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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 Relapsed/Refractory Multiple Myeloma (RRMM) Who Had Received 2-4 Prior Regimens: Updated Results from the Phase 3 KarMMa-3 Trial

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Background: An interim analysis (data cutoff date April 18, 2022) of the international, open-label, phase 3 KarMMa-3 trial (NCT03651128) showed the chimeric antigen receptor T cell therapy idecabtagene vicleucel (ide-cel) significantly improved progression-free survival and treatment response rates, as well as HRQoL, as compared with standard regimens, in patients with triple-class exposed (TCE) RRMM who had received 2-4 prior regimens (Rodriguez-Otero P, et al. *N Engl J Med* 2023;388:1002-1014; Delforge M, et al., *HemaSphere*, 2023;7(S3):P905). The aim of the present study was to analyze the effect of ide-cel versus standard regimens (daratumumab [DARA], pomalidomide, and dexamethasone [DEX]; DARA, bortezomib, and DEX; ixazomib, lenalidomide, and DEX; carfilzomib and DEX; or elotuzumab, pomalidomide, and DEX) on HRQoL in KarMMa-3 trial participants with an extended follow-up of patient-reported outcomes (PRO) data collection (data cutoff date April 28, 2023).
Methods: In KarMMa-3, HRQoL was assessed using the European Organisation 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. HRQoL assessments were completed at screening (baseline); the day of ide-cel infusion or the first dose of standard treatment; and monthly from 2 to 28 months; and every 3 months thereafter. The prespecified primary outcomes of interest were 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 visual analog scale (EQ-VAS). Least squares (LS) mean changes from baseline through month 25 for ide-cel and standard regimens were compared by constrained longitudinal data analysis (cLDA). Effect sizes were estimated by Hedges' g. The effect of ide-cel versus standard regimens on time to confirmed improvement and deterioration in HRQoL (defined by prespecified change thresholds and sustained duration) were compared by stratified Cox proportional hazards regression. There was no adjustment for multiple testing, and all *P* values reported are nominal.
Results: Overall, 254 patients were randomized to the ide-cel arm and 132 to the standard regimens arm. Baseline characteristics were well balanced across treatment arms; both arms had a median age of 63 years, a median of 3 prior anti-myeloma regimens, and median time from MM diagnosis to screening was 4 years. The baseline HRQoL scores were generally compa-

rable between treatment arms. Overall LS mean changes from baseline to month 25 showed significant differences (nominal *P* value < 0.05) in favor of ide-cel for 18 out of 21 HRQoL domains, with effect sizes (Hedges' g) of 0.27 to 0.82 (Table). For 13 of these domains (including 6 primary domains of interest), the difference in overall LS mean change from baseline exceeded the prespecified minimum important difference (MID) threshold. Time to confirmed improvement was significantly shorter in the ide-cel arm than the standard regimens arm for 19 domains, including all primary domains of interest (Table). Time to confirmed deterioration showed trends of being longer in the ide-cel arm than the standard regimens arm for most domains and was significantly longer for emotional functioning, cognitive functioning, social functioning, dyspnea, and constipation as measured by the EORTC QLQ-C30. The time to confirmed deterioration in side effects of treatment (based on the EORTC QLQ-MY20) was significantly longer for patients in the ide-cel arm and time to confirmed improvement was significantly faster, as compared with the standard regimens arm (Table).
Conclusions: In the KarMMa-3 trial, patients with TCE RRMM who had received 2-4 prior regimens, ide-cel significantly and meaningfully improved MM-relevant symptoms, functioning, and overall health status/HRQoL compared with standard regimens. Confirmed HRQoL improvements in the ide-cel arm occurred sooner than standard regimens. PRO improvements were sustained over more than 2 years, which is notable after a single infusion treatment with ide-cel. These patient-reported findings further support the benefit of ide-cel in this patient population.

Disclosures Delforge: *Janssen:* Consultancy, Research Funding, Speakers Bureau; *Sanofi:* Consultancy, Speakers Bureau; *Stemline:* Consultancy, Speakers Bureau; *Bristol Myers Squibb:* Consultancy, Speakers Bureau. **Patel:** *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; *Takeda:* Consultancy; *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:** *Pharmaceutical Product Development Inc.:* Current Employment; 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Table. Overall LS mean change from baseline to month 25 and time to confirmed HRQoL improvement and deterioration

Instrument/domain	Difference in LS mean change from baseline (ide-cel vs standard regimens) (95% CI)	MID[a]	Hedges' g (95% CI)[b]	Time to confirmed improvement HR (95% CI)	Time to confirmed deterioration HR (95% CI)
EORTC QLQ-C30					
QoL/functioning					
Global health status/QoL[c]	7.49* (4.78 to 10.20)	4	0.58 (0.37 to 0.80)	4.56* (2.27 to 9.15)	0.94 (0.51 to 1.74)
Physical functioning[c]	5.99* (3.50 to 8.48)	5	0.51 (0.29 to 0.73)	3.32* (1.70 to 6.51)	0.71 (0.43 to 1.17)
Role functioning	5.66* (1.97 to 9.34)	6	0.33 (0.11 to 0.54)	1.94* (1.01 to 3.72)	0.90 (0.51 to 1.60)
Emotional functioning	5.45* (2.85 to 8.05)	3	0.44 (0.23 to 0.66)	2.66* (1.54 to 4.60)	0.49* (0.26 to 0.90)
Cognitive functioning[c]	6.21* (3.65 to 8.77)	3	0.51 (0.3 to 0.73)	3.81* (1.47 to 9.87)	0.33* (0.18 to 0.64)
Social functioning	9.65* (5.93 to 13.37)	5	0.55 (0.33 to 0.76)	5.52* (2.34 to 13.05)	0.49* (0.27 to 0.89)
Symptoms					
Fatigue[c]	−7.60* (−10.74 to −4.46)	−5	−0.51 (−0.73 to −0.3)	4.86* (2.33 to 10.16)	0.95 (0.54 to 1.67)
Nausea and vomiting	−1.51 (−3.21 to 0.19)	−3	−0.19 (−0.40 to 0.02)	4.77* (1.02 to 22.22)	0.69 (0.23 to 2.05)
Pain[c]	−6.64* (−10.22 to −3.05)	−6	−0.39 (−0.61 to −0.18)	2.23* (1.15 to 4.33)	0.80 (0.43 to 1.48)
Dyspnea	−9.27* (−12.68 to −5.86)	−4	−0.58 (−0.79 to −0.36)	3.39* (1.17 to 9.83)	0.35* (0.17 to 0.72)
Insomnia	−7.27* (−11.22 to −3.33)	−4	−0.39 (−0.60 to −0.18)	2.27* (1.09 to 4.69)	0.52 (0.25 to 1.08)
Appetite loss	−3.0 (−6.04 to 0.05)	−5	−0.21 (−0.42 to 0.00)	3.94* (1.46 to 10.63)	1.00 (0.39 to 2.55)
Constipation	−5.84* (−8.91 to −2.78)	−5	−0.40 (−0.62 to −0.19)	5.20* (1.55 to 17.46)	0.40* (0.16 to 1.00)
Diarrhea	−2.66 (−5.84 to 0.52)	−3	−0.18 (−0.39 to 0.04)	1.55 (0.66 to 3.67)	0.64 (0.29 to 1.41)
Financial difficulties	−4.61* (−8.25 to −0.98)	−3	−0.27 (−0.48 to −0.06)	2.31 (0.86 to 6.23)	0.81 (0.35 to 1.88)
EORTC QLQ-MY20					
Symptoms					
Disease symptoms[c]	−3.68* (−6.01 to −1.34)	−10	−0.33 (−0.55 to −0.12)	3.30* (1.38 to 7.91)	0.75 (0.36 to 1.59)
Side effects of treatment[c]	−6.87* (−8.63 to −5.1)	−10	−0.82 (−1.04 to −0.60)	5.86* (2.10 to 16.38)	0.43* (0.23 to 0.84)
Functioning					
Body image	7.27* (3.51 to 11.03)	13	0.41 (0.2 to 0.62)	2.47* (1.02 to 5.98)	0.72 (0.36 to 1.44)
Future perspective	9.38* (6.26 to 12.49)	9	0.64 (0.42 to 0.85)	2.71* (1.64 to 4.47)	0.53 (0.25 to 1.13)
EQ-5D-5L					
Health utility index	0.04* (0.01 to 0.07)	0.08	0.29 (0.08 to 0.50)	2.21* (1.01 to 4.83)	0.65 (0.36 to 1.20)
EQ-VAS[c]	8.43* (5.98 to 10.88)	7	0.73 (0.51 to 0.95)	2.94* (1.61 to 5.38)	0.67 (0.36 to 1.27)

For EORTC QLQ-C30 global health status/QoL and functioning domains, EORTC QLQ-MY20 body image and future perspective, EQ-5D-5L health utility index, and EQ-VAS, a positive difference in LS mean change from baseline favors ide-cel over standard regimens. For EORTC QLQ-C30 symptom domains and EORTC QLQ-MY20 disease symptoms and side effects of treatment, a negative difference in LS mean change from baseline favors ide-cel over standard regimens. An HR > 1 for confirmed improvement and an HR < 1 for confirmed deterioration favor ide-cel over standard regimens.

[a]MID for improvement (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); [b]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; [c]Primary domains of interest.

*Difference between ide-cel and standard regimens statistically significant (nominal *P* value <0.05).

CI, confidence interval; EORTC, European Organization for Research and Treatment of Cancer; HR, hazard ratio; LS, least squares; MID, minimum important difference; 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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