

## Supplementary Appendix

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This appendix has been provided by the authors to give readers additional information about the work.

## Supplementary Appendix

### Ide-cel or Standard Regimens in Relapsed and Refractory Multiple Myeloma

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**KarMMa-3 Study Countries and Sites.**

<b>Belgium</b> Universitaire Ziekenhuizen Leuven
<b>Canada</b> Tom Baker Cancer Center-University of Calgary University Health Network Princess Margaret Hospital
<b>France</b> Centre Hospitalier Univ De Nantes Hotel-Dieu CHU Lille, Université de Lille Hospital Saint-Louis – APHP IUCT Oncopole
<b>Germany</b> Medizinische Universitätsklinik Heidelberg Universitätsklinikum Würzburg University Hospital of Cologne
<b>Italy</b> Azienda Ospedaliero Universitaria di Bologna - Policlinico S. Orsola-Malpighi - Istituto di Ematologia
<b>Japan</b> Japanese Red Cross Medical Center Nagoya City University Hospital Tokai University Hospital
<b>The Netherlands</b> Erasmus MC Vrije Universiteit University Medical Centre
<b>Norway</b> Oslo Universitetssykehus, Rikshospitalet
<b>Spain</b> Clinica Universitaria de Navarra Hospital Clinico Universitario de Salamanca
<b>Switzerland</b> Department of Medical Oncology, University Hospital Inselspital and University of Bern, Bern, Switzerland
<b>United Kingdom</b> King's College Hospital-King's College Hospital NHS Foundation Trust
<b>United States</b>

Baylor University Medical Center  
Dana-Farber Cancer Institute  
Duke University Medical Center  
Fox Chase Cancer Center  
Hackensack University Medical Center  
H. Lee Moffitt Cancer Center and Research Institute  
Indiana University Melvin and Bren Simon Comprehensive Cancer Center  
Massachusetts General Hospital  
Mayo Clinic Arizona  
Mayo Clinic Florida  
Mayo Clinic, Rochester, Minnesota  
MD Anderson, University of Texas  
Memorial Sloan Kettering Cancer Center  
Mount Sinai Medical Center  
Northside Hospital Cancer Institute  
Northwestern University Feinberg School of Medicine  
Thomas Jefferson University  
UCLA Medical Center - Santa Monica Hematology and Oncology  
University of Alabama Birmingham - Bone and Marrow Transplantation and Cellular  
Therapy Program  
University of Colorado Anschutz Cancer Pavilion  
University of Kansas Hospital  
University of Maryland - Greenebaum Comprehensive Cancer Center  
University of Texas Southwestern  
University of Utah Huntsman Cancer Center  
University of Wisconsin Carbone Cancer Center  
Washington University School of Medicine  
Weill Cornell Medicine/New York Presbyterian Hospital  
Winship Cancer Institute of Emory University

## Methods

### Study Design and Patients

Key exclusion criteria included non-secretory multiple myeloma (MM) or central nervous system involvement with myeloma, previous B-cell maturation antigen (BCMA)-targeted treatment, or autologous stem cell transplantation  $\leq 12$  weeks prior to randomization.

Idecabtagene vicleucel (ide-cel) treatment consisted of 3 periods: pretreatment (leukapheresis and bridging therapy [if needed]), treatment (lymphodepleting chemotherapy and infusion with ide-cel), and post-treatment follow-up (after ide-cel infusion). If necessary, per investigator discretion, patients could receive antimyeloma bridging therapy prior to lymphodepleting chemotherapy while ide-cel was being manufactured, provided the last dose of bridging therapy was administered  $\geq 14$  days prior to lymphodepleting chemotherapy initiation. Bridging therapy may include up to 1 cycle of daratumumab/pomalidomide/dexamethasone (DPd), daratumumab/bortezomib/dexamethasone (DVd), ixazomib/lenalidomide/dexamethasone (IRd), carfilzomib/dexamethasone (Kd), or elotuzumab/pomalidomide/dexamethasone (EPd). The choice of bridging therapy was dependent on the most recent antimyeloma treatment regimen based on the following criteria per investigator discretion and was assigned prior to randomization:

- Patients who have received daratumumab in combination with pomalidomide with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive up to 1 cycle of DVd, IRd, Kd, or EPd.
- Patients who have received daratumumab in combination with bortezomib with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive up to 1 cycle of DPd, IRd, Kd, or EPd.
- Patients who have received ixazomib in combination with lenalidomide with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive up to 1 cycle of DPd, DVd, Kd, or EPd.

- Patients who have received carfilzomib with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive up to 1 cycle of DPd, DVd, IRd, or EPd.
- Patients who have received elotuzumab in combination with pomalidomide with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive up to 1 cycle of DPd, DVd, IRd, or Kd.

Patients who met at least one of the following criteria on the day of scheduled ide-cel infusion had their infusion delayed: suspected or active systemic infection, onset of fever  $\geq 38^{\circ}\text{C}/100.4^{\circ}\text{F}$  (not related to underlying disease), requirement for supplemental oxygen to keep saturation  $>91\%$ , cardiac arrhythmia not controlled with medical management, hypotension requiring vasopressor support, new onset or worsening of other non-hematologic organ dysfunction grade  $\geq 3$ , or taking any of the prohibited medications.

Patients randomly assigned to the standard regimen arm received DPd, DVd, IRd, Kd, or EPd, per investigator discretion, based on individual patient's conditions and prior treatment history:

- Patients who have received daratumumab in combination with pomalidomide with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive DVd, IRd, Kd, or EPd.
- Patients who have received daratumumab in combination with bortezomib with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive DPd, IRd, Kd, or EPd.
- Patients who have received ixazomib in combination with lenalidomide with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive DPd, DVd, Kd, or EPd.
- Patients who have received carfilzomib with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive DPd, DVd, IRd, or EPd.

- Patients who have received elotuzumab in combination with pomalidomide with or without dexamethasone as part of their most recent antimyeloma treatment regimen may receive DPd, DVd, IRd, or Kd.
- Patients who have not received DP±d, DV±d, IR±d, K±d, or EP±d as part of their most recent antimyeloma treatment regimen may receive DPd, DVd, IRd, Kd, or EPd.

These treatment options reflect the best available choices for standard of care at the time of the study. As part of a protocol amendment 2.0 (December 2019), EPd and Kd were added as standard regimen options after the study was designed and enrollment started.

DPd cycles were 28 days in duration. Patients received intravenous daratumumab 16 mg/kg weekly in cycles 1 and 2 and then every 2 weeks in cycles 3 to 6 and every 4 weeks thereafter; pomalidomide 4 mg per day orally on days 1 to 21; dexamethasone 40 mg (20 mg per week in patients >75 years of age) was administered weekly and before and after the daratumumab infusions.

With DVd, patients received eight 21-day cycles of intravenous daratumumab 16 mg/kg weekly in cycles 1 to 3 and on day 1 in cycles 4 to 8, and every 4 weeks thereafter; eight 21-day cycles of 1.3 mg/m<sup>2</sup> subcutaneous bortezomib (days 1, 4, 8, and 11) and 20 mg oral dexamethasone (days 1, 2, 4, 5, 8, 9, 11, and 12).

With IRd, patients received ixazomib 4 mg on days 1, 8, and 15 in 28-day cycles; oral lenalidomide 25 mg on days 1 to 21 in 28-day cycles; and dexamethasone 20–40 mg on days 1, 8, 15, and 22 in 28-day cycles.

With Kd, carfilzomib was administered intravenously at 20 mg/m<sup>2</sup> in cycle 1 on days 1 and 2 in a 28-day cycle, and 56 mg/m<sup>2</sup> on days 8, 9, 15, and 16 of cycle 1 and on days 1, 2, 8, 9, 15, and 16 thereafter; dexamethasone 20 mg was administered on days 1, 2, 8, 9, 15, 16, 22, and 23 in 28-day cycles.

EPd cycles were 28 days in duration. Patients received intravenous elotuzumab at a dose of 10 mg/kg on days 1, 8, 15, and 22 during cycles 1 and 2 and 20 mg/kg on day 1 of each cycle thereafter; oral pomalidomide at 4 mg per day on days 1 through 21 of each cycle; oral dexamethasone 40 mg (patients ≤75 years) or 20 mg (patients >75 years) per

week, except on the days of elotuzumab administration, when patients in the elotuzumab arm received dexamethasone both orally (28 mg in patients  $\leq 75$  years or 8 mg in patients  $> 75$  years) and intravenously (8 mg).

Measurable disease was defined by serum ( $\geq 0.5$  g/dL) or urine ( $\geq 200$  mg/24 hours) monoclonal protein or serum free light chains (FLCs; involved FLCs  $\geq 10$  mg/dL with abnormal ratio). Patients in the standard regimen arm were eligible to receive ide-cel after confirmed evidence of PD by Independent Response Committee (IRC) assessment. The full study protocol is available with the full text of this article at NEJM.org.

Demographic representation of patients enrolled into KarMMa-3 compared with real-world myeloma patients is shown in Table S3. SEER Cancer Stat Facts for Myeloma<sup>1</sup> were used as a starting point to determine differences in age, sex/gender, and race/ethnicity as compared with the KarMMa-3 study population. The European, Canadian, and Japanese SEER equivalents were then searched, as patients in KarMMa-3 study were also enrolled from these locations. Further information on other considerations was found by searching key terms in PubMed, including 'multiple myeloma' in conjunction with one or more of the following key terms: 'patient characteristics', 'racial disparity', 'Black or African American', and 'demographics'. References that were deemed related were read to determine relevance. In addition, census data, where available, were used to infer racial proportions in the relevant regions.

### **Long-term Follow-up**

All patients who were treated with ide-cel would enroll into a separate long-term follow-up study upon completion of the survival follow-up period or upon premature discontinuation from study. Patients would be monitored for up to 15 years from the date of their last ide-cel infusion.

### **Endpoints and Assessments**

Follow-up duration was defined as the randomization to data cutoff date. Additional secondary objectives include percentage of patients achieving minimal residual disease



negative status, pharmacokinetics of ide-cel, time to next myeloma treatment, changes in health-related quality of life, and impact of ide-cel on health utility values.

Overall survival (OS) was defined as the time from randomization to time of death due to any cause. Time to response (TTR) was defined as the time from randomization to first documentation of a partial response or better, based on International Myeloma Working Group guidelines. Duration of response (DOR) was defined as the time from first documentation of a partial response or better to disease progression. TTR and DOR were analyzed based on responders in the ITT patient population. Minimal residual disease (MRD) negative status was assessed in bone marrow aspirate and determined at a sensitivity level of least  $10^{-5}$  and  $10^{-6}$  nucleated cells using next-generation sequencing (ClonoSEQ®). The primary analysis for MRD negative response used the sensitivity level of  $10^{-5}$ . MRD negativity was determined by at least one negative MRD value within 3 months prior to achieving CR or above until time of progression/death (exclusive) based on the ITT population. The MRD negative rate with 2-sided 95% confidence intervals (CIs) was provided. Safety assessments included complete physical examination including neurologic examination and vital signs, weight, Eastern Cooperative Oncology Group performance status, Mini Mental State Examination, clinical laboratory evaluations, pregnancy testing, concomitant medications and procedures, and adverse events.

The cellular kinetic–pharmacokinetic (PK) profile of ide-cel was determined by time course of vector transgene copies per microgram genomic DNA, as measured by digital droplet PCR. Using the PK data, non-compartmental analysis was performed to calculate parameters, including time to maximum measurable CAR T cell concentration ( $t_{max}$ ), time to last measurable CAR T cell concentration ( $t_{last}$ ), maximum measurable CAR T cell concentration occurring at  $t_{max}$  ( $C_{max}$ ), and area under the curve from day 0 to day 28 ( $AUC_{0-28d}$ ), using Phoenix WinNonlin version 8.2 (Certara, Princeton, NJ). The PK parameters were further analyzed for exposure–response relationships.

Tumor-associated BCMA expression was assessed from bone marrow biopsies by immunohistochemistry using a monoclonal antibody directed against an intracellular BCMA

epitope. Biopsies with any CD138+ cells ( $\geq 3\%$ ) were evaluated for BCMA expression. Soluble BCMA (sBCMA) was longitudinally assessed in serum (day 1 through disease progression) using Luminex immunoassay to monitor antitumor responses and infer tumor BCMA expression at disease progression in patients with no available bone marrow biopsies.

### **Statistical Analyses**

The primary analysis for the study is to compare progression-free survival (PFS) between ide-cel and standard regimen arms. It is assumed that the overall PFS distribution is exponential with a constant failure (hazard) rate. With 2:1 randomization and two interim analyses for PFS (1 for futility at approximately 33% information and 1 for superiority at approximately 80% information) a total of approximately 289 events is required for the final PFS analysis providing approximately 94% overall power to detect a hazard rate ratio of 0.643 (an improvement in median PFS from 9 months to 14 months) using a one-sided log rank test with an overall significance level of 0.025. O'Brien–Fleming type of alpha spending and beta spending will be used for superiority and futility boundaries, respectively. Considering the potential nonproportional hazard function due to delayed study treatment in the ide-cel arm by 1-month post-randomization, the statistical power was still estimated to be  $>85\%$ . At the time of the second PFS interim analysis, the null hypotheses would be rejected if the P-value associated with the test was  $\leq 0.012$  at 80% information fraction (IF) with approximately 232 PFS events. However, based on the actual information fraction observed (242 out of 289 planned PFS events; IF 84%), the null hypothesis would be rejected if the P-value associated with the test was  $\leq 0.014$  (one-sided per statistical plan; two-sided test also conducted). PFS final analysis would be conducted if the superiority boundary is not crossed at the second interim analysis; the null hypothesis would be rejected if the P-value associated with the test is  $\leq 0.021$  for PFS. PFS was censored upon subsequent therapy with no documented progression by IRC, according to US Food and Drug Administration guidelines.

A hierarchical test procedure was conducted to control the multiplicity among the primary and key secondary efficacy endpoints. Overall response rate (ORR) is second in the statistical testing hierarchy and was tested at the same level as PFS following a positive PFS result. The sample size of 381 patients will provide at least 90% power for ORR with one interim analysis for ORR (conducted at the second PFS interim analysis for superiority) and one final analysis of ORR (conducted at the PFS final analysis) by assuming that ORR is approximately 68% in the ide-cel arm and 50% in the standard regimen arm. The 95% CIs for ORR were based on two-sided Wald CI. For the comparison of ORR between treatment arms, the associated two-sided P-values were calculated using the Cochran–Mantel–Haenszel test stratified by study stratification factors.

OS is third in the hierarchy with two interim analyses planned at the time of the second interim and final PFS analyses, and a final analysis at 222 OS events. A one-sided superiority boundary of 0.01 will be used for the OS interim analysis conducted at the PFS final analysis. The superiority boundary for the final OS analysis will be determined following the Haybittle–Peto boundary based on the actual alpha spent and actual information fraction used at the two OS interim analyses to retain the overall alpha of 0.025 one-sided (per statistical plan; two-sided test will also be conducted). TTR were estimated with the use of summary statistics. DOR event analyses and associated 95% CIs were estimated using Kaplan–Meier methods.

The proportional hazards assumption was checked for the primary PFS analysis by addition of a time-dependent covariate, defined by treatment by log(time) interaction, into the stratified Cox regression model. The Wald chi-square test showed a two-sided P-value of >0.05, indicating that the proportional hazards assumption is not violated.

Apart from the primary endpoint and key secondary endpoints, no adjustment for multiplicity was conducted for other analyses including subgroup analyses and these analyses are presented in a descriptive manner.

## **Results**

### **Patients and Treatment**

Among the 29 patients randomized to ide-cel who did not receive treatment, 5 patients did not undergo leukapheresis (1 patient due to adverse event, 2 failed to meet treatment criteria, and 2 patients withdrew consent); 7 did not receive ide-cel due to physician decision, 6 failed to meet treatment criteria, 4 did not receive ide-cel due to adverse events, 4 died, and 3 experienced manufacturing failures. Median time from leukapheresis to ide-cel infusion in 225 patients was 49.0 days (range, 34.0–117.0 days).

At data cutoff, of 254 patients randomized to the ide-cel arm and 132 patients randomized to the standard regimens arm, 91 patients were ongoing for PFS in the ide-cel arm, and in the standard regimens arm, 20 patients were ongoing for treatment and PFS (Figure 1). In total, 76 patients were in survival follow-up after confirmed disease progression: 67 and 9 patients in the ide-cel arm and in standard regimens arm, respectively. In the standard regimens arm, after confirmed disease progression, 69 patients underwent leukapheresis with the intent of receiving ide-cel. Discontinuations from the study occurred in 96 (38%) and 34 (26%) patients in the ide-cel and in the standard regimens arms, respectively, after the initial treatment, most commonly due to death (n=75; 30% vs. n=20; 15%).

### **Odds Ratio for Overall Response Rate**

Odds ratios favor ide-cel treatment when compared with standard regimens overall (3.47; 95% CI, 2.24 to 5.39) and across prespecified patient subgroups, including age, number of prior regimens, high-risk cytogenetics, extramedullary disease, high tumor burden, and triple-class–refractory status (Figure S3).

### **Cellular Kinetics-Pharmacokinetics**

Exploratory analyses indicate that higher quartiles of ide-cel expansion measured by PK exposure ( $AUC_{0-28d}$ ) were associated with longer PFS, with the median PFS in the lowest quartile of PK exposure as ~6 versus ~15 months or more in the higher three quartiles of PK

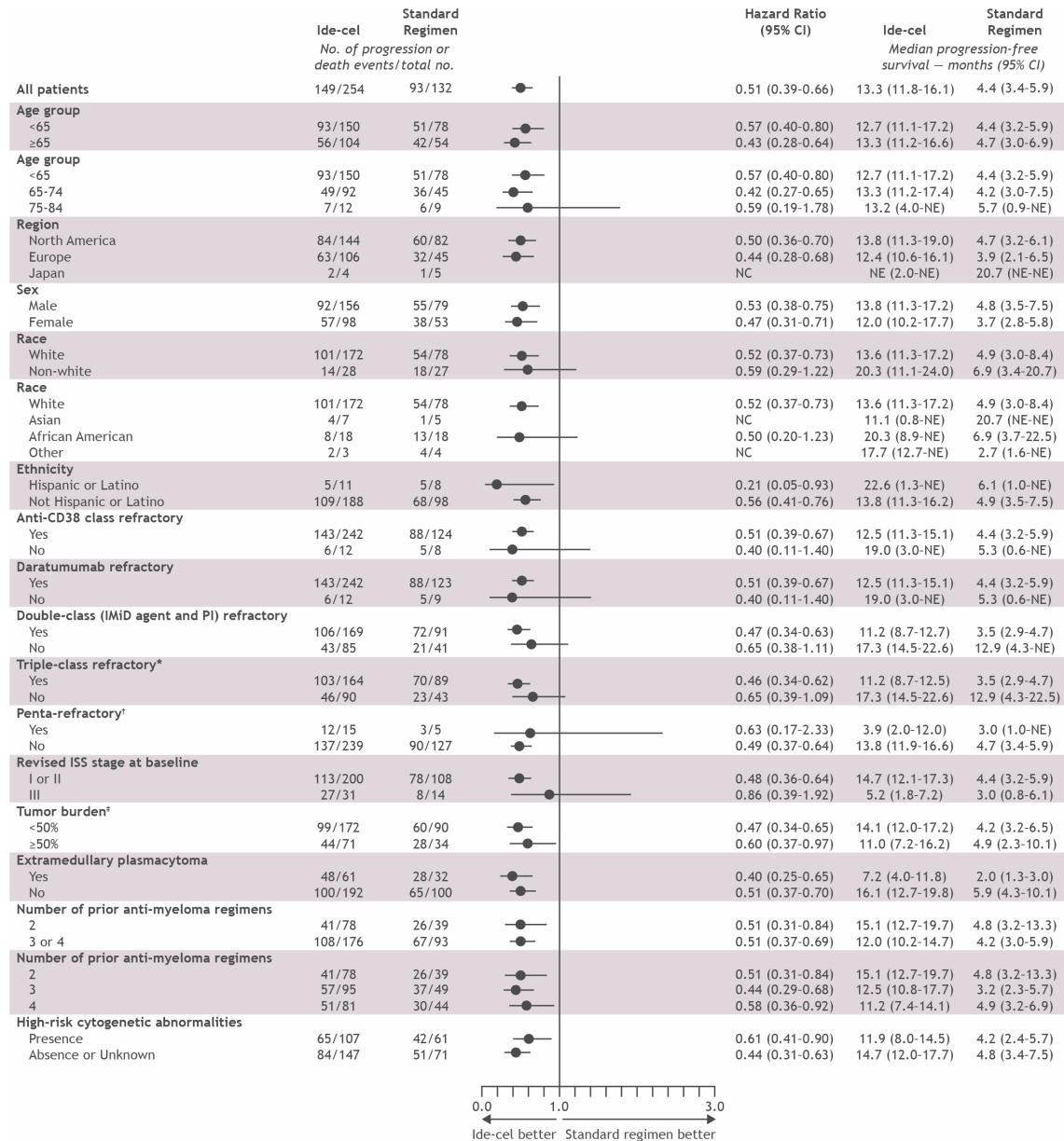
exposure (Figure S4). Inherent to CAR T biology, considerable inter-patient variability in cell expansion was observed for ide-cel in patients with RRMM, and the lowest quartile (Q1) of ide-cel expansion was present across all actual dose levels.

### **BCMA Expression**

BCMA-expressing bone marrow tumor cells were observed in 6 of 6 evaluable biopsies obtained at disease progression from patients treated with ide-cel. As an indirect measure of BCMA expression on tumor cells, serum sBCMA level at disease progression was also measured in patients treated with ide-cel. Of the 84 ide-cel–treated patients with evaluable sBCMA data at disease progression, 82 (98%) had detectable sBCMA, suggesting that BCMA-expressing cells were present.

## Figures

**Figure S1. Subgroup Analysis of Progression-free Survival.**



Per IRC based on IMWG criteria. Assumption of proportional hazards was assessed using a treatment\*log(time) interaction term in each model.

\* Triple-class–refractory is defined as refractory to at least one each of an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody.

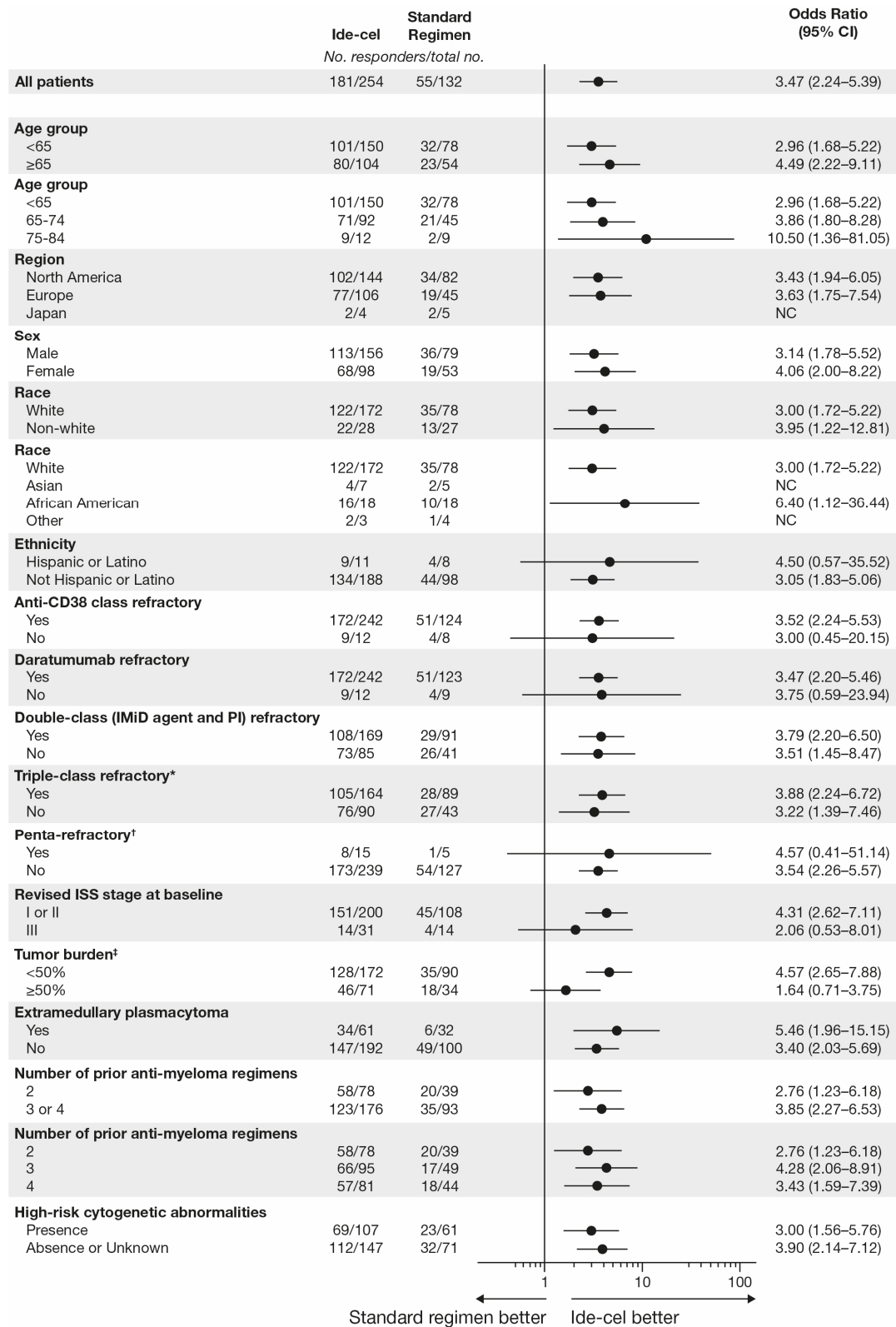
† Penta-refractory is defined as refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib, and daratumumab.

‡ Determined by the higher value between bone marrow aspiration and bone marrow biopsy CD138+ plasma cell. Low tumor burden: <50%, High tumor burden:  $\geq$ 50%.

HR is unstratified based on the univariate Cox proportional hazards model.

CI denotes confidence interval, ide-cel idecabtagene vicleucel, IRC Independent Response Committee, IMWG International Myeloma Working Group, ISS International Staging System, NC not calculated, NE, not evaluable, and PI proteasome inhibitor.

**Figure S2. Odds Ratio for Overall Response Rate (ITT Population).**





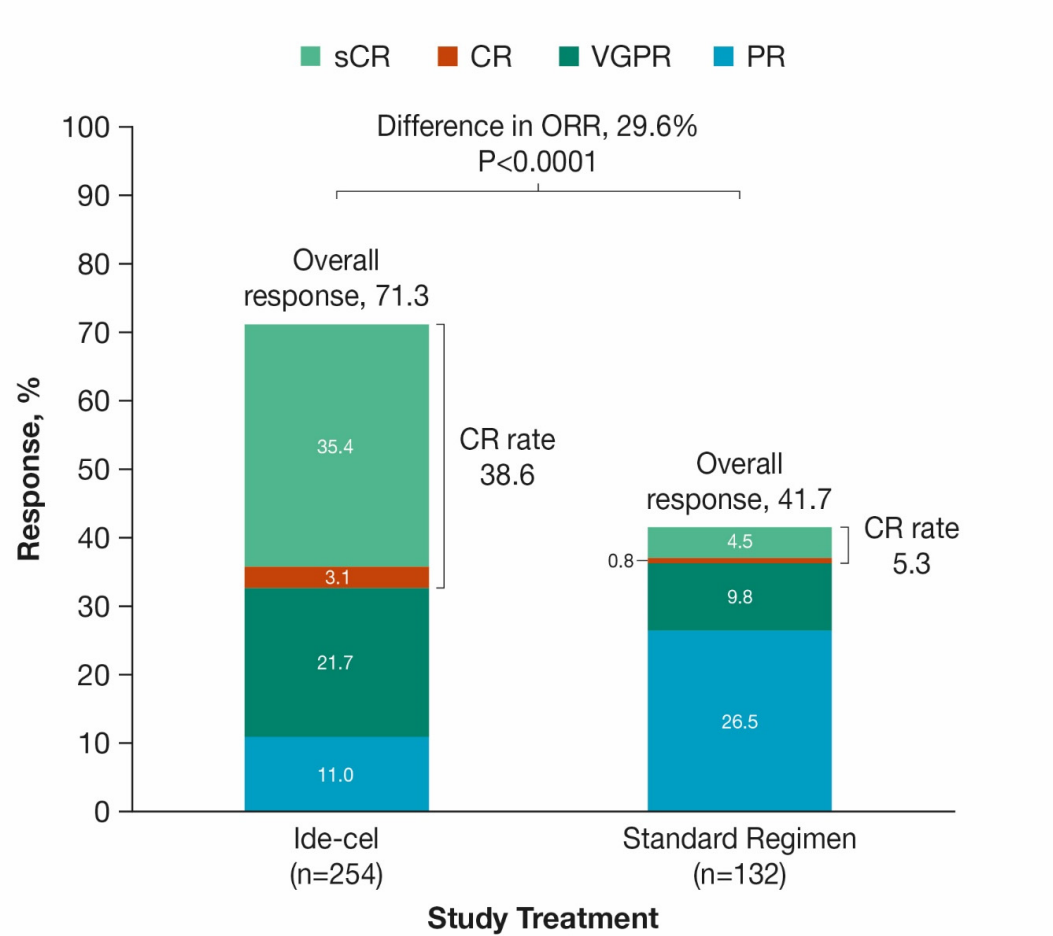
Cochran–Mantel–Haenszel test stratified by study stratification factors was used to compare ORR. The 95% CIs for ORR were based on two-sided Wald CI.

\* Triple-class–refractory is defined as refractory to at least one each of an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody.

† Penta-refractory is defined as refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib, and daratumumab.

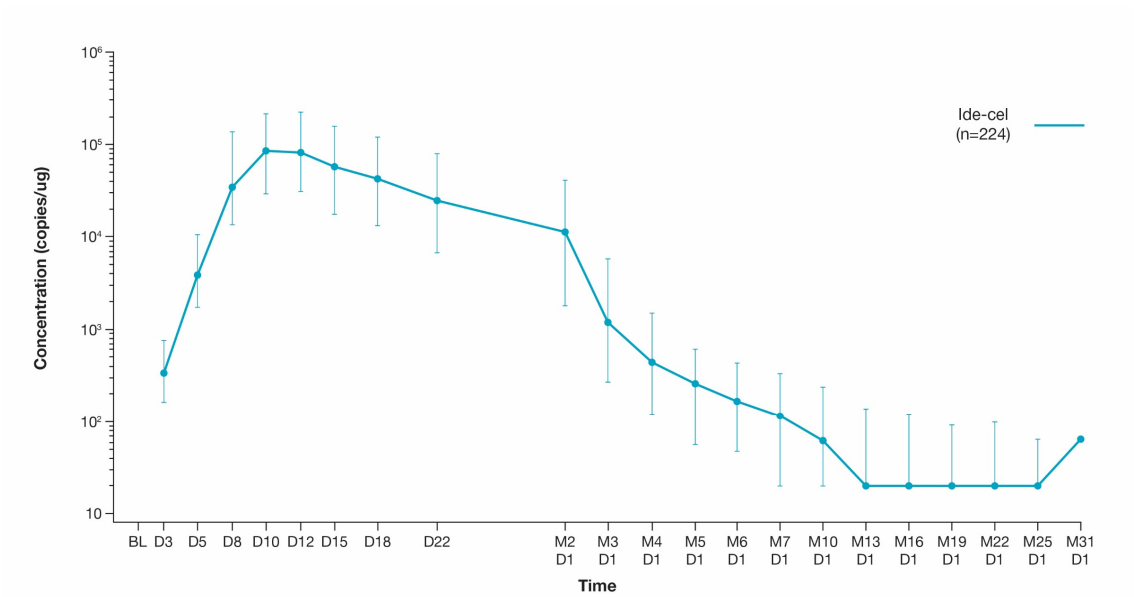
‡ Determined by the higher value between bone marrow aspiration and bone marrow biopsy CD138+ plasma cell. Low tumor burden: <50%, high tumor burden: ≥50%.

**Figure S3.** Overall Response Rate (ITT Population).



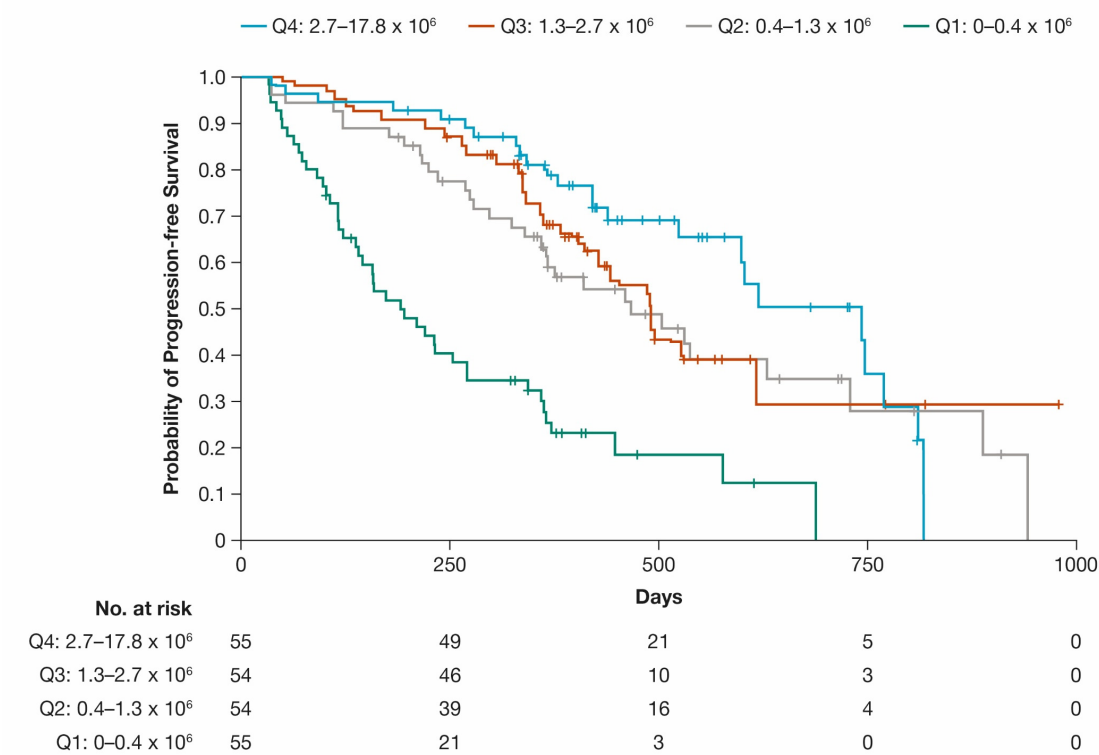
Cochran–Mantel–Haenszel test stratified by study stratification factors was used to compare ORR. The 95% CIs for ORR were based on two-sided Wald CI.

**Figure S4.** Median Ide-cel Transgene Level Over Time in Whole Blood Matrix in the Ide-cel Arm



Error bars indicate first and third quartiles. Post-infusion concentrations recorded as “not detected” were imputed as half of the lower limit of quantification (40 copies/μg for whole blood matrix). Time courses of transgene levels were measured by droplet digital polymerase chain reaction in whole blood. BL denotes baseline, D day, and M month.

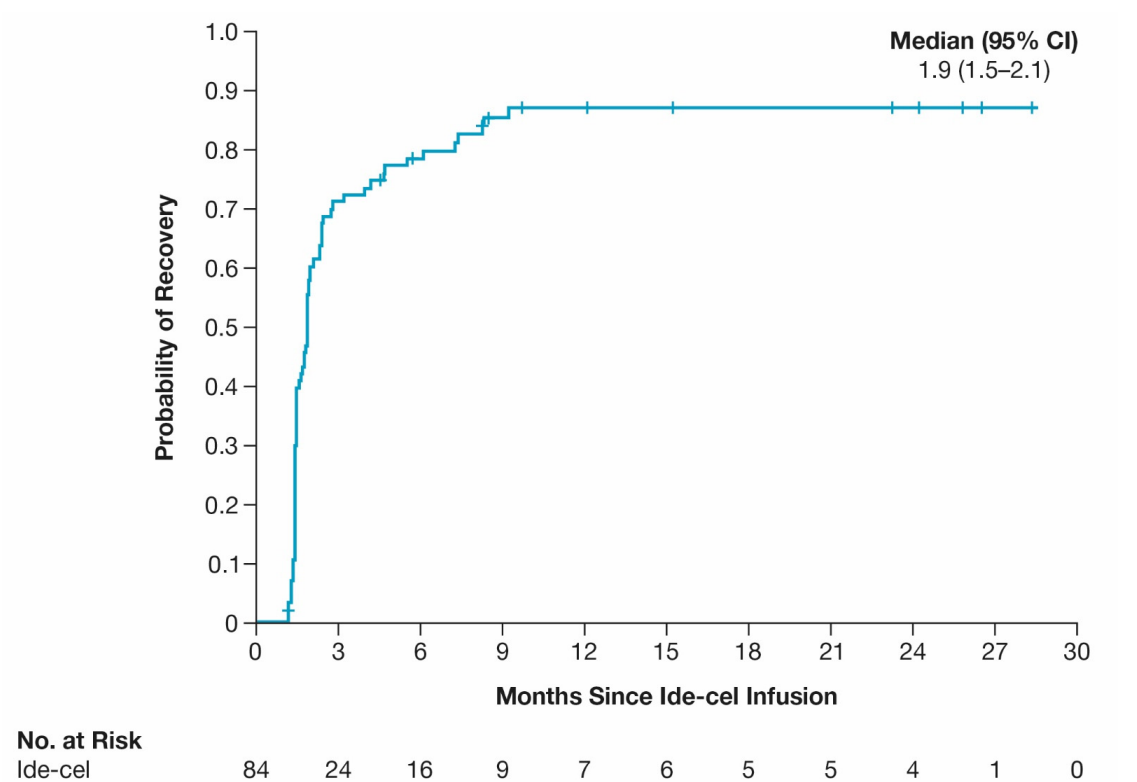
**Figure S5.** Progression-free Survival According to PK Exposure ( $AUC_{0-28d}$ ) in Patients Treated with Ide-cel.



$AUC_{0-28d}$  denotes area under the curve from day 0 to day 28, and is measured in days\*copies/ $\mu$ g.

Q denotes quartile.

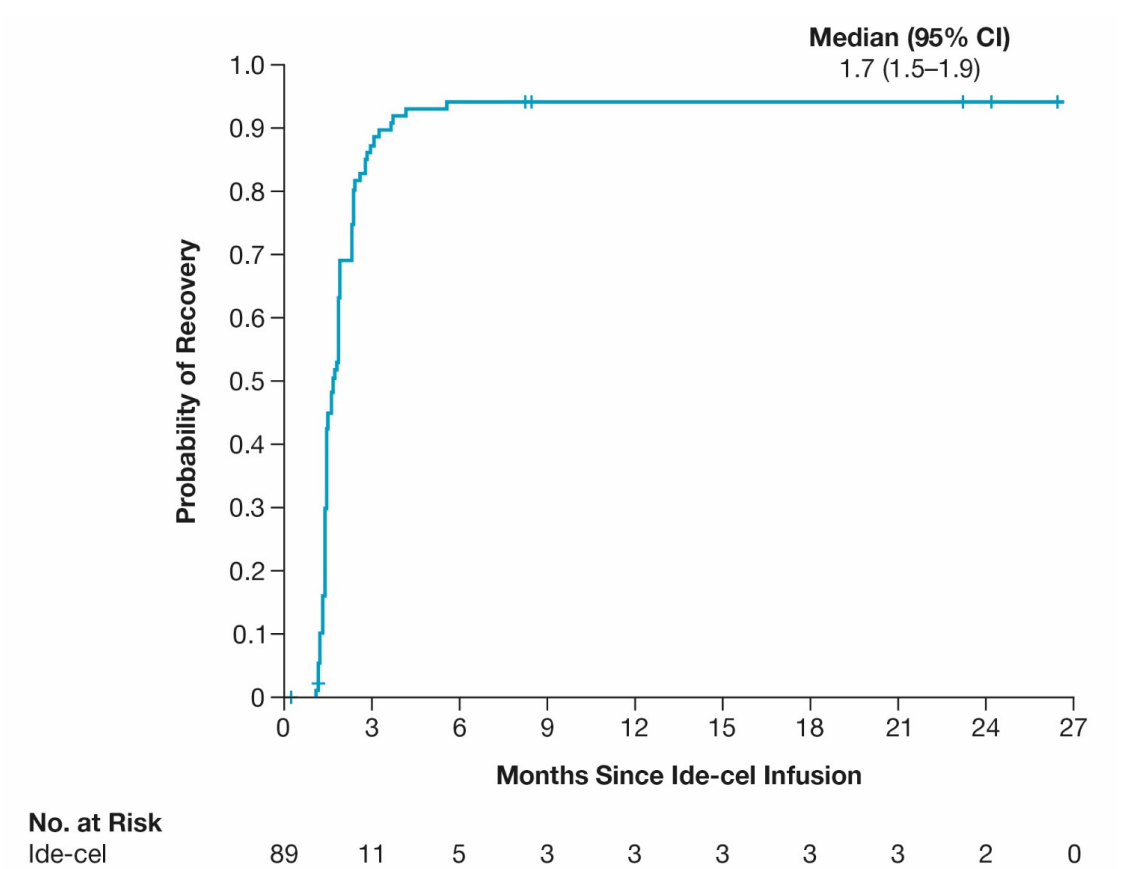
**Figure S6.** Time to Recovery of Grade 3/4 Thrombocytopenia in Patients Without Recovery by Month 1\* (Safety Population).



Patients in the safety population in the ide-cel arm with last lab within month 1 of ide-cel infusion date indicating grade 3/4 thrombocytopenia. Time to recovery of grade 3 or 4 thrombocytopenia is defined as the time from ide-cel infusion date to the time when recovery was first met after month 1 post infusion. The median and recovery rate are based on Kaplan–Meier estimates. Patients who did not recover after month 1 without death, including ongoing at the cutoff date or lost to follow-up before recovery, are censored to last non-missing assessment date after month 1, and patients who died before recovery are censored to current data cutoff date.

\* Grade 3/4 thrombocytopenia is defined as platelet count <50,000/μL. Recovery from thrombocytopenia is achieved when platelet count is ≥50,000/μL.  
CI denotes confidence interval.

**Figure S7.** Time to Recovery of Grade 3/4 Neutropenia in Patients Without Recovery by Month 1\* (Safety Population).



Patients in the safety population in the ide-cel arm with last lab within month 1 of ide-cel infusion date indicating grade 3/4 neutropenia.

Time to recovery of grade 3 or 4 neutropenia is defined as the time from ide-cel infusion date to the time when recovery was first met after month 1 post infusion. The median and recovery rate are based on Kaplan–Meier estimates. Patients who did not recover after month 1 without death, including ongoing at the cutoff date or lost to follow-up before recovery, are censored to last non-missing assessment date after month 1, and patients who died before recovery are censored to current data cutoff date.

\* Grade 3/4 neutropenia is defined as absolute neutrophil count <1000/ $\mu$ L. Recovery from neutropenia is achieved when absolute neutrophil count is  $\geq$ 1000/ $\mu$ L.

CI denotes confidence interval.

## Tables

**Table S1.** International Myeloma Working Group Uniform Response Criteria.

Response	Criteria
sCR	CR (as defined below), plus normal serum FLC ratio, and absence of clonal plasma cells by immunohistochemistry
CR	Negative immunofixation of serum and urine, disappearance of any soft tissue plasmacytomas, and <5% plasma cells in bone marrow In patients in whom the only measurable disease is by serum FLC levels: a normal FLC ratio of 0.26 to 1.65
VGPR	Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥90% reduction in serum M-protein plus urine M-protein level <100 mg/24 hours In patients in whom the only measurable disease is by serum FLC levels: a >90% decrease in the difference between involved and uninvolved FLC levels
PR	≥50% reduction of serum M-protein and reduction in 24-hour urine M-protein by ≥90% or to <200 mg/24 hours If the serum and urine M-protein are unmeasurable, a ≥50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria If serum and urine M-protein are unmeasurable, and the serum FLC assay is also unmeasurable, a ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was ≥30% In addition to the above-listed criteria, if present at baseline, a ≥50% reduction in the size measured by the sum of the products of the maximal perpendicular diameters of soft tissue plasmacytomas is also required
MR	≥25% but ≤49% reduction of serum M-protein and reduction in 24-hour urine M-protein by 50–89% In addition to the above criteria, if present at baseline, ≥50% reduction in the size of soft tissue plasmacytomas is also required
SD	Not meeting criteria for CR, VGPR, PR, MR, or PD
PD	Increase of 25% from lowest response value in any of the following: <ul style="list-style-type: none"> <li>Serum M-component (absolute increase must be ≥0.5 g/dL) and/or</li> </ul>

	<ul style="list-style-type: none"> <li>• Urine M-component (absolute increase must be <math>\geq 200</math> mg/24 hour) and/or</li> <li>• Only in patients without measurable serum and urine M-protein levels: the difference between involved and uninvolved FLC levels (absolute increase must be <math>\geq 10</math> mg/dL)</li> <li>• Only in patients without measurable serum and urine M-protein levels and without measurable disease by FLC levels, bone marrow plasma cell percentage (absolute increase must be <math>\geq 10\%</math>)</li> <li>• Appearance of a new lesion(s), <math>\geq 50\%</math> increase from nadir in the sum of the products of <math>&gt;1</math> lesion, or <math>\geq 50\%</math> increase in the longest diameter of a previous lesion <math>&gt;1</math> cm in short axis; <math>\geq 50\%</math> increase in circulating plasma cells (minimum of 200 cells/<math>\mu</math>L) if this is the only measure of disease</li> </ul>
Relapse	<p>Clinical relapse requires <math>\geq 1</math> of the following criteria:</p> <ul style="list-style-type: none"> <li>• Direct indicators of increasing disease and/or end organ dysfunction (CRAB features) that are considered related to the underlying plasma cell proliferative disorder</li> <li>• Development of new soft tissue plasmacytomas or bone lesions</li> <li>• Definite increase in the size of existing plasmacytomas or bone lesions. A definite increase is defined as a 50% (and <math>\geq 1</math> cm) increase as measured serially by the sum of the products of the measurable lesion</li> <li>• Hypercalcemia (<math>&gt;11</math> mg/dL)</li> <li>• Decrease in hemoglobin of <math>&gt;2</math> g/dL not related to therapy or other non-myeloma-related conditions</li> <li>• Rise in serum creatinine of <math>\geq 2</math> mg/dL</li> <li>• Hyperviscosity related to serum paraprotein</li> </ul>

CR denotes complete response, CRAB calcium, renal insufficiency, anemia, or bone lesions, FLC free light chain, MR minor response, PD progressive disease, PR partial response, sCR stringent complete response, SD stable disease, and VGPR very good partial response.



**Table S2.** Cytokine Release Syndrome Revised Grading System.<sup>2</sup>

Grade	Toxicity
1	Symptoms are not life threatening and require symptomatic treatment only (e.g., fever, nausea, fatigue, headache, myalgias, malaise)
2	Symptoms require and respond to moderate intervention: oxygen requirement <40%, hypotension responsive to fluids or low dose of one vasopressor, or grade 2 organ toxicity
3	Symptoms require and respond to aggressive intervention: oxygen requirement $\geq$ 40%, hypotension requiring high dose or multiple vasopressors, or grade 3 organ toxicity or grade 4 transaminitis
4	Life-threatening symptoms: requirement for ventilator support or grade 4 toxicity (excluding transaminitis)

**Table S3.** Representativeness of Study Participants.

Category	Example
<b>Disease, problem, or condition under investigation</b>	(relapsed and/or refractory) MM
<b>Special considerations related to:</b> Age Sex/gender Race/ethnic group	<ul style="list-style-type: none"> <li>• Prevalence increases with age, and peaks at a median of 64–69 years in the USA<sup>1,3</sup></li> <li>• The incidence rate of MM is higher in male patients compared with female patients<sup>1,3,4</sup></li> <li>• MM affects non-Hispanic Black or African American patients disproportionately in the USA, with an incidence rate per 100,000 that is twice as that of all races<sup>1</sup></li> </ul>
<b>Other considerations</b>	<ul style="list-style-type: none"> <li>• MM is diagnosed at a younger age in Black or African American patients compared with White patients<sup>1</sup></li> <li>• Black or African American patients may have differences in cytogenetic or molecular abnormalities compared with White patients<sup>5-7</sup></li> <li>• Black patients are less likely to undergo ASCT; if received, ASCT usually occurs later in the disease course<sup>5,8,9</sup></li> <li>• In a real-world analysis from the SEER–Medicare database (2007–2013 from SEER, 2007/2014 from Medicare) to examine treatment and outcome disparities among White, African American, and Hispanic patients with MM<sup>10</sup>: <ul style="list-style-type: none"> <li>○ OS was similar across cohorts, but African American and Hispanic patients received novel MM therapies later than White patients and thus may not be reaping the full benefits from the introduction of these treatments</li> <li>○ The use of novel therapies has increased over time, but the increase was more pronounced in Whites than in African Americans</li> <li>○ Healthcare costs were similar between African Americans and Whites with MM</li> </ul> </li> </ul>
<b>Overall representativeness of this trial</b>	<ul style="list-style-type: none"> <li>• In the KarMMa-3 trial, patients had a median age of 63 years, which was slightly lower than the median age of diagnosis from SEER (69 years)<sup>1</sup></li> <li>• The proportion of male patients was 61%, which was lower than that reported in the SEER and ECIS databases but higher than that reported from the 19 trials summarized in a meta-analysis by Kanapuru et al (55%).<sup>1,3,4</sup></li> </ul>

	<ul style="list-style-type: none"> <li>• The proportion of Black or African American patients randomized to the ide-cel group was 7%, which was less than that reported in the US population (12% from 2020 US Census<sup>11</sup>), but 18% from the 19 US trials in a meta-analysis.<sup>3</sup> This may be attributed to the lower proportions observed in other countries (Canadian census, 2021<sup>12</sup>), as patients were also enrolled from Canada, Europe, and Japan</li> </ul> <p>Various enrollment strategies were implemented in the USA and globally, including multimedia, digital, and print outreach to increase awareness of the study, addition of new sites, additional investigator meetings, and ad hoc site visits. Furthermore, travel cost reimbursement for patients was made available to sites in the USA to help overcome economic barriers to participation.</p> <p>The study sponsor, Bristol Myers Squibb, is committed to strengthening clinical trial diversity and has identified specific focus areas globally to reach this goal. These areas include the identification and activation of sites in racially and ethnically diverse communities in the USA. Additional details can be found at:  <a href="https://www.bms.com/about-us/global-diversity-and-inclusion/our-commitments.html?linkId=131649043">https://www.bms.com/about-us/global-diversity-and-inclusion/our-commitments.html?linkId=131649043</a></p>
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ASCT denotes autologous stem cell transplant, ECIS European Cancer Information System, MM multiple myeloma, OS overall survival

**Table S4.** Treatment Exposure (Safety Population).

Regimen			
CAR T cell therapy	Patients who received treatment		Median number of CAR+ T cells infused
	— no. (%)		— 10 <sup>6</sup> cells (range)
Ide-cel	225 (100)		445 (175–529)
Standard regimen	Patients who received		Median number of cycles
	treatment — no. (%) <sup>*</sup>	Median duration of treatment — days (range) <sup>†</sup>	— no (range) <sup>‡</sup>
DPd	41 (33)	178.0 (11.0–967.0)	6.0 (1.0–35.0)
EPd	30 (24)	119.5 (14.0–399.0)	4.5 (1.0–14.0)
Kd	28 (22)	178.0 (28.0–604.0)	6.5 (2.0–21.0)
IRd	20 (16)	120.0 (21.0–623.0)	5.0 (1.0–22.0)
DVd	7 (6)	86.0 (15.0–195.0)	5.0 (1.0–10.0)

<sup>\*</sup> Percentages calculated based on 126 total patients in the standard regimen arm.

<sup>†</sup> Treatment duration defined as the period from the first dose to last dose date of a regimen.

<sup>‡</sup> Cycle refers to the "month" defined per protocol, which is 21 days for DVd, and 28 days for all other standard regimens.

CAR denotes chimeric antigen receptor, DPd daratumumab/pomalidomide/dexamethasone, DVd daratumumab/bortezomib/dexamethasone, EPd elotuzumab/pomalidomide/dexamethasone, ide-cel idecabtagene vicleucel, IRd ixazomib/lenalidomide/dexamethasone, and Kd carfilzomib/dexamethasone.

**Table S5.** Prior treatment (ITT Population).

ITT population	Ide-cel (n=254)	Standard regimens (n=132)
Patients — no. (%)		
<b>Patients with &gt;1 prior therapy</b>	254 (100)	132* (100)
<b>Corticosteroids</b>	254 (100)	132 (100)
Dexamethasone	254 (100)	132 (100)
Prednisone	8 (3)	5 (4)
Methylprednisolone	7 (3)	3 (2)
<b>Immunomodulatory agents</b>	254 (100)	132 (100)
Lenalidomide	250 (98)	131 (99)
Pomalidomide	142 (56)	78 (59)
Thalidomide	59 (23)	26 (20)
<b>Monoclonal antibodies</b>	254 (100)	132 (100)
Daratumumab	254 (100)	132 (100)
Elotuzumab	20 (8)	17 (13)
<b>Proteasome inhibitors</b>	254 (100)	132 (100)
Bortezomib	238 (98)	128 (97)
Carfilzomib	144 (57)	57 (43)
Ixazomib	38 (15)	21 (16)

\* In the standard regimens arm, of the 43 patients treated with DPd, none had received prior DPd; of the 7 patients treated with DVd, none had received prior DVd; of the 22 patients treated with IRd, none had received prior IRd; of the 30 patients treated with Kd, 5 had received prior Kd; of the 30 patients treated with EPd, 1 had received prior EPd.

Ide-cel denotes idecabtagene vicleucel.

**Table S6.** Minimal Residual Disease Negativity in Patients With At Least a Complete Response (ITT Population).

	Sensitivity level* at 10 <sup>-5</sup>		Sensitivity level* at 10 <sup>-6</sup>	
	Ide-cel (n=254)	Standard regimens (n=132)	Ide-cel (n= 254)	Standard regimens (n = 132)
Patients who achieved CR and MRD-negative status <sup>†</sup>				
MRD negativity — no. (%)	51 (20)	1 (1)	32 (13)	0
95% CI	15.2–25.0	0–2.2	8.5–16.7	0–0

\* The primary analysis for MRD negativity used a sensitivity level of 10<sup>-5</sup> per IMWG Uniform Response Criteria for Multiple Myeloma, as specified by the protocol. 95% CI calculated using two-sided Wald interval.

<sup>†</sup> Any time within 3 months prior to achieving at least CR until progression or death.

CI denotes confidence interval, CR complete response, ide-cel idecabtagene vicleucel, ITT intent-to-treat, and MRD minimal residual disease.

**Table S7.** Grade 5 All-causality Adverse Events (Treated Population).

<b>System organ class</b> Preferred term	<b>Ide-cel</b> <b>(n=250)</b>	<b>Standard regimens</b> <b>(n=126)</b>
	Patients — no. (%)	
<b>Grade 5 all-cause event*</b>	36 (14)	8 (6)
<b>General disorders and administration site conditions</b>	15 (6)	4 (3)
General physical health deterioration <sup>†,‡</sup>	14 (6)	3 (2)
Sudden death	1 (<1)	0
Multiple organ dysfunction	0	1 (1)
<b>Infections and infestations</b>	11 (4)	3 (2)
Sepsis <sup>§</sup>	6 (2)	2 (2)
Pneumonia	2 (1)	0
Bronchopulmonary aspergillosis	1 (<1)	0
COVID-19	1 (<1)	1 (1)
COVID-19 pneumonia	1 (<1)	0
<b>Benign, malignant, and unspecified neoplasms (including cysts and polyps)</b>	4 (2)	0
Leukemia	1 (<1)	0
Plasma cell leukemia <sup>‡</sup>	1 (<1)	0
Plasma cell myeloma <sup>‡</sup>	1 (<1)	0
Small intestine adenocarcinoma	1 (<1)	0
<b>Immune system disorders</b>	2 (1)	0
Cytokine release syndrome	2 (1)	0
<b>Nervous system disorders</b>	2 (1)	0
Amyotrophic lateral sclerosis	1 (<1)	0
Cerebrovascular accident	1 (<1)	0
<b>Respiratory, thoracic, and mediastinal disorders</b>	2 (1)	1 (1)
Respiratory failure <sup>‡</sup>	2 (1)	1 (1)
<b>Renal and urinary disorders</b>	1 (<1)	0
Renal failure <sup>‡</sup>	1 (<1)	0

\* Grade 5 all-cause adverse events that occurred in  $\geq 1$  patient. In the standard regimens arm, for patients who underwent leukapheresis in preparation of planned ide-cel treatment upon documented disease progression on standard regimen, only adverse events before leukapheresis were included.

† General physical health deterioration was defined as patients with no clear or dominant signs or symptoms.

‡ Of the grade 5 adverse events by system organ class in the ide-cel and standard regimen arms, 18 of the 36 patients in the ide-cel arm (14 patients with general health deterioration, 1 patient with plasma cell leukemia, 1 patient with plasma cell myeloma, 1 patient with respiratory failure, and 1 patient with renal failure) and 3 of the 8 patients in the standard regimens arm had verbatim terms consistent with progression of myeloma; 6 of the 18 patients randomized to the ide-cel arm never received ide-cel.

§ In the ide-cel arm there were n=3 of sepsis, and n=1 each of *Candida* sepsis, *Klebsiella* sepsis, and pulmonary sepsis; in the standard regimens arm there was n=1 each of *Escherichia* sepsis, and neutropenia sepsis.

Ide-cel denotes idecabtagene vicleucel.



**Table S8.** Recovery from Grade 3/4 Adverse Events of Thrombocytopenia or Neutropenia (Safety Population).

Ide-cel arm (n=225)	Thrombocytopenia	Neutropenia
Patients with grade 3/4 event at any time on/before month 1 of ide-cel infusion — no. (%) <sup>*</sup>	120 (53)	217 (96)
Patients who recovered at last assessment on/before month 1 — no. (%) <sup>†</sup>	36 (30)	128 (59)
Patients who did not recover at last assessment on/before month 1 — no. (%) <sup>‡</sup>	84 (70)	89 (41)
Recovery status after month 1 <sup>‡</sup>		
Recovered	71 (85)	82 (92)
Censored	13 (15)	7 (8)
Died without recovery	8 (10)	5 (6)
Lost to follow-up	2 (2)	1 (1)
Ongoing	3 (4)	1 (1)
Median time to recovery in all patients — months (range) <sup>§</sup>	1.9 (1.1–28.3)	1.7 (0.3–26.5)
Median time to recovery in patients who recovered — months (range) <sup>§</sup>	1.7 (1.1–9.2)	1.6 (1.1–5.6)

Grade 3/4 thrombocytopenia is defined as platelet count <50,000/μL. Recovery from thrombocytopenia is achieved when platelet count is ≥50,000/μL. Grade 3/4 neutropenia is defined as absolute neutrophil count <1000/μL. Recovery from neutropenia is achieved when absolute neutrophil count is ≥1000/μL.

\* Percentage is calculated using the safety population (n=225) as the denominator.

† After month 1. Percentage is calculated using patients who had grade 3/4 event at any time on or before month 1 as the denominator.

‡ After month 1. Percentage is calculated using patients who did not recover from grade 3/4 event at the last assessment on or before month 1 as the denominator.

§ Time to recovery of grade 3/4 neutropenia was defined as the time from ide-cel infusion to the time when recovery criteria were first met (month 1 post infusion). The median and recovery rate are based on Kaplan–Meier estimates. Patients who did not recover after month 1 without death, including ongoing as cutoff date or lost to follow-up before recovery, were censored to last non-missing assessment date after month 1, and patients who died

before recovery were censored at the data cutoff date. The summary statistics are univariate statistics without adjusting for censoring.

Ide-cel denotes idecabtagene vicleucel.

**Table S9.** Serious Adverse Events (Treated Population).

<b>System organ class</b> Preferred term	<b>Ide-cel</b> <b>(n=250)</b>	<b>Standard regimens</b> <b>(n=126)</b>
Patients — no. (%)		
<b>Any</b>	130 (52)	48 (38)
<b>Infections and infestations*</b>	61 (24)	25 (20)
<b>General physical health deterioration</b>	34 (14)	8 (6)
General physical health deterioration†	17 (7)	4 (3)
Pyrexia	12 (5)	1 (1)
<b>Neoplasms</b>	23 (9)	4 (3)
Plasma cell leukemia	3 (1)	0
<b>Hematologic</b>	20 (8)	4 (3)
Febrile neutropenia	10 (4)	2 (2)
Neutropenia	5 (2)	1 (1)
Thrombocytopenia	2 (1)	2 (2)
<b>Musculoskeletal and connective tissue disorders</b>	17 (7)	5 (4)
Pathologic fracture	6 (2)	0
Back pain	4 (2)	2 (2)
Bone pain	3 (1)	1 (1)
Pain in extremity	0	2 (2)
<b>Nervous system disorders</b>	16 (6)	5 (4)
Depressed level of consciousness	4 (2)	0
Aphasia	3 (1)	1 (1)
Encephalopathy	3 (1)	0
Spinal cord compression	3 (1)	2 (2)

<b>Renal and urinary disorders</b>	14 (6)	2 (2)
Acute kidney injury	8 (3)	2 (2)
Renal failure	3 (1)	0
<b>Immune system disorders</b>	12 (5)	0
Cytokine release syndrome	10 (4)	0
Hemophagocytic lymphohistiocytosis	5 (2)	0
<b>Respiratory, thoracic, and mediastinal disorders</b>	12 (5)	6 (5)
Dyspnea	3 (1)	1 (1)
<b>Cardiac disorders</b>	11 (4)	7 (6)
Atrial fibrillation	4 (2)	3 (2)
<b>Metabolism and nutrition disorders</b>	11 (4)	4 (3)
Hypercalcemia	5 (2)	1 (1)
<b>Psychiatric disorders</b>	9 (4)	2 (2)
Confusional state	6 (2)	1 (1)
<b>Gastrointestinal disorders</b>	6 (2)	3 (2)
Diarrhea	1 (<1)	2 (2)
<b>Vascular disorders</b>	6 (2)	1 (1)
Deep vein thrombosis	3 (1)	0

Shown are serious adverse events that occurred from randomization in  $\geq 1\%$  of patients from either treatment arm. In the standard regimens arm, for patients who underwent leukapheresis in preparation of planned ide-cel treatment upon documented disease progression on standard regimen, only adverse events before leukapheresis were included.

\* Included pneumonia, influenza, sepsis, COVID-19, COVID-19 pneumonia, and pneumonia legionella.

† General physical health deterioration was defined as patients with no clear or dominant signs or symptoms.

Ide-cel denotes idecabtagene vicleucel.

**Table S10.** Treatment-related Adverse Events (Safety Population).

<b>System organ class</b> Preferred term	<b>Ide-cel</b> <b>(n=225)</b>	<b>Standard regimens</b> <b>(n=126)</b>
<b>≥1 grade 5 treatment-related event*</b>	6 (3)	1 (1) <sup>†</sup>
<b>Infections and infestations</b>	5 (2)	1 (1)
Sepsis <sup>‡</sup>	5 (2)	1 (1)
<b>Immune system disorders</b>	2 (1)	0
Cytokine release syndrome	2 (1)	0

\* In the standard regimens arm, for patients who underwent leukapheresis in preparation of planned ide-cel treatment upon documented disease progression on standard regimen, only adverse events before leukapheresis were included.

<sup>†</sup> Patient received elotuzumab/pomalidomide/dexamethasone (EPd).

<sup>‡</sup> In the ide-cel arm there was n=1 each of *Candida* sepsis, *Klebsiella* sepsis, and pulmonary sepsis; in the standard regimens arm there was n=1 neutropenia sepsis.

Relatedness to study treatment was assessed by investigator.

Ide-cel denotes idecabtagene vicleucel.

**Table S11.** Second Primary Malignancy (Safety Population).

<b>Second primary malignancy category</b> <b>Second primary malignancy</b> <b>subcategory</b> Preferred term	<b>Ide-cel</b> <b>(n=225)</b>	<b>Standard regimens*</b> <b>(n=126)</b>
Patients — no. (%)		
<b>Any second primary malignancy</b>	13 (6)	5 (4)
<b>Invasive second primary malignancy</b>	9 (4)	3 (2)
<b>Hematological malignancy</b>	3 (1)	0
Myelodysplastic syndrome	2 (1)	0
Acute myeloid leukemia	1 (<1)	0
<b>Solid tumor</b>	6 (3)	3 (2)
Malignant melanoma	2 (1)	0
Breast cancer (of bilateral origin)	1 (<1)	0
Breast cancer	1 (<1)	0
Rectal adenocarcinoma	1 (<1)	0
Small intestine adenocarcinoma	1 (<1)	0
Gastrointestinal stromal tumor	0	1 (1)
Lentigo maligna	0	1 (1)
Bronchial carcinoma	0	1 (1)
<b>Non-invasive second primary malignancy (non-melanoma skin cancer)</b>	4 (2)	2 (2)
Basal cell carcinoma	2 (1)	1 (1)
Squamous cell carcinoma	2 (1)	1 (1)
Squamous cell carcinoma of skin	1 (<1)	0
Bowen's disease	0	1 (1)

\* In the standard regimens arm, for patients who underwent leukapheresis in preparation of planned ide-cel treatment upon documented disease progression on standard regimen, only adverse events before leukapheresis were included.

ide-cel denotes idecabtagene vicleucel.

**Table S12.** Characteristics and Management of Cytokine Release Syndrome (Safety Population).

Parameter	Ide-cel (n=225)
<b>Patients with a CRS event — no. (%)<sup>*</sup></b>	197 (88)
Grade 1	124 (55)
Grade 2	62 (28)
Grade 3	6 (3)
Grade 4	3 (1)
Grade 5	2 (1) <sup>†</sup>
<b>Median (range) time to onset — days<sup>‡</sup></b>	1.0 (1.0–14.0)
<b>Median (range) duration — days<sup>§</sup></b>	3.5 (1.0–51.0)
<b>Medications used for management of CRS — no. (%)</b>	
Tocilizumab use	161 (72)
1 dose	92 (41)
>1 dose	69 (31)
Siltuximab use	3 (1)
Anakinra use	8 (4)
Steroid use <sup>¶</sup>	64 (28)

<sup>\*</sup> CRS is graded according to modified Lee's Criteria.<sup>2</sup>

<sup>†</sup> Two patients experienced grade 5 CRS. The first patient developed grade 1 CRS on the same day of ide-cel infusion, rising to grade 2 on day 3. Following a decline in organ function, acute myocardial infarction potentially related to anemia, and rapid atrial flutter, the patient died on day 6. The second patient died 21 days after ide-cel infusion from grade 5 CRS and concomitant grade 5 *Candida* sepsis, having had prolonged grade 4 CRS, hemophagocytic lymphohistiocytosis, infection due to multiple pathogens, and neurotoxicity. Both patients were treated with tocilizumab, anakinra, and dexamethasone for their CRS.

<sup>‡</sup> Time to first onset of CRS: first start date of CRS – infusion date +1.

<sup>§</sup> Algorithm for duration: if the gap between two events  $\leq 1$  day, then these two events are considered as one event regardless grade change, drug relationship change, or severity change.

<sup>¶</sup> Steroid use was not mandated in the protocol and was used based on clinical judgement. CRS denotes cytokine release syndrome and ide-cel idecabtagene vicleucel.



**Table S13.** Characteristics and Management of Neurologic Toxicity Events (Safety Population).

Parameter	Ide-cel (n=225)
<b>Patients with a neurotoxicity event — no. (%)<sup>*</sup></b>	34 (15)
Grade 1	13 (6)
Grade 2	14 (6)
Grade 3	5 (2)
Grade 4	2 (1)
Grade 5	0
<b>Median (range) time to onset — days<sup>†</sup></b>	3.0 (1.0–317.0 <sup>‡</sup> )
<b>Median (range) duration — days<sup>§</sup></b>	2.0 (1.0–37.0)
<b>Medications used for management of neurotoxicity — no. (%)</b>	
Steroids	15 (7)

<sup>\*</sup> Neurotoxicity includes immune effector cell–associated neurotoxicity syndrome reported by investigator as a neurological toxicity adverse event. No Parkinsonism was reported.

<sup>†</sup> Time to first onset of neurotoxicity: first start date of neurotoxicity – infusion date + 1.

<sup>‡</sup> One patient developed encephalopathy at day 317, which was not considered by the investigator to be related to ide-cel but related to worsening pneumonia and *C. difficile* colitis. The next longest duration of onset to a neurotoxicity event was 46 days.

<sup>§</sup> Algorithm for duration: if the gap between two events  $\leq 1$  day, then these two events are considered as one event regardless grade change, drug relationship change, or severity change.

ide-cel denotes idecabtagene vicleucel.

**Table S14.** Deaths (ITT population).

Parameter	Ide-cel (n=254)	Standard regimens (n=132)
Patients — no. (%)		
<b>Overall number of deaths</b>	75 (30)	34 (26)
Disease progression	44 (17)	23 (17)
AEs*	15 (6)	8 (6)
Other causes†	14 (6)	3 (2)
Second primary malignancies	2 (1)‡	0

\* Deaths due to AEs in the ide-cel arm were sepsis (n=3), COVID-19 (n=2), septic shock (n=2), bronchopulmonary aspergillosis (n=1), *Candida* sepsis (n=1), cytomegalovirus infection (n=1), pneumonia (n=1), pulmonary sepsis (n=1), amyotrophic lateral sclerosis (n=1), cerebrovascular accident (n=1), and cytokine release syndrome (n=1). Deaths due to AEs in the standard regimens arm were sepsis (n=2), COVID-19 (n=2), *Escherichia* sepsis (n=1), neutropenic sepsis (n=1) multiple organ dysfunction syndrome (n=1), and respiratory failure (n=1).

† Other causes for ide-cel arm included death (n=9), hemothorax (n=1), respiratory failure (n=1), cardiac failure (n=1), sepsis (n=1), and cerebral hemorrhage (n=1). Other causes for standard regimens arm included death (n=2) and euthanasia (n=1).

‡ Included leukemia (n=1) and pancreatic adenocarcinoma (n=1).

AE denotes adverse event, ide-cel idecabtagene vicleucel, and ITT intent-to-treat.

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