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Secondary quality-of-life domains in patients with relapsed and refractory multiple myeloma treated with the BCMA-directed CAR T cell therapy idecabtagene vicleucel (ide-cel, bb2121): results from the KarMMa clinical trial

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INTRODUCTION

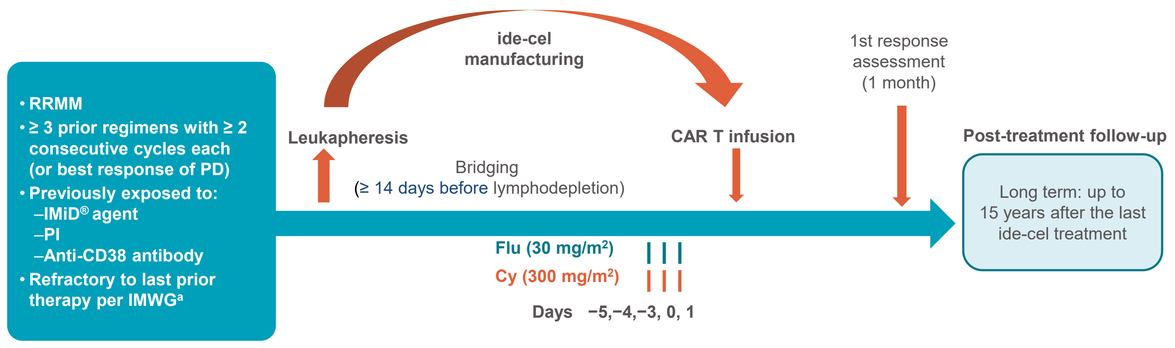
- Patients with RRMM who are triple-class exposed to IMiD® agents, PIs, and anti-CD38 antibodies have few treatment options and no standard of care[1–3]
- The symptom burden of MM is high; fatigue and bone pain adversely affect HRQoL[4,5]
  - As their symptoms become more severe, patients also report poorer HRQoL, including worsening physical and social functioning[5,6]
- Idecabtagene vicleucel (ide-cel, bb2121), a B cell maturation antigen-directed CAR T cell therapy, demonstrated a favorable clinical benefit-risk profile in triple-class exposed patients with RRMM in the phase 2, single-arm KarMMa clinical trial (NCT03361748)[7]
  - ORR was 73% (33% CR) and median PFS was 8.8 months for patients treated with ide-cel (target dose: 150–450 × 10^6 CAR+ T cells)
  - Among patients treated with the highest target dose (450 × 10^6 CAR+ T cells), the ORR was 82% (39% CR) and median PFS was 12.1 months
- Analysis of the impact of ide-cel therapy on primary domains of HRQoL showed that ide-cel provides meaningful improvements in HRQoL and self-reported symptoms associated with RRMM[8]
- To report the impact of ide-cel treatment on secondary HRQoL domains of interest and health utility scores in patients with RRMM in the KarMMa clinical trial
  - Group-level analysis
  - Individual-level analysis

CAR, chimeric antigen receptor; CR, complete response; HRQoL, health-related quality of life; IMiD, immunomodulatory drug; MM, multiple myeloma; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; RRMM, relapsed and refractory multiple myeloma.

1. Gandhi UH, et al. Leukemia 2019;33:2266-2275. 2. Nijhof IS, et al. Drugs 2018;78:19-37. 3. Mikhael J. Clin Lymphoma Myeloma Leuk 2020;20:1-7. 4. Johnsen AT, et al. Eur J Haematol 2009;83:139-148. 5. Jordan K, et al. Support Care Cancer 2014;22:417-426. 6. Despiégel N, et al. Clin Lymphoma Myeloma Leuk 2019;19:e13-e28. 7. Munshi NC, et al. J Clin Oncol 2020;38:8503. 8. Delforge M, et al. HemaSphere 2020:4:EP1000.

METHODS

Figure 1. KarMMa study design and HRQoL assessments



In the KarMMa trial, HRQoL is assessed at screening, baseline, on day of infusion (Day 1), monthly during months 1–6, and every 3 months until month 24 or end of study, and at disease progression or complete remission

- 3 HRQoL instruments were used (ide-cel-treated patients):
  - EORTC QLQ-C30 – a generic cancer validated instrument (n = 121)
  - EORTC QLQ-MY20 – an MM-specific module assessed with EORTC QLQ-C30 (n = 120)
  - EQ-5D-5L – a generic instrument to assess health status (index) and to assess global health using the visual analogue scale (VAS) (n = 120)
- The compliance rate was ≥ 80% for most visits

EudraCT: 2017-002245-29; ClinicalTrials.gov: NCT03361748

[a]Defined as documented disease progression during or within 60 days from last dose of prior antimyeloma regimen.

Cy, cyclophosphamide; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life C30; EQ-5D-5L, EuroQol 5 dimensions 5 levels; Flu, fludarabine; IMWG, International Myeloma Working Group; MY20, Myeloma Module; PD, progressive disease.

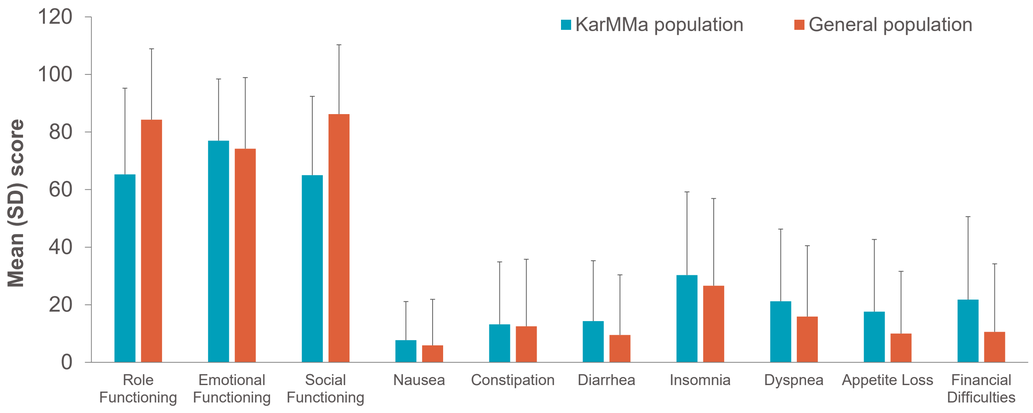
Statistical analyses

- Group-level analysis
  - Mean changes from baseline were considered clinically meaningful if the point estimate was above/below the prespecified threshold (minimal important difference [MID])
  - Mean changes from baseline were considered statistically significant where the 95% confidence interval boundaries were above/below the pre-specified threshold (MID)
  - MIDs were predefined for each subscale based on published definitions[1,2]
- Individual-level analysis
  - A patient's score was considered improved/deteriorated if it crossed the prespecified threshold (responder definition [RD])[3]

1. Cocks K, et al. Eur J Cancer 2012;48:1713-1721. 2. Sully K, et al. Eur J Haematol 2019;103:500-509. 3. Cocks K, Buchanan J. Presented at 22nd Annual Conference for the International Society for Quality of Life Research; 2015; Vancouver, Canada.

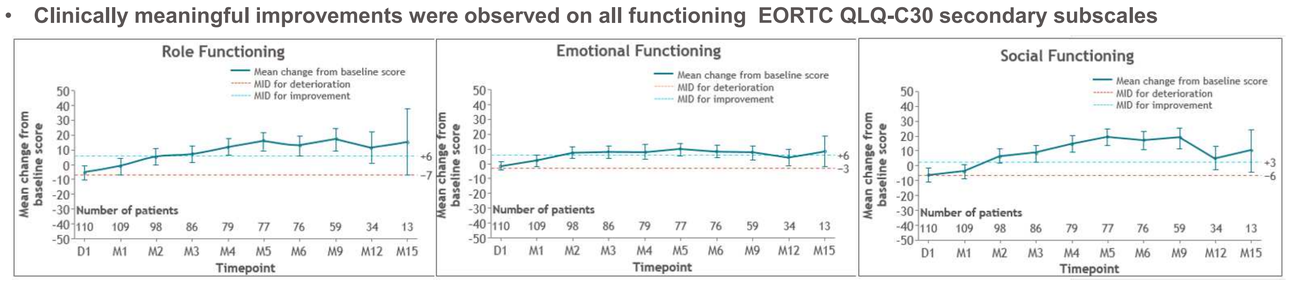
RESULTS

- At baseline, patients in the KarMMa trial had a lower level of functioning and higher symptom burden than the general population
- **Comparison of baseline HRQoL scores from KarMMa with general population normative data[1] (EORTC QLQ-C30)**



SD, standard deviation. 1. Nolte S, et al. Eur J Cancer 2019;107:153-163.

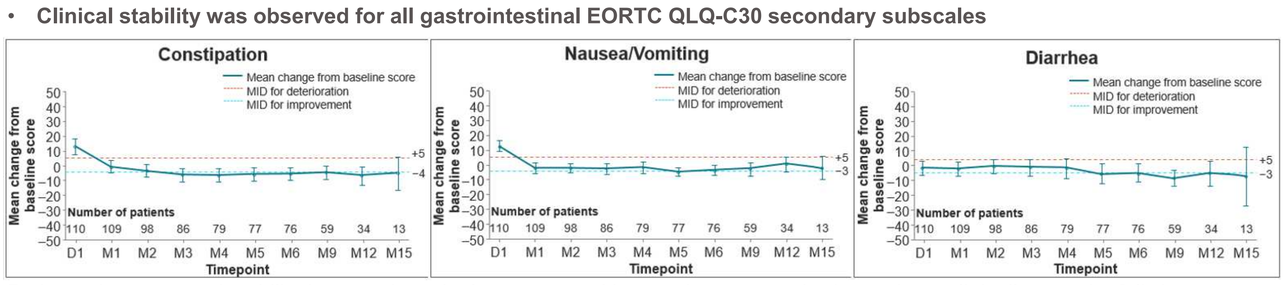
- **Clinically meaningful improvements were observed on all functioning EORTC QLQ-C30 secondary subscales**



These improvements were statistically significant for the Role Functioning and Social Functioning subscales at multiple time points

Day 1 is day of infusion. Error bars denote 95% confidence intervals. D1, Day 1; M, month; MID, minimal important difference.

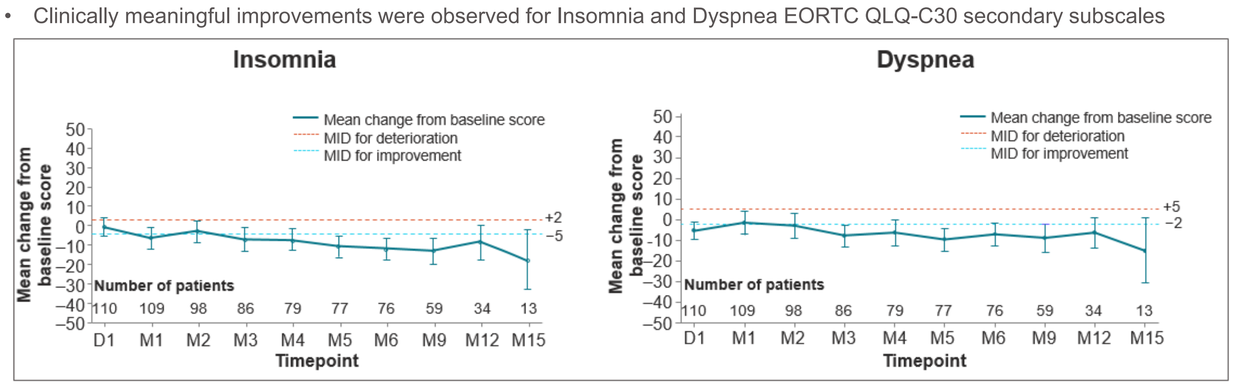
- **Clinical stability was observed for all gastrointestinal EORTC QLQ-C30 secondary subscales**



Patients demonstrated stability in gastrointestinal symptoms with a tendency toward a (sometimes clinically meaningful) decrease

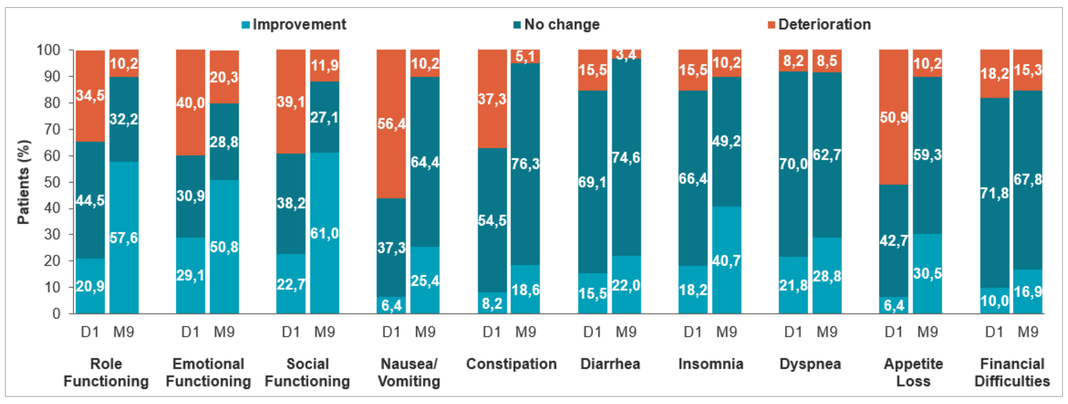
RESULTS

- Clinically meaningful improvements were observed for Insomnia and Dyspnea EORTC QLQ-C30 secondary subscales



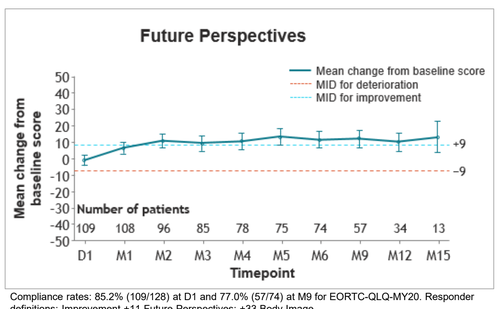
Insomnia and Dyspnea subscale scores improved over the course of treatment with a clinically meaningful (and sometimes statistically significant) decrease observed at most time points

- Clinically meaningful improvements or stability were observed for all EORTC QLQ-C30 secondary subscales
- Most patients achieved a clinically meaningful improvement or stability on all EORTC QLQ-C30 secondary subscales at Month 9

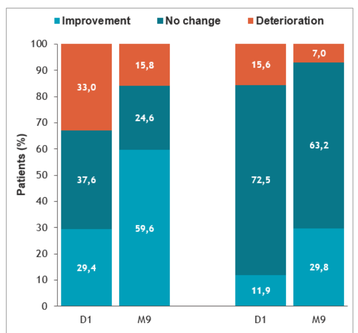


Compliance rates: 85.9% (110/128) at D1 and 79.7% (59/74) at M9 for EORTC QLQ-C30. Responder definitions: Improvement: +15 Role Functioning; +5 Emotional Functioning; +15 Social Functioning; −15 Nausea/Vomiting; −30 Constipation; −30 Diarrhea; −30 Insomnia; −30 Dyspnea; −30 Appetite Loss; −30 Financial Difficulties. Response is calculated relative to baseline.
Cocks K, Buchanan J. Presented at 22nd Annual Conference for the International Society for Quality of Life Research; 2015; Vancouver, Canada.

- Patients showed improvement or stability in Future Perspectives and Body Image EORTC QLQ-MY20 secondary subscales

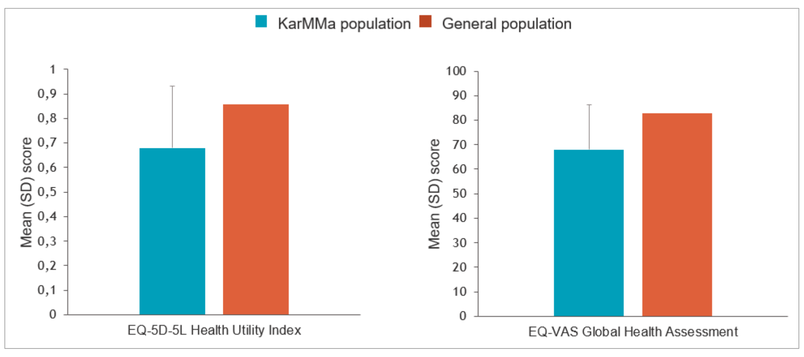


Compliance rates: 85.2% (109/128) at D1 and 77.0% (57/74) at M9 for EORTC-QLQ-MY20. Responder definitions: Improvement +11 Future Perspectives; +33 Body Image.



- Patients demonstrated stability in the Future Perspectives subscale from baseline to Months 2 through 15
- A greater proportion of patients demonstrated a clinically meaningful improvement or stability in Future Perspectives and Body Image subscales at Month 9 than at Day 1, from baseline

- At baseline, EQ-5D-5L index and EQ-VAS scores were lower for patients in the KarMMa trial versus the general population



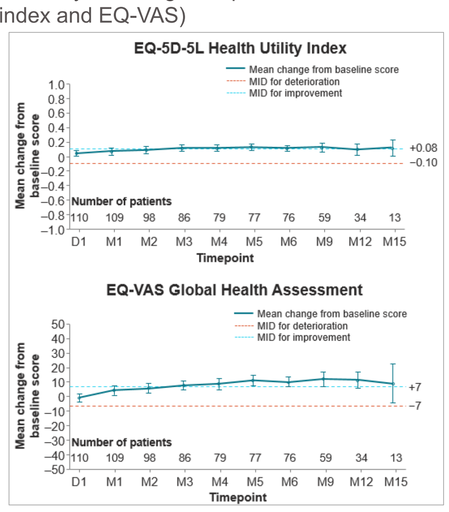
Both the EQ-5D-5L Health Utility Index and EQ-VAS Global Health Assessment scores were meaningfully lower than the UK general population[1] scores (below MID) at baseline[a]

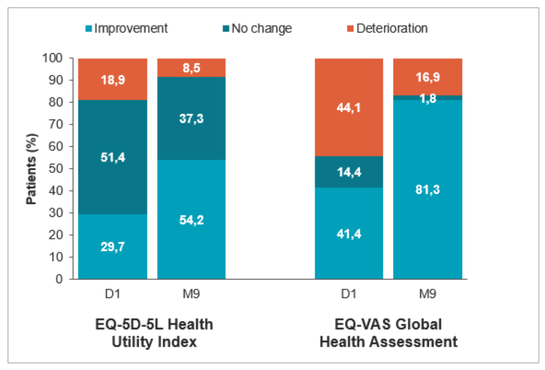
aNo statistical comparisons were conducted. SD data were not available for general population data.

Responder definitions: Improvement +0.08 EQ-5D-5L Health Utility Index; +15 EQ-VAS. Pickard AS, et al. Health Qual Life Outcomes 2007;5:70. EQ-VAS, EuroQoL Visual Analogue Scale.

1. Janssen B, Szende A. In: Self-reported population health: an international perspective based on EQ-5D. Dordrecht:Springer;2014. Chapter 3.

- Clinically meaningful improvements in Health Utility Index and Global Health Assessment were observed (EQ-5D-5L index and EQ-VAS)





In most patients, a clinically meaningful improvement from baseline was observed for the EQ-5D-5L Health Utility Index and EQ-VAS Global Health Assessment

Compliance rates: 79.7% (59/74) at M9 for EQ-5D-5L. Responder definitions: Improvement +0.08 EQ-5D-5L Health Utility Index; +15 EQ-VAS

CONCLUSION

- Patients in the KarMMa trial demonstrated group-level improvements in most functional and symptom EORTC QLQ-C30 secondary subscale scores from baseline to Month 3 through Month 15
  - Stable status was most frequently observed among individuals for symptom and financial difficulties subscales
- Scores for the EORTC QLQ-MY20 Future Perspectives and Body Image subscales were stable over time
- At baseline, EQ-5D-5L Health Utility Index and EQ-VAS Global Health Assessment scores were lower compared with the UK general population, but improved over time following treatment with ide-cel

Overall, these data confirm that in triple-class exposed RRMM patients, the clinical benefits associated with ide-cel treatment provide clinically meaningful HRQoL improvements without compromising any HRQoL domains

ACKNOWLEDGMENTS

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