Poster
58

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

Caron A. Jacobson, MD, MMSc[1]; Frederick L. Locke, MD[2]; Armin Ghobadi, MD[3]; David B. Miklos, MD, PhD[4]; Lazaros J. Lekakis, MD[5]; Olalekan O. Oluwole, MBBS, MPH[6]; Yi Lin, MD, PhD[7]; Brian T. Hill, MD, PhD[8]; John M. Timmerman, MD[9]; Abhinav Deol, MD[10]; Patrick M. Reagan, MD[11]; Patrick Stiff, MD[12]; Ian W. Flinn, MD, PhD[13]; Umar Farooq, MD[14]; Andre H. Goy, MD[15]; Javier Muñoz, MD, MS, MBA, FACP[16]; Tanya Siddiqi, MD[17]; Rhine R. Shen, PhD[18]; Adrian A. Bot, MD, PhD[18]; Jinghui Dong, PhD[18]; Kanwarjit Singh, MD[18]; Clare Spooner, MBBS[18]; Roshan Karalliyadda, PhD[18]; Jenny J. Kim, MD, MS[18]; Yan Zheng, MS[18]; and Sattva S. Neelapu, MD[19]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Moffitt Cancer Center, Tampa, FL, USA; [3]Washington University School of Medicine, St Louis, MO, USA; [4]Stanford University School of Medicine, Stanford, CA, USA; [5]Sylvester Comprehensive Cancer Center, University of Miami Health System, Miami, FL, USA; [6]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [7]Mayo Clinic, Rochester, MN, USA; [8]Cleveland Clinic Foundation, Cleveland, OH, USA; [9]UCLA David Geffen School of Medicine, Los Angeles, CA USA; [10]Karmanos Cancer Center, Wayne State University, Detroit, MI, USA; [11]University of Rochester School of Medicine, Rochester, NY, USA; [12]Loyola University Chicago Stritch School of Medicine, Maywood, IL, USA; [13]Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA; [14]University of Iowa, Iowa City, IA, USA; [15]John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ, USA; [16]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [17]City of Hope National Medical Center, Duarte, CA, USA; [18]Kite, a Gilead Company, Santa Monica, CA, USA; [19]The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

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[1,2]
- ZUMA-1 (NCT02348216) is the multicenter, single-arm, registrational Phase 1/2 study of axi-cel in patients with refractory LBCL[3,4]
- 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 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%[4]
- 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%[5]
- 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

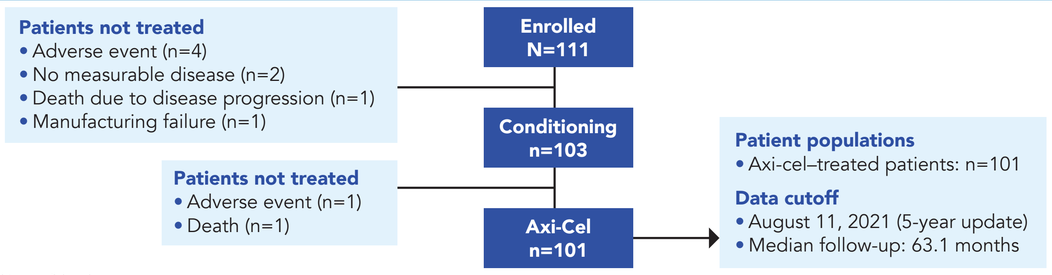
- To present the 5-year updated analysis of Cohorts 1 and 2 from Phase 2 of ZUMA-1
- To explore the potential role of EFS at 12 and 24 months as a surrogate endpoint for OS

METHODS

- The study protocol for Phase 2 Cohorts 1 and 2 of ZUMA-1 was previously described[3]
- 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

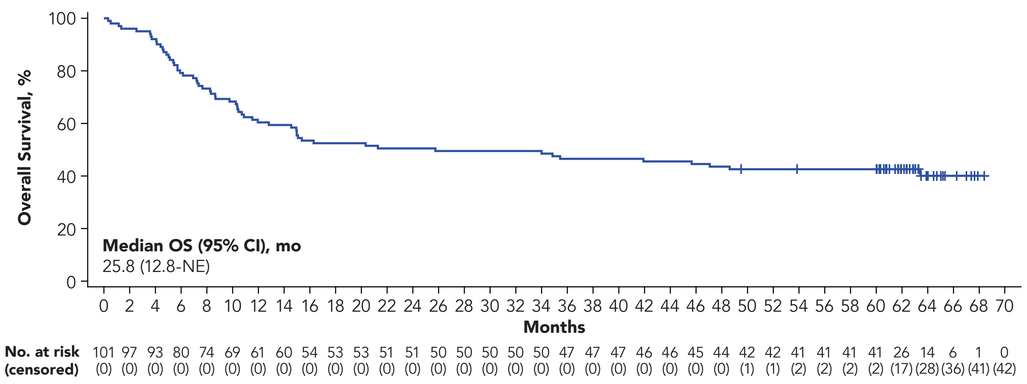
RESULTS

Figure 1. ZUMA-1 Phase 2 Patient Disposition



Axi-cel, axicabtagene ciloleucel.

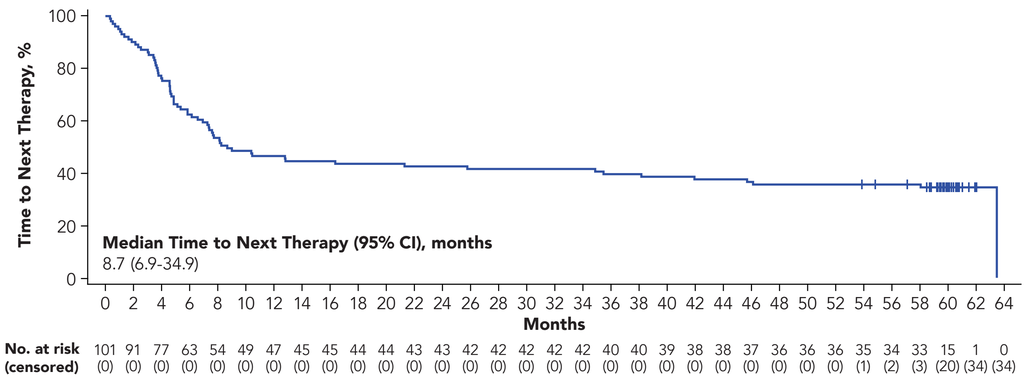
Figure 2. 5-Year Overall Survival



One patient's event time was updated from Month 42 to 39 after data cutoff and is not reflected in this figure.
NE, not estimable; OS, overall survival.

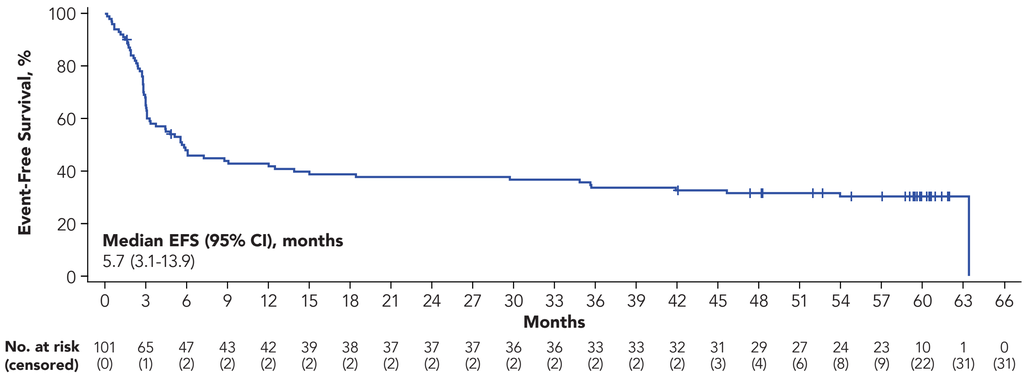
- With ≥5 years of follow-up, the 5-year OS rate was 42.6% (95% CI, 32.8-51.9) among patients treated with axi-cel
- The 5-year OS rate among complete responders was 64.4% (95% CI, 50.8-75.1); the median survival time among complete responders was not reached (95% CI, 63.4-not estimable); 37 of 59 CR 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 (partial response) were observed

Figure 3. 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[5]
- 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,[5] 2 patients (2%) who had previously progressed received new anticancer therapy

Figure 4. Event-Free Survival (Exploratory Analysis)

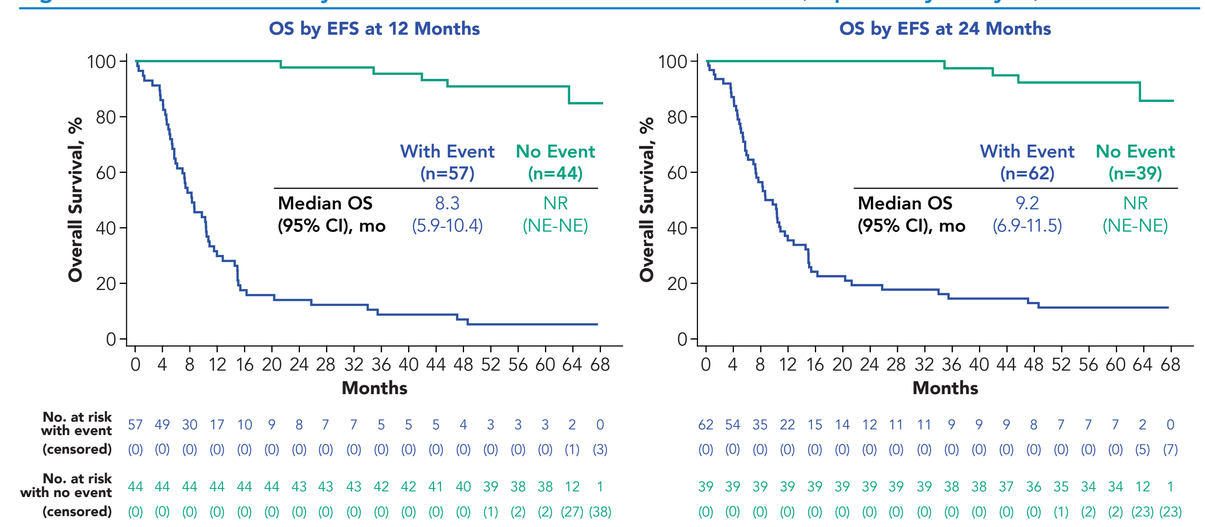


EFS, event-free survival

- 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)

RESULTS *(continued)*

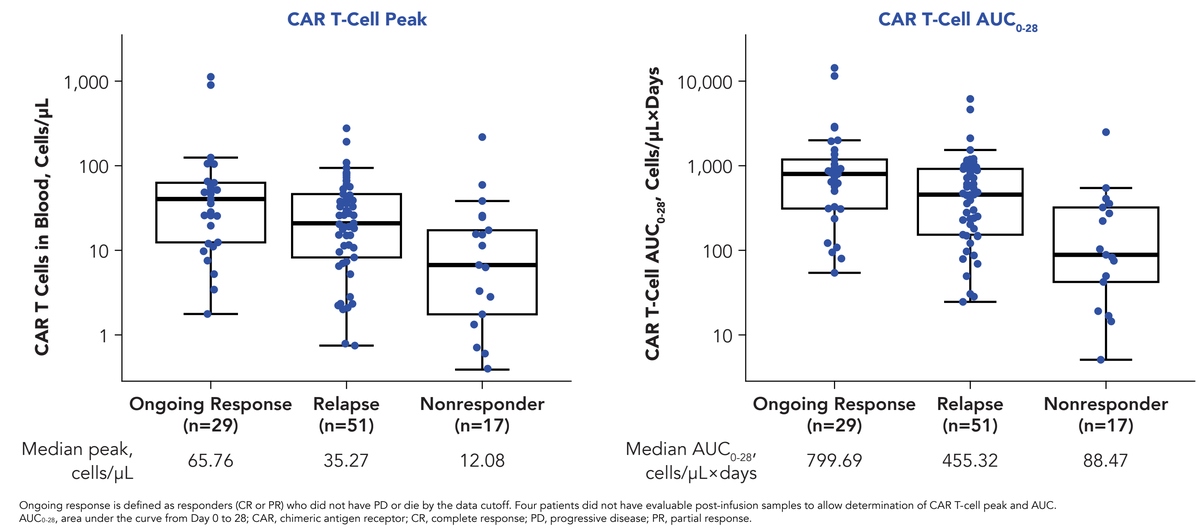
Figure 5. Overall Survival by Event-Free Survival at 12 and 24 Months (Exploratory Analysis)



EFS, event-free survival; NE, not estimable; NR, not reached; OS, overall survival.

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



Ongoing response is defined as responders (CR or PR) who did not have PD or die by the data cutoff. Four patients did not have evaluable post-infusion samples to allow determination of CAR T-cell peak and AUC.
$AUC_{0\text{-}28}$, area under the curve from Day 0 to 28; CAR, chimeric antigen receptor; CR, complete response; PD, progressive disease; PR, partial response.

- 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
Patients who died	**59 (58)**	**40 (40)**	**10 (10)**	**4 (4)**	**3 (3)**	**1 (1)**	**1 (1)**
Primary cause of death							
Progressive disease[a]	45 (45)	32 (32)	9 (9)	3 (3)	0	1 (1)	0
Other[b]	9 (9)	5 (5)	0	1 (1)	3 (3)	0	0
Adverse event[c]	4 (4)	3 (3)	1 (1)	0	0	0	0
Secondary malignancy	1 (1)	0	0	0	0	0	1 (1)

[a] 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. [b] Events included infection (n=3), cardiac arrest (n=2), pulmonary nocardiosis (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). [c] 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; CNS, central nervous system; MDS, myelodysplastic syndrome.

- Among treated patients, 58% have died as of the data cutoff date (**Table 1**)
- Following the 4-year data cutoff date[5]
  - 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 OS 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,[3-5] 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

REFERENCES

1. YESCARTA® (axicabtagene ciloleucel) Prescribing information. Kite Pharma, Inc; 2021.
2. YESCARTA® (axicabtagene ciloleucel) Summary of product characteristics. Kite Pharma EU B.V.; 2021.
3. Neelapu SS, et al. *N Engl J Med*. 2017;377:2531-2544.
4. Locke FL, et al. *Lancet Oncol*. 2019;20:31-42.
5. Jacobson C, et al. ASH 2020. #1187.

ACKNOWLEDGMENTS

- The patients, families, friends, and caregivers
- The study investigators, coordinators, and health care staff at each study site
- We would like to thank Debbie Mirjah-Jablonski, MD, of Kite, a Gilead Company, for her contributions as the study safety physician
- Medical writing support was provided by Grace Lewis, PharmD, of Nexus Global Group Science LLC, funded by Kite, a Gilead Company

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, Ispen, and AbbVie; speakers' bureau participation for Axis and Clinical Care Options; research funding from Pfizer; and travel support from Kite, a Gilead Company, Celgene, Novartis, Precision Biosciences, Lonza, Pfizer, and Humanigen.

Full author disclosures are available at the following Quick Response (QR) code:

FULL AUTHOR 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, Ispen, and AbbVie; speakers' bureau participation for Axis and Clinical Care Options; research funding from Pfizer; and travel support from Kite, a Gilead Company, Celgene, Novartis, Precision Biosciences, Lonza, Pfizer, and Humanigen. **FLL:** consulting or advisory role with ecoR1, Emerging Therapy Solutions Gerson Lehman Group, Allogene, Amgen, bluebird bio, Bristol Myers Squibb (BMS)/Celgene, Calibr, Iovance, Kite, a Gilead Company, Janssen, Legend Biotech, Novartis, Umoja, 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 (unlicensed) 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. **DBM:** consultancy or advisory role for Kite, a Gilead Company, Novartis, Juno-Celgene-BMS, Allogene, Precision Bioscience, Adicet, Pharmacyclics, Janssen, Takeda, Adaptive Biotechnologies and Miltenyi Biotechnologies; 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 Pharmacyclics. **LJL:** no relevant financial relationships to disclose. **OOO:** consultancy or advisory role for Kite, a Gilead Company, Janssen, Pfizer, Novartis, Janssen, and Curio Science; honoraria from Kite, a Gilead Company; and research funding from Kite, a Gilead Company. **YL:** consultancy or advisory role for Kite, a Gilead Company, Janssen, Novartis, Celgene, bluebird bio, Juno, Legend, Sorrento, Gamida Cell, and Vineti; research funding from Kite, a Gilead Company, Janssen, Celgene, bluebird bio, Merck, and Takeda. **BTH:** honoraria from Kite, a Gilead Company; consultancy or advisory role for Kite, a Gilead Company; research funding from Kite, a Gilead Company; and travel support from Kite, a Gilead Company. **JMT:** 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 CRISPR Therapeutics; and research funding from Kite, a Gilead Company, Amgen, MacroGenics, BMS, Janssen, Gamida-Cell, Seattle Genetics. **IWF:** 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, Iksuda Therapeutics, Janssen, Juno Therapeutics, Kite, a Gilead Company, MorphoSys, Novartis, Nurix Therapeutics, Pharmacyclics, Roche, Seattle Genetics, Takeda, TG Therapeutics, Unum Therapeutics (Cogent Biosciences), Verastem, Vincerx Pharma and Yingli Pharmaceuticals; and research funding from AbbVie, Acerta Pharma, Agios, ArQule, 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, Pharmacyclics, Portola Pharmaceuticals, Rhizen Pharmaceuticals, Roche, Seattle Genetics, Takeda, Teva, TG Therapeutics, Trillium Therapeutics, Triphase Research & Development Corp., Unum Therapeutics (Cogent Biosciences), and Verastem. **UF:** honoraria from Kite, a Gilead Company. **AHG:** employment with Regional Cancer Care Associates/OMI; leadership role at COTA (Cancer Outcome Tracking Analysis) and Genomic Testing Cooperative; stock or other ownership in COTA and Genomic Testing Cooperative; honoraria from Celgene, Elsevier PracticeUpdate: Oncology, Kite, a Gilead Company, AstraZenca, Xcenda, OncLive Peer Exchange, Janssen, Novartis, MorphoSys, Incyte, Pharmacyclics, BMS and Vincerx; consultancy or advisory role for Physicians' Education Resource, Celgene, Elsevier PracticeUpdate: Oncology, Janssen, Kite, a Gilead Company, Medscape, Michael J. Hennessy Associates, Inc., Novartis, BMS, AbbVie, and Pharmacyclics; research funding from Acerta, AstraZeneca, Celgene, Genentech, Hoffmann-La Roche, Infinity Pharmaceuticals, Janssen, Karyopharm, and Pharmacyclics; and other relationships with MorphoSys, Incyte Steering Committee, AstraZeneca MCL Steering Committee and Vincerx- Scientific Advisory Board. **JM:** honoraria from Targeted Oncology, OncView, Curio, Kyowa Kirin, Physicians' Education Resource, and Seattle Genetics; consultancy or advisory role for Pharmacyclics/AbbVie, Bayer, Kite, a Gilead Company, Pfizer, Janssen, Juno/Celgene, BMS, Kyowa Kirin, Alexion, Fosun Kite, Innovent, Seattle Genetics, BeiGene, Debiopharm, Epizyme, Karyopharm, ADC Therapeutics, Servier, and Genmab; speakers' bureau participation for Kite, a Gilead Company, Kyowa, Bayer, Pharmacyclics/Janssen, Seattle Genetics, Acrotech/Aurobindo, BeiGene, Verastem, AstraZeneca, Celgene/BMS, and Genentech/Roche; and research funding (paid to institution) from Bayer, Gilead/Kite Pharma, Celgene, Merck, Portola, Incyte, Genentech, Pharmacyclics, Seattle Genetics, Janssen, Millennium. **TS:** consultancy or advisory role for AstraZeneca, PCYC, Celgene, Juno, Kite, a Gilead Company, and BeiGene; speakers' bureau participation for PCYC, Janssen, AstraZeneca, and Seattle Genetics; and research funding from PCYC, Juno, Kite, a Gilead Company, AstraZeneca, BeiGene, Oncternal, TG Therapeutics, and Celgene. **RRS:** employment with Kite, a Gilead Company and Atara; leadership role with Kite, a Gilead Company and Atara; stock or other ownership in Kite, a Gilead Company and Atara; and patents, royalties and other intellectual property from Kite, a Gilead Company and Atara. **AAB:** employment with Kite, a Gilead Company and Gilead Sciences; stock or other ownership in Gilead Sciences; consultancy or advisory role for Gilead Sciences; travel support from Gilead Sciences. **JD:** employment with Kite, a Gilead Company; stock or other ownership in Gilead Sciences; consultancy or advisory role for GliaCure/Tufts; and patents, royalties, or other intellectual property from GliaCure/Tufts. **KS:** employment with Kite, a Gilead Company; and stock or other ownership in Kite, a Gilead Company. **CS:** employee with Kite, a Gilead Company; stock or other ownership with Gilead Sciences. **RK:** employment with Kite, a Gilead Company and Gilead Sciences; stock or other ownership with Gilead Sciences. **JJK:** employment with Kite, a Gilead Company; and stock or other ownership in Gilead. **YZ:** employment with Kite, a Gilead Company; and stock or other ownership in Gilead. **SSN:** consulting fees or honorarium from Kite, a Gilead Company, Merck, BMS, Novartis, Celgene, Pfizer, Allogene Therapeutics, Cell Medica/Kuur, Incyte, Precision Biosciences, Legend Biotech, Adicet Bio, Calibr, Unum Therapeutics, and bluebird bio, Medscape, Aptitude Health, Bio Ascend, and MJH Life Sciences; personal fees from Kite, a Gilead Company, Merck, BMS, Novartis, Celgene, Pfizer, Allogene, Kuur, Incyte, Precision BioSciences, Legend, Adicet Bio, Calibr, and Unum Therapeutics; grants, contracts, or research funding from Kite, a Gilead Company, BMS, Merck, Poseida, Cellectis, Celgene, Karus Therapeutics, Unum Therapeutics (Cogent Biosciences), Allogene, Precision BioSciences, Acerta and Adicet Bio; and patents, royalties, or other intellectual property from Takeda Pharmaceuticals and related to cell therapy.