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ORAL ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Effects of Idecabtagene Vicleucel (Ide-Cel) Versus Standard Regimens on Health-Related Quality of Life (HRQoL) in Patients with Triple-Class-Exposed (TCE) Relapsed/Refractory Multiple Myeloma (RRMM) Who Received at Least 3 Lines of Prior Antimyeloma Regimens in the KarMMa-3 Phase 3 Randomized Controlled Trial

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Introduction: Patients with TCE RRMM have a high disease burden and often report worsening HRQoL with additional lines of therapy. The single-arm, phase 2 KarMMa study demonstrated that ide-cel, a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T cell therapy, improved HRQoL from baseline in patients with TCE RRMM who had received ≥ 3 prior regimens (Delforge M, et al. *Blood Adv* 2022;6:1309-1318). Furthermore, in the phase 3 KarMMa-3 clinical trial (NCT03651128), ide-cel significantly improved progression-free survival and response compared with standard regimens in patients with TCE RRMM who had received 2-4 prior regimens (Rodriguez-Otero P, et al. *N Engl J Med* 2023;388:1002-1014). Here we assessed the comparative effects of ide-cel versus standard regimens on HRQoL in patients with TCE RRMM who had received 3-4 prior regimens including an immunomodulatory agent, a proteasome inhibitor, and daratumumab (an anti-CD38 monoclonal antibody) using data from the KarMMa-3 study.
Methods: Patient-reported outcomes (PROs) were assessed by the European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire-Core 30 (QLQ-C30), EORTC Quality of Life Questionnaire Multiple Myeloma Module (QLQ-MY20), and EQ-5D-5L. The pre-specified primary domains of interest included EORTC QLQ-C30 global health status/QoL, physical functioning, cognitive functioning, fatigue, and pain; EORTC QLQ-MY20 disease symptoms and side effects of treatment; and the EQ-5D-5L visual analog scale (EQ-5D VAS). PROs were collected at screening (baseline), the day of ide-cel infusion (ide-cel) or first treatment dose (standard regimens), monthly from 2 to 28 months, and thereafter every 3 months. Comparisons were performed on least squares (LS) mean changes from baseline through 28 months between arms using constrained longitudinal data analysis (cLDA). Effect size was estimated by Hedges' g. The comparative effects of ide-cel versus standard regimens on time to confirmed improvement and time to confirmed deterioration (defined by prespecified change thresholds) were assessed via stratified Cox proportional hazards regression analyses. All *P* values are nominal and not adjusted for multiple testing. Statistical significance was set at $P < 0.05$.
Results: Baseline characteristics were well balanced among the patients in the ide-cel arm (n = 167) and the standard regimen arm (n = 93), with a median age of 63 years and a median time of 4.7 years from RRMM diagnosis to study screening. Completion rates of HRQoL assessments were high over time for most visits (> 75%). At baseline, mean HRQoL domain scores

were similar between arms. Overall LS mean changes from baseline to 28 months showed significant differences in favor of ide-cel versus standard regimens (nominal $P < 0.05$) for 11 domains (effect sizes of 0.26-0.82), and 7 (4 primary: global health status/QoL, cognitive functioning, pain, EQ-5D VAS; 3 secondary: dyspnea, insomnia, constipation) of them exceeded the prespecified MID thresholds (Table).
Time to confirmed improvement was significantly shorter (nominal $P < 0.05$) in the ide-cel arm than in the standard regimen arm for 10 domains, including all primary domains except pain. Time to confirmed deterioration was longer in the ide-cel arm than the standard regimen arm for most domains, with significant differences in emotional functioning, cognitive functioning, and dyspnea (EORTC QLQ-C30). Finally, side effects of treatment favored the ide-cel versus standard regimen arm (EORTC QLQ-MY20) (Table).
Conclusions: These patient-reported findings demonstrate that compared with standard regimens, treatment with ide-cel improved MM-relevant disease symptoms, functioning, and overall health status/HRQoL of patients with TCE RRMM in the KarMMa-3 trial. These data further substantiate the superior treatment outcomes of ide-cel over standard regimens in this patient population. Overall, treatment with ide-cel may help alleviate detriments to HRQoL in these patients with complex disease.

Disclosures Delforge: *Janssen:* Consultancy, Research Funding, Speakers Bureau; *Stemline:* Consultancy, Speakers Bureau; *Sanofi:* Consultancy, Speakers Bureau; *Bristol Myers Squibb:* Consultancy, Speakers Bureau. **Patel:** *Takeda:* Consultancy; *AbbVie; Allogene Therapeutics, Inc.; Arcellx; Bristol Myers Squibb/Celgene Corporation; Cellectis; Janssen Pharmaceuticals, Inc.; Nektar Therapeutic; Poseida Therapeutics; Precision BioSciences, Inc.; and Takeda Pharmaceuticals U.S.A., Inc.:* Research Funding; *AbbVie; Arcellx, AstraZeneca; Bristol Myers Squibb/Celgene Corporation; Caribou Science; Cellectis; Curio Bioscience; Genentech; Janssen Pharmaceuticals, Inc.; Karyopharm; Legend Biotech; Merck & Co., Inc.; Oncopeptides; Pfizer; Precision BioSciences:* Consultancy. **Eliason:** *GlaxoSmith-Kline:* Ended employment in the past 24 months; *Bristol Myers Squibb:* Current Employment, Current equity holder in publicly-traded company. **Dhanda:** *Bristol Myers Squibb:* Current Employment, Current equity holder in publicly-traded company. **Shi:** *Thermo Fisher:* Current holder of *stock options* in a privately-held company; 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Table. cLDA overall LS mean change from baseline to month 28 and time to confirmed HRQoL improvement and deterioration

Instrument/domain	Difference in BL to month 28 (ide-cel vs standard) LS mean change[a] (95% CI)	MID[b] (Imp)	Hedges' g[c] (95% CI)	Confirmed improvement[d] HR (95% CI)	Confirmed deterioration[e] HR (95% CI)
EORTC QLQ-C30					
QoL/Functioning					
Global health status/QoL[f]	6.69* (2.72 to 10.67)	4	0.43 (0.17 to 0.68)	3.80 (1.60 to 9.03)	0.79 (0.38 to 1.64)
Physical functioning[f]	3.91 (−0.54 to 8.36)	5	0.22 (−0.03 to 0.48)	2.21 (1.01 to 4.81)	0.72 (0.39 to 1.34)
Role functioning	1.92 (−3.50 to 7.33)	6	0.09 (−0.16 to 0.34)	1.29 (0.62 to 2.67)	0.89 (0.43 to 1.87)
Emotional functioning	3.50 (−0.23 to 7.23)	3	0.24 (−0.02 to 0.49)	1.82 (0.95 to 3.49)	0.47 (0.22 to 0.99)
Cognitive functioning[f]	6.17* (2.49 to 9.85)	3	0.42 (0.17 to 0.68)	5.96 (1.37 to 25.90)	0.20 (0.09 to 0.46)
Social functioning	3.49 (−2.03 to 9.01)	5	0.16 (−0.09 to 0.42)	3.31 (1.23 to 8.87)	0.85 (0.38 to 1.86)
Symptoms					
Fatigue[f]	−4.66 (−9.28 to −0.04)	−5	−0.26 (−0.511 to 0)	3.11 (1.38 to 6.99)	0.96 (0.46 to 2.01)
Nausea and vomiting	−2.36 (−5.09 to 0.38)	−3	−0.22 (−0.47 to 0.04)	NE	0.74 (0.18 to 3.08)
Pain[f]	−7.67* (−12.98 to −2.36)	−6	−0.37 (−0.62 to −0.11)	1.45 (0.64 to 3.28)	0.77 (0.35 to 1.69)
Dyspnea	−7.50* (−12.67 to −2.32)	−4	−0.37 (−0.62 to −0.11)	4.32 (0.97 to 19.24)	0.26 (0.11 to 0.63)
Insomnia	−6.09* (−12.14 to −0.04)	−4	−0.26 (−0.51 to 0)	1.46 (0.58 to 3.68)	0.49 (0.18 to 1.32)
Appetite loss	−2.41 (−7.33 to 2.52)	−5	−0.12 (−0.38 to 0.13)	3.87 (1.11 to 13.47)	1.60 (0.45 to 5.67)
Constipation	−5.83* (−10.31 to −1.36)	−5	−0.33 (−0.59 to −0.08)	3.48 (0.75 to 16.13)	0.56 (0.17 to 1.82)
Diarrhea	−2.55 (−7.49 to 2.40)	−3	−0.13 (−0.39 to 0.12)	1.48 (0.49 to 4.48)	0.63 (0.19 to 2.10)
EORTC QLQ-MY20					
Symptoms					
Disease symptoms[f]	−5.34 (−8.99 to −1.69)	−10	−0.37 (−0.63 to −0.12)	3.57 (1.04 to 12.21)	0.61 (0.24 to 1.51)
Side effects of treatment[f]	−8.22 (−10.77 to −5.67)	−10	−0.82 (−1.08 to −0.55)	5.10 (1.54 to 16.85)	0.30 (0.13 to 0.69)
Functioning					
Body image	3.56 (−2.02 to 9.14)	13	0.16 (−0.09 to 0.42)	1.30 (0.46 to 3.67)	1.36 (0.50 to 3.70)
Future perspective	5.33 (0.77 to 9.88)	9	0.30 (0.04 to 0.55)	1.84 (1.01 to 3.35)	0.64 (0.24 to 1.73)
EQ-5D-5L					
EQ-5D VAS[f]	7.18* (3.55 to 10.81)	7	0.50 (0.25 to 0.76)	3.80 (1.60 to 9.03)	0.68 (0.31 to 1.46)

[a]Negative differences in LS means for symptom domains and positive differences for functioning and overall health domains favor the ide-cel arm versus the standard regimens arm; [b]MID values (Cocks K, et al. *J Clin Oncol* 2011;29:89–96; Pickard AS, et al. *Health Qual Life Outcomes* 2007;5:70; Scully K, et al. *Eur J Haem* 2019;103:500–509) were the threshold for between-group changes over time; [c]Guidelines for interpretation of Hedges' g values: 0.20 is indicative of small effects; 0.50 for medium effects; 0.80 for large effects (Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale, NJ: Erlbaum; 1988); [d]Estimated from stratified Cox proportional hazards regression analysis. HR > 1 for confirmed improvement is in favor of the ide-cel arm versus the standard regimens arm; [e]Estimated from stratified Cox proportional hazards regression analysis. HR < 1 for confirmed deterioration is in favor of the ide-cel arm versus the standard regimens arm; [f]Primary domains.

*Nominally statistically significant (P <0.05) and clinically meaningful (exceeding the prespecified MID thresholds) difference between ide-cel and the standard regimens.

BL, baseline; cLDA, constrained longitudinal data analysis; CI, confidence interval; EORTC, European Organization for Research and Treatment of Cancer; HR, hazard ratio; Imp, improvement; LS, least squares; MID, minimum important difference; NE, not evaluable; QLQ-C30, Quality-of-Life Questionnaire-Core 30; QLQ-MY20, Quality of Life Questionnaire Multiple Myeloma Module; QoL, quality of life; VAS, visual analog scale.

Figure 1

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