS was defined as time from axi-cel infusion until disease progression, initiation of new anticancer therapy (excluding SCT), or any-cause death
  - Kaplan-Meier methodology was used to estimate median OS, 5-year OS rates, median EFS, EFS rates, and comparisons of OS by EFS outcomes

## RESULTS

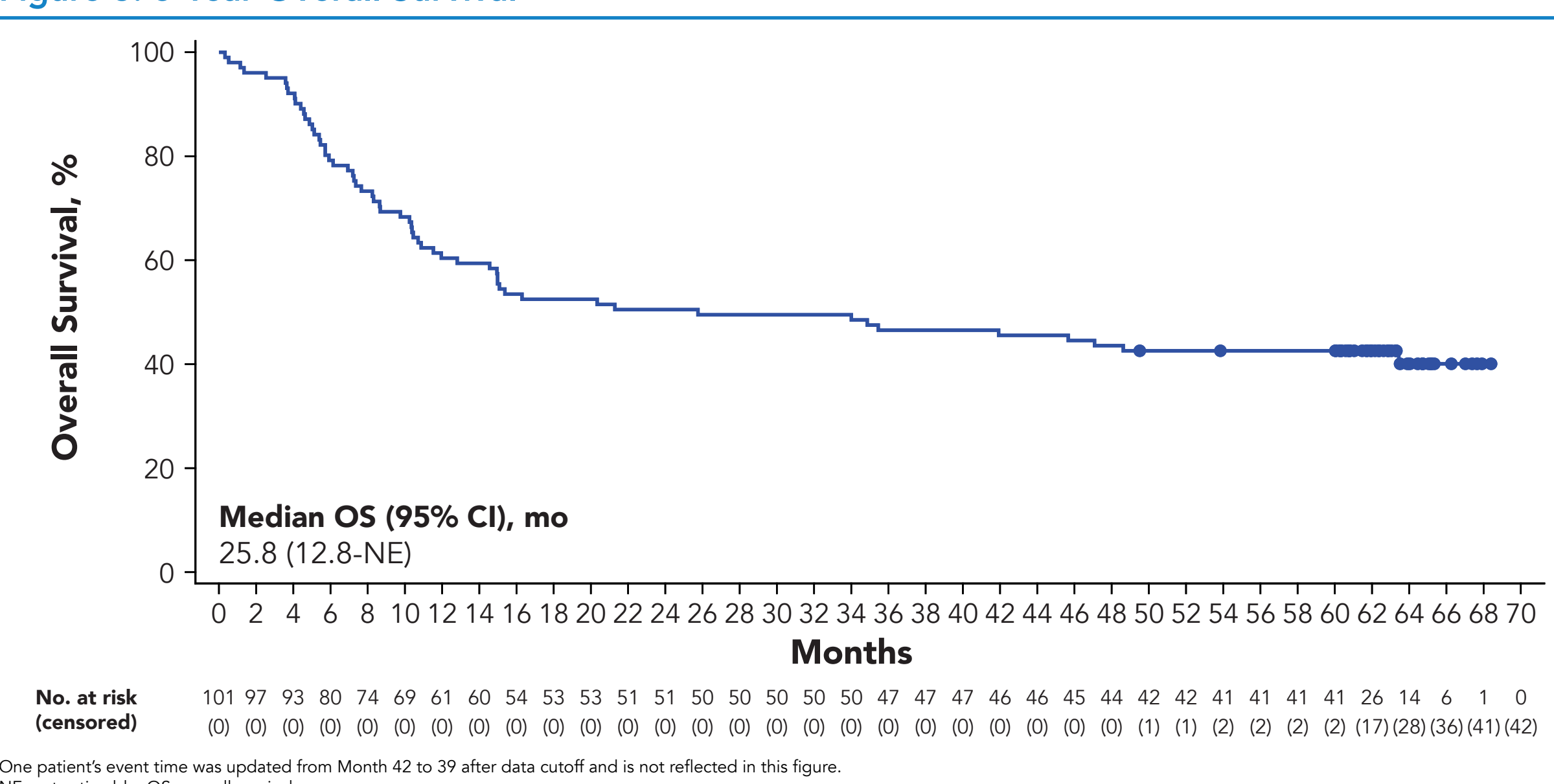
Figure 2. ZUMA-1 Phase 2 Patient Disposition



Axi-cel, axicabtagene ciloleucel.

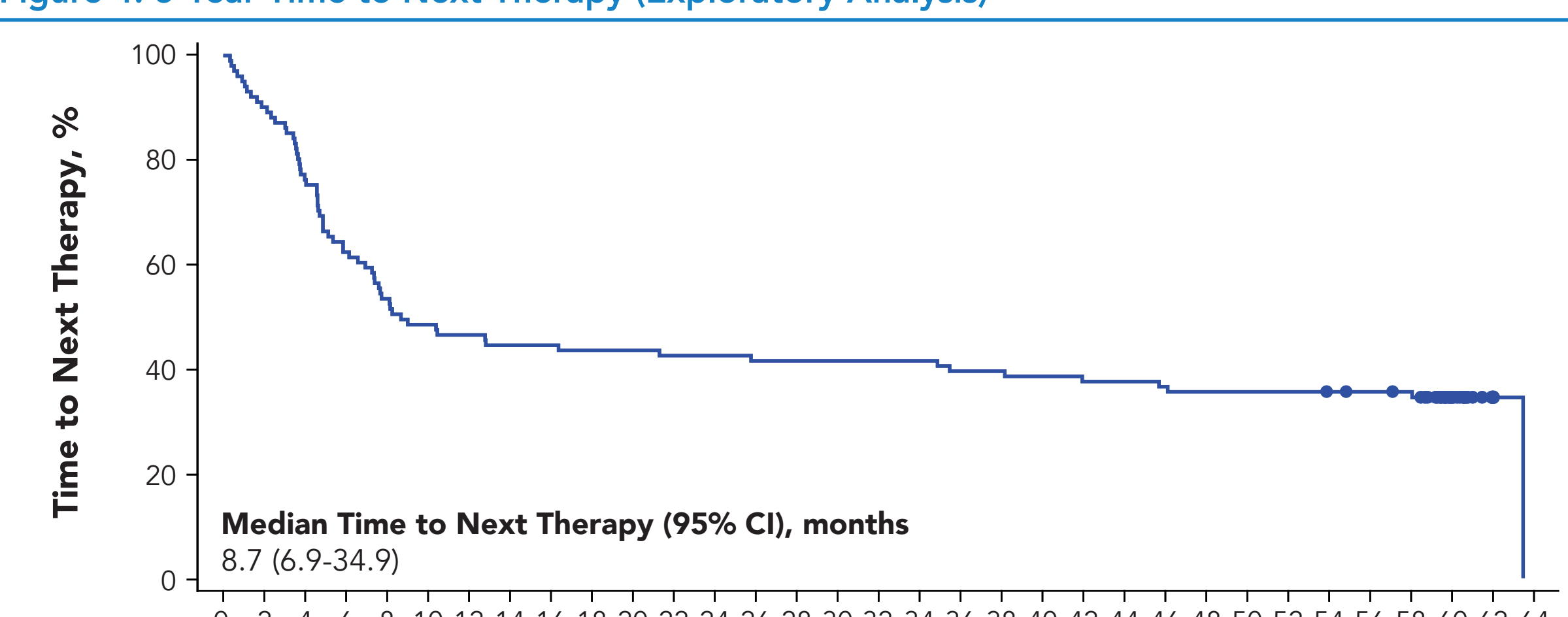
## RESULTS (continued)

Figure 3. 5-Year Overall Survival



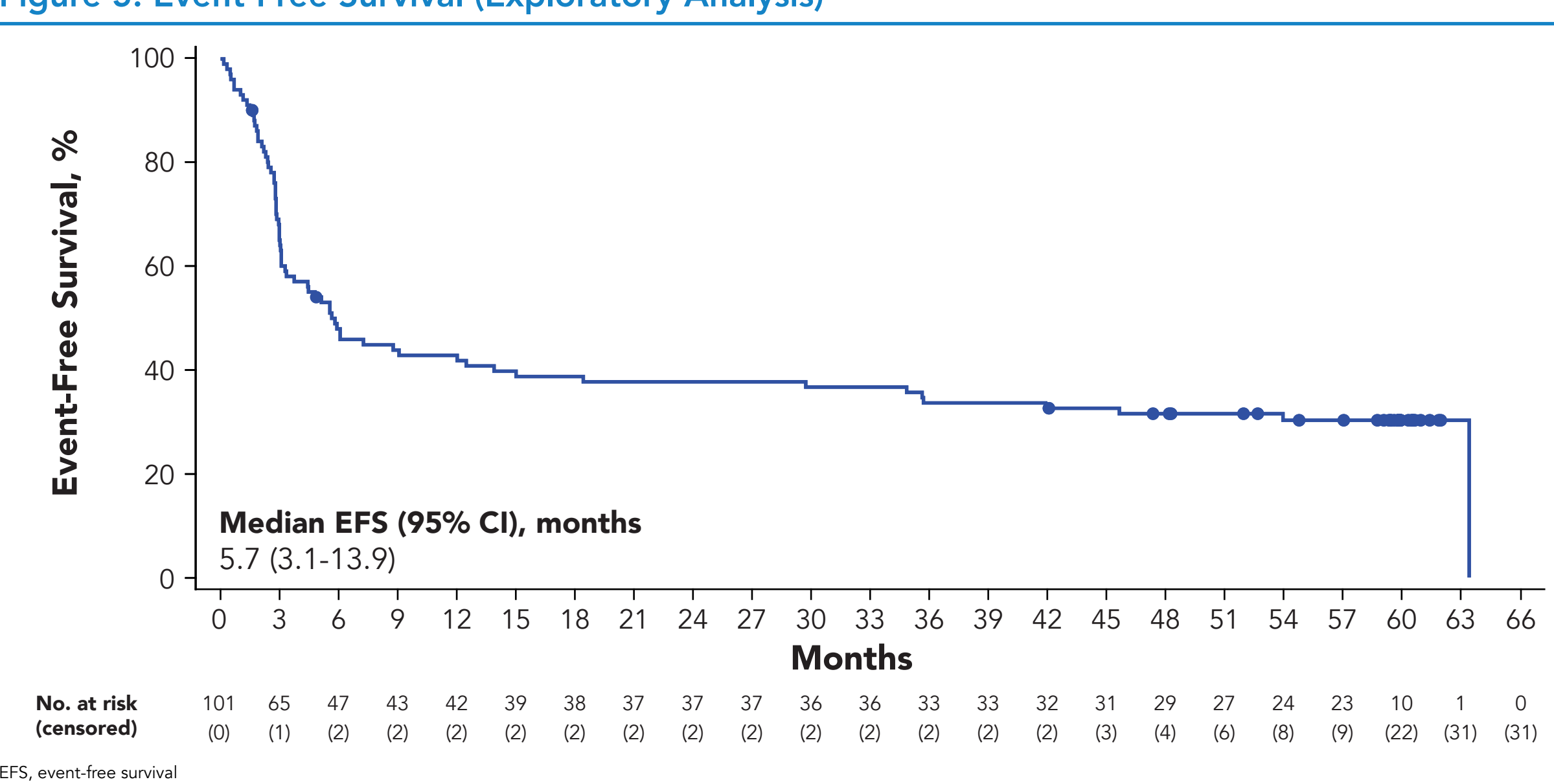
- With ≥5 years of follow-up, the 5-year OS rate was 42.6% (95% CI, 32.8-51.9) among patients treated with axi-cel
- The 5-year OS rate among complete responders was 64.4% (95% CI, 50.8-75.1); the median survival time among complete responders was not reached (95% CI, 63.4-NE); 37 of 59 CR patients (63%) are still alive at the 5-year data cutoff
- Since the 4-year data cutoff, 1 death at Month 63 (CR) and 1 progressive disease at month 54 (PR) were observed

Figure 4. 5-Year Time to Next Therapy (Exploratory Analysis)



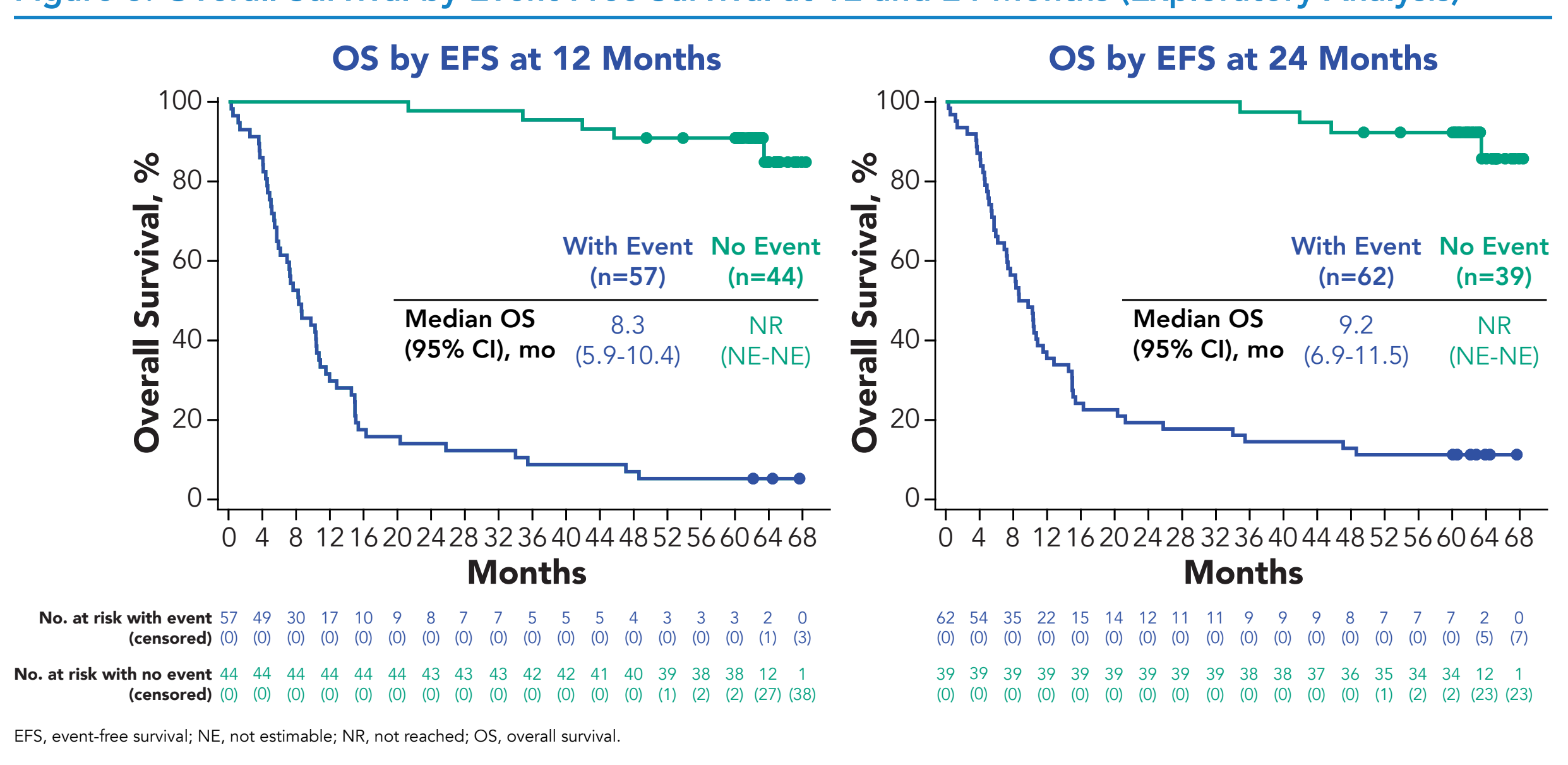
- Median time to next anticancer therapy was 8.7 months (range, 0.3-63.4) after axi-cel infusion, unchanged from previous reports<sup>5</sup>
- By the Year 5 data cutoff, 34 patients (34%) were still alive and received no subsequent therapy (excluding SCT) or retreatment with axi-cel
- Compared with the Year 4 data,<sup>5</sup> 2 patients (2%) who had previously progressed received new anticancer therapy

Figure 5. Event-Free Survival (Exploratory Analysis)



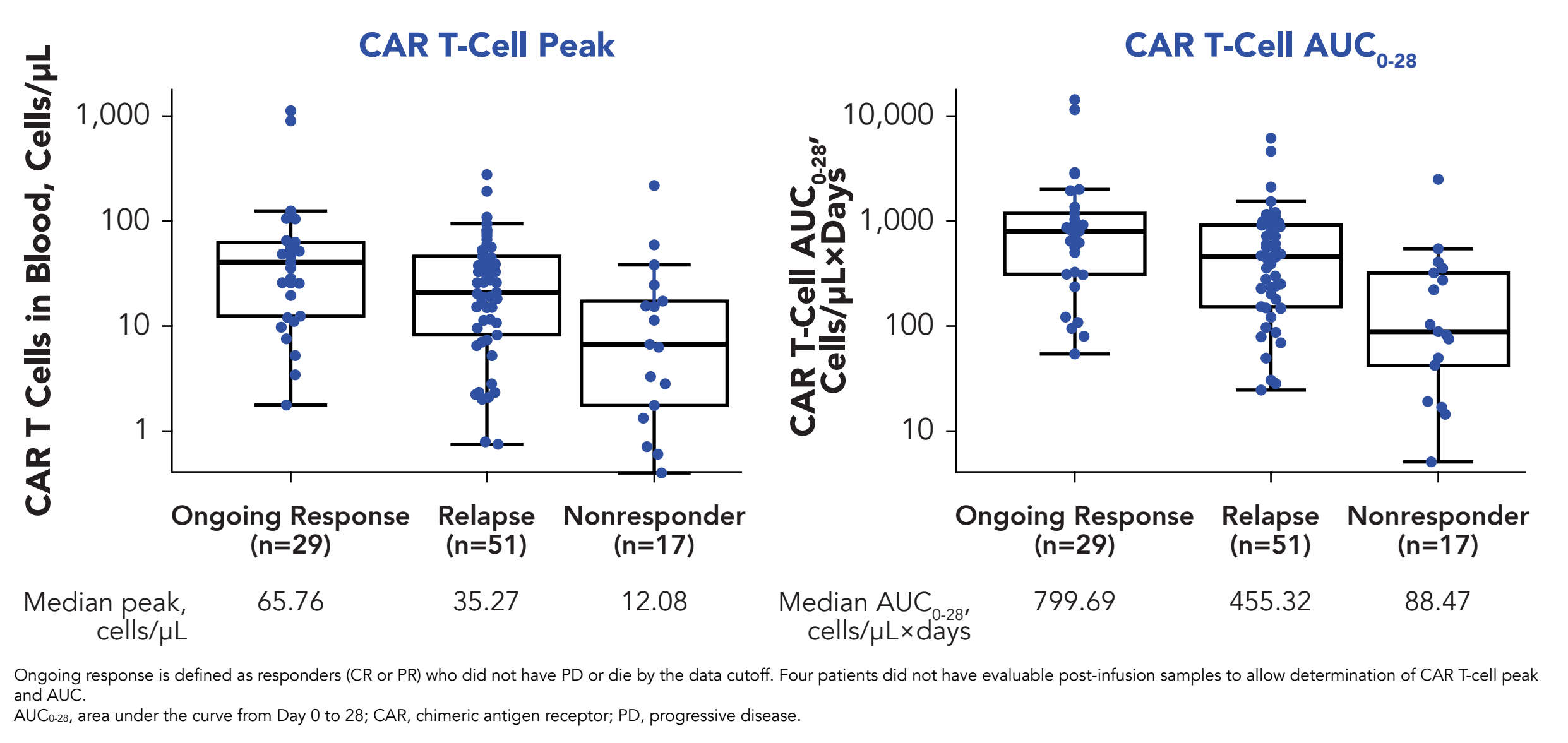
- Among all treated patients, the 12-month EFS rate was 42.8% (95% CI, 33.0-52.3) and the 24-month EFS rate was 37.7% (95% CI, 28.3-47.2)

Figure 6. Overall Survival by Event-Free Survival at 12 and 24 Months (Exploratory Analysis)



- Among patients with (n=57) and without (n=44) an EFS event by Month 12, respectively, 5-year OS rates were 5.3% (95% CI, 1.4-13.2) and 90.9% (95% CI, 77.6-96.5)
- Among patients with (n=62) and without (n=39) an EFS event by Month 24, respectively, 5-year OS rates were 11.3% (95% CI, 5.0-20.5) and 92.3% (95% CI, 78.0-97.5)

Figure 7. Early CAR T-Cell Expansion Associates With Ongoing Response at Month 60



- Median peak CAR T-cell levels were numerically higher in patients with ongoing response at Month 60 and were considerably lower in patients who relapsed and nonresponders
- A similar trend was observed with CAR T-cell expansion by area under the curve from Day 0 to 28

Table 1. Deaths

n (%)	Total N=101	Year 1	Year 2	Year 3	Year 4	Year 5	Year >5
<b>Patients who died</b>	<b>59 (58)</b>	<b>40 (40)</b>	<b>10 (10)</b>	<b>4 (4)</b>	<b>3 (3)</b>	<b>1 (1)</b>	<b>1 (1)</b>
<b>Primary cause of death</b>							
Progressive disease <sup>a</sup>	45 (45)	32 (32)	9 (9)	3 (3)	0	1 (1)	0
Other <sup>b</sup>	9 (9)	5 (5)	0	1 (1)	3 (3)	0	0
Adverse event <sup>c</sup>	4 (4)	3 (3)	1 (1)	0	0	0	0
Secondary malignancy	1 (1)	0	0	0	0	0	1 (1)

<sup>a</sup>During ongoing safety monitoring after the data cutoff, one event of CNS lesion which was not amenable to biopsy was reported. Treatment for presumed progressive disease for diffuse large B-cell lymphoma was initiated by the investigator. <sup>b</sup>Events included infection (n=3), cardiac arrest (n=2), pulmonary neoplasm (n=1), sepsis (n=1), complications of allogeneic transplant for previous treatment-related MDS not related to axi-cel (n=1), and unknown (n=1). <sup>c</sup>Two events had no causal relationship (sepsis, pulmonary embolism) and 2 events were related to axi-cel (brain injury due to cardiac arrest and hemophagocytic lymphohistiocytosis). Axi-cel, axicabtagene ciloleucel; MDS, myelodysplastic syndrome.

- Among treated patients, 58% have died as of the data cutoff date (Table 1)
- Following the 4-year data cutoff date<sup>5</sup>
  - There has been 1 death which was due to secondary malignancy (prior therapy- and/or conditioning chemotherapy-related myelodysplastic syndrome while in CR for LBCL)
    - No patients received intravenous immunoglobulin
- As of the 5-year data cutoff, no new safety signals have been reported, including
  - No serious adverse events related to axi-cel
  - No secondary malignancies related to axi-cel

## CONCLUSIONS

- In this updated, 5-year analysis of the Phase 2 pivotal cohorts of ZUMA-1, axi-cel induced long-term overall survival with no new safety signals in patients with refractory LBCL
  - In treated patients, the 5-year OS rate was 42.6%
  - Between the 4-year and 5-year analyses, the time to next therapy curve remained stable, and 92% of patients remained alive without need of subsequent therapy, which may be suggestive of a cure for these patients
  - Safety findings were similar to those in previous reports,<sup>3-5</sup> with no new safety signals observed
- Durable responses were strongly associated with peak CAR T-cell expansion
- The exploratory analysis of long-term OS by EFS status appears highly correlative in refractory LBCL
  - These findings can potentially support use of 1-year and 2-year EFS as a surrogate endpoint for long-term OS in R/R LBCL

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## DISCLOSURES

**CAJ:** honoraria from Kite, a Gilead Company, Celgene, Novartis, bluebird bio, Epizyme, Humanigen, Pfizer, Precision BioSciences, Nkarta, Lonza, and AbbVie; consultancy or advisory role for Kite, a Gilead Company, Celgene, Novartis, Pfizer, Humanigen, Precision BioSciences, Nkarta, bluebird bio, Lonza, Pfizer, Ipsen and AbbVie; speakers' bureau participation for AstraZeneca, Celgene, and Seattle Genetics; research funding from Pfizer; and travel support from Kite, a Gilead Company, Celgene, Novartis, Precision BioSciences, Lonza, Pfizer, and Humanigen. **FLJ:** consulting or advisory role with ecoRI, Emerging Therapy Solutions Geneva Lehman Group, Allogene, Amgen, bluebird bio, Bristol Myers Squibb (BMS)/Celgene, Calibr, Invance, Kite, a Gilead Company, Janssen, Legend Biotech, Novartis, Umajo, Cowen, Cellular Biomedicine Group, GammaDelta Therapeutics, Wugen; research funding from Kite, a Gilead Company, Allogene and Novartis; and patents, royalties, other intellectual property from several patents held by the institution in my name (licensed) in the field of cellular immunotherapy. **AG:** consultancy or advisory role for Kite, a Gilead Company, Amgen, Atara, Wugen Inc., and Celgene; research funding from Kite, a Gilead Company, and Amgen; and honoraria from Kite, a Gilead Company. **BBM:** consultancy or advisory role for Kite, a Gilead Company, Novartis, Juno-Celgene-BMS, Allogene, Precision BioScience, Adicet, Pharmaclytics, Janssen, Takeda, Adaptive Biotechnologies and Miltenyi Biotechonologies; research funding from Kite, a Gilead Company, Novartis, Juno-Celgene-BMS, Allogene, Precision BioSciences, Adicet, Adaptive Biotechnologies; and patents, royalties, or other intellectual property from Pharmaclytics, Legend Biotech, and Humanigen. **JNT:** stock or other ownership in Genmab, Corvus, Marker Therapeutics, TG Therapeutics and bluebird bio; consultancy or advisory role for Kite, a Gilead Company, and research funding from BMS, Kite, a Gilead Company, Spectrum Pharmaceuticals, and Merck. **AD:** consultancy or advisory role for Kite, a Gilead Company, Janssen, and Adicet. **PMR:** consultancy or advisory role for Kite, a Gilead Company, and Curis; and research funding from Seattle Genetics and Genentech. **PS:** honoraria from MorphoSys and Karyopharm; consultancy or advisory role for MorphoSys, Karyopharm, and Bristol Myers Squibb (BMS), Kite, a Gilead Company, Janssen, and Genentech. **BT:** honoraria from Kite, a Gilead Company, Janssen, and Celgene. **MR:** honoraria from Kite, a Gilead Company, Janssen, and Celgene. **PF:** employment with Sarah Cannon Research Institute, stock or other ownership in Johnson & Johnson; consultancy or advisory role for AbbVie, AstraZeneca, BeiGene, Genentech, Gilead, Great Point Partners, Hutchison MediPharma, Ikusuda Therapeutics, Janssen, Juno Therapeutics, Kite, a Gilead Company, MorphoSys, Novartis, Nurix Therapeutics, Pharmaclytics, Roche, Seattle Genetics, Takeda, TG Therapeutics, Unum Therapeutics (Cogent BioSciences), Verastem, Vincer Pharma and Yngli Pharmaceuticals; and research funding from AbbVie, Acerta Pharma, Agios, Aduro, AstraZeneca, BeiGene, Calithera Biosciences, Celgene, Constellation Pharmaceuticals, Curis, Forma Therapeutics, Forty Seven, Genentech, Gilead Sciences, IGM Biosciences, Incyte, Infinity Pharmaceuticals, Janssen, Juno Therapeutics, Karyopharm Therapeutics, Kite, a Gilead Company, Loxo Oncology, Merck, MorphoSys, Novartis, Pfizer, Pharmaclytics, Portola Pharmaceuticals, Phizen Pharmaceuticals, Roche, Seattle Genetics, Takeda, Teva, TG Therapeutics, Trillium Therapeutics, Triphase Research & Development Corp., Unum Therapeutics (Cogent BioSciences), Verastem, Vincer Pharma and Yngli Pharmaceuticals; and research funding from Regional Cancer Care Associates/OMI; leadership role at COA (Cancer Outcome Tracking Analysis) and Genomic Testing Cooperative; stock or other ownership in COA and Genomic Testing Cooperative; honoraria from Celgene, Elsevier PracticeUpdate; Oncology, Kite, a Gilead Company, AstraZeneca, Xcenda, OnLive Peer Exchange, Janssen, Novartis, MorphoSys, Incyte, Pharmaclytics, BMS and Vincer; consultancy or advisory role for Physicians' Education Resource, Celgene, Elsevier PracticeUpdate; Oncology, Janssen, Kite, a Gilead Company, Medscape, Michael J. 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