The Burden of Relapsed/Refractory Multiple Myeloma: An Indirect Comparison of Health-Related Quality of Life Burden Across Different Types of Advanced Cancers at Baseline and After Treatment Based on HORIZON (OP-106) Study of Melflufen Plus Dexamethasone

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BACKGROUND

- Due to advances in therapy, outcomes have improved in multiple myeloma (MM). However, the improvement in overall survival (OS) is associated with a greater proportion of patients living with the burden of symptoms and complications of relapsed/refractory MM (RR MM) and prior lines of therapy¹
- Treatment options are limited for late-stage RR MM refractory to pomalidomide (pom) and/or daratumumab (dara). Treatment goals for these latestage patients should include extending OS but also preserving health-related quality of life (HRQoL) and managing disease-related symptoms²
- HRQoL assessment may increase understanding of the impact that cancer and cancer treatment have on the physical, mental, and emotional well-being of patients³
- Melflufen is a novel peptide-drug conjugate that rapidly delivers a cytotoxic payload into tumor cells⁴⁻⁸
- Phase 2 HORIZON (OP-106), an ongoing, pivotal study of melflufen + dexamethasone (dex), has demonstrated encouraging efficacy and safety in patients with heavily pretreated, poor-risk RR MM refractory to pom and/or dara⁹

OBJECTIVES

• This analysis examines baseline HRQoL in the HORIZON study as well as other published studies in RR MM and other advanced cancers to help characterize the burden of relapsed/refractory disease

METHODS

- In the HORIZON trial, HRQoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) and the EQ-5D-3L questionnaire
- HRQoL was added to HORIZON via a protocol amendment specifying inclusion of a minimum of 50 evaluable patients
- Questionnaires in HORIZON were administered at cycle (C) 1 day (D) 1, C2D1, C4D1, C6D1, C8D1, and end of treatment
- A literature search was conducted to identify other studies of baseline HRQoL in comparable patient populations with RR MM and other advanced cancers
- A stepwise analysis approach was used in which HORIZON baseline HRQoL was compared with other studies with similar patient populations with RR MM where HRQoL has been reported
- This comparison was based on 2 widely used patientreported outcome measures: EORTC QLQ-C30 and EQ-5D
- Next, HRQoL of HORIZON (as representative for RR MM) was compared with other advanced cancer types (Pickard et al³), based on EQ-5D-3L
- US time trade-off value set (44% of patients in HORIZON are from the United States) was used to calculate EQ-5D index

RESULTS

Table 1. Baseline Patient Characteristics for the HRQoL-Evaluable **Population, HORIZON Study**

Characteristic

Age, median (range), y

Gender (male/female), %

Time since diagnosis at study ent

No. of prior lines at study entry,

ISS stage I / II / III / unknown, %

Albumin level at study entry

≥3.5 g/dL, n (%)

<3.5 g/dL, n (%)

High-risk cytogenetics at study e

High LDH (1.5 × ULN) at study ent

Triple-class refractory,^d n (%)

Alkylator refractory, n (%)

nformation is missing for 4 patients. ^bHigh-risk cytogenetics at study entry were based on fluorescence in situ hybridization defined as t(4;14), del(17/17p), t(14;16), t(14;20), gain(1q) ber Sonneveld P, et al¹⁰; data are currently missing for 32 patients. ^cInformation is missing for 1 patient. ^dTriple-class refractory is defined as refractory to at least 1 PI, at least 1 IMiD, and at least 1 anti-CD38 monoclonal antibody. HRQoL, health-related quality of life; ISS, International Staging System; LDH, lactate dehydrogenase; ULN, upper limit of normal; PI, proteasome inhibitor.

- data, 63 of whom also had baseline data available (**Table 1**)
- International Staging System stage II/III disease at study entry

Table 2. Studies in RR MM With HRQoL Information

Study	Median Prior Lines	Age (range)	Treatment	Ν
Chari A, et al (2016) ¹¹	≥3	65 (27-94)	Daratumumab	348
Cook G, et al (2019) ¹²	≥3	64 (32-85)	Daratumumab	293
Steward AK, et al (2016) ¹³	2 2	64 (38-87) 65 (31-91)	KRd Rd	396 396
Leleu X, et al (2017) ¹⁴	≥2 ≥2		BOR LEN	96 162
Richardson PG, et al (2018) ¹⁵	3 3	61 (33-79) 61 (32-77)	PBd Pla+Bd	73 74
Robinson D Jr, et al (2016) ¹⁶	Late stage Late stage	<65 65-75	BOR BOR	153 77

BOR, bortezomib; KRd, carfilzomib, lenalidomide, and dexamethasone; LEN, lenalidomide; PBd, panobinostat, bortezomib, and dexamethasone; Pla+Bd, placebo + bortezomib and dexamethasone; Rd, lenalidomide and dexamethasone

- (Table 2)
- (Figure 1)

-Symptoms previously described to have the largest impact on HRQoL, including pain, fatigue, and role functioning,^{17,18} were comparable across RR MM studies

- was 0 (range -66.6 to 50)
- of RR MM populations

	HRQoL-Evaluable Patients (N=63)		
	67 (46-84)		
	54/46		
ntry,ª median (range), y	7 (0.7-17.1)		
, median (range)	5 (2-10)		
	38 / 22 / 37 / 3		
	49 (78)		
	14 (22)		
v entry,⁵ n (%)	25 (40)		
ntry, ^c n (%)	6 (10)		
	40 (63)		
	30 (48)		

• As of data cutoff (21 October 2019), 64 patients in HORIZON had baseline HRQoL

• Patients were heavily pretreated, with a median of 5 prior lines of therapy, and most (63%) were triple-class refractory. More than half (59%) of patients had

• Six studies with baseline EORTC QLQ-C30 HRQoL data, representing 2068

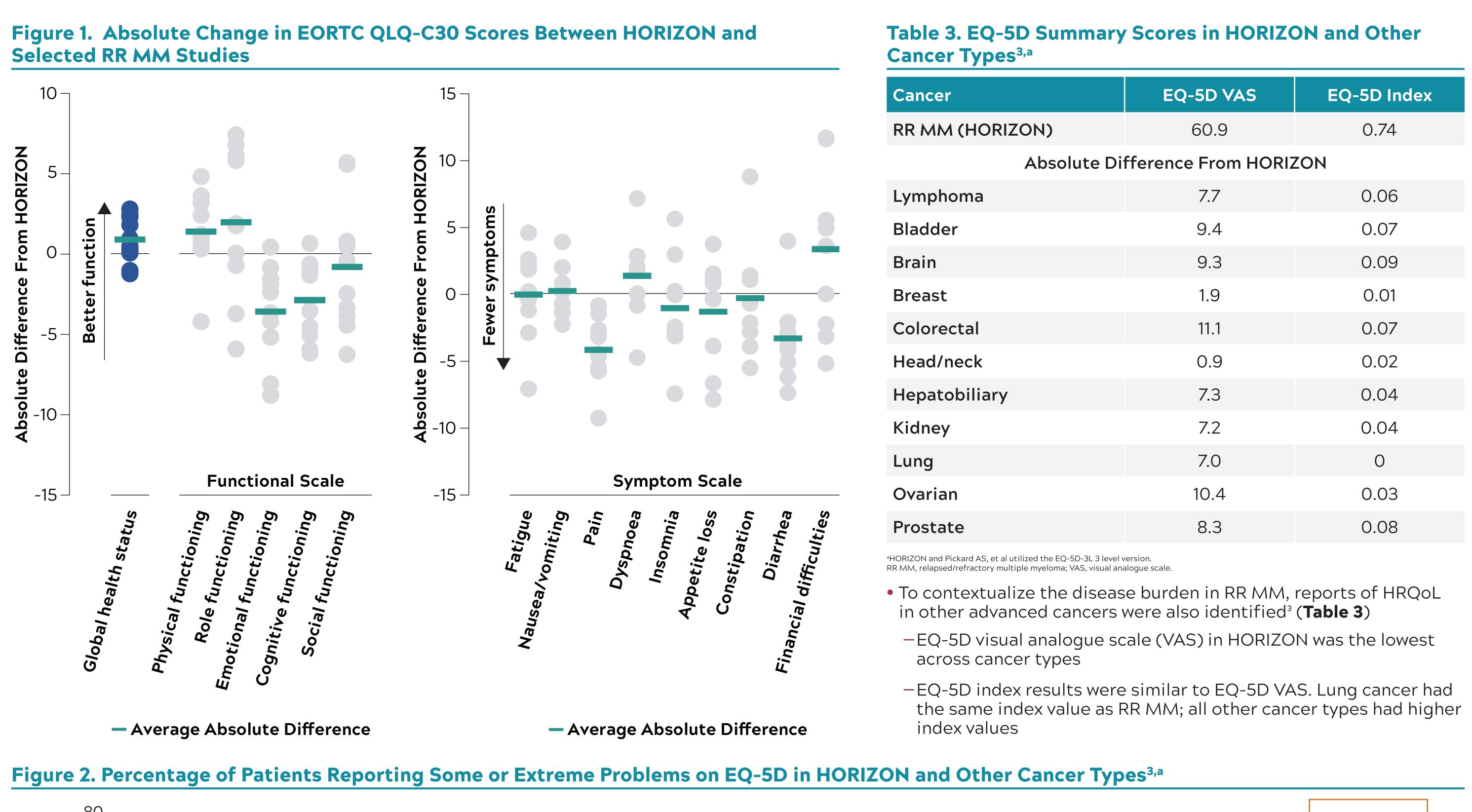
patients with RR MM with at least 2 prior lines, were identified in the literature

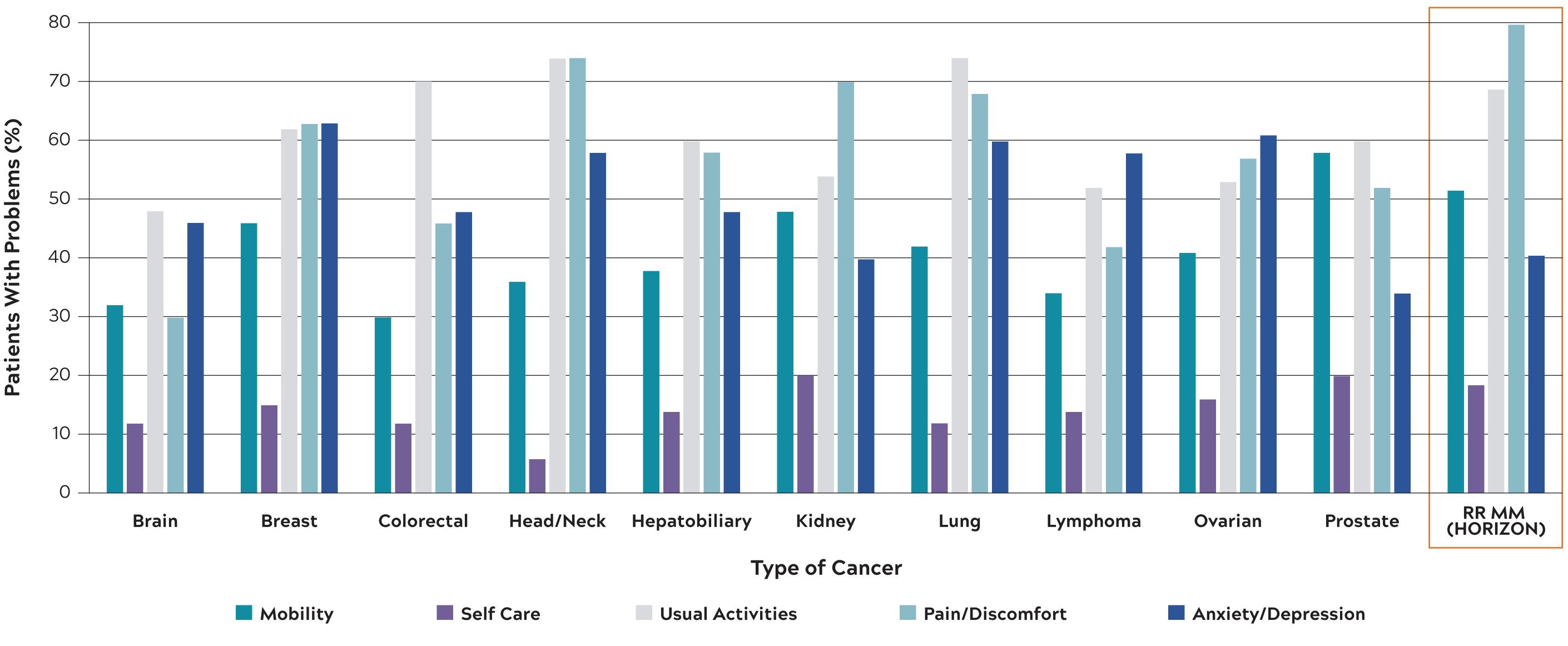
• EORTC QLQ-C30 baseline Global Health Status, Functional Domain, and Symptom Domain scores for HORIZON were comparable with those of other RR MM studies

• At the data cutoff, 53 patients had at least 1 follow-up visit; 2 patients had 7 follow-up visits, while the median number of follow-up visits was 3. The median change in EORTC QLQ-C30 Global Health Status from baseline to last treatment

• Overall, these data suggest that HORIZON HRQoL baseline data are representative

Selected RR MM Studies





^aHORIZON and Pickard AS, et al utilized the EQ-5D-3L 3 level version

• HORIZON data indicate a high HRQoL burden in RR MM relative to other cancer types³ (**Figure 2**)

- A higher percentage of patients with RR MM in HORIZON (80%) reported problems with pain/discomfort compared with any other cancer type (range, 30%-74%) -The percentage of patients reporting mobility problems in HORIZON (52%) was second only to those with prostate cancer (58%)

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-5D VAS	EQ-5D Index			
60.9	0.74			
From HORIZON				
7.7	0.06			
9.4	0.07			
9.3	0.09			
1.9	0.01			
11.1	0.07			
0.9	0.02			
7.3	0.04			
7.2	0.04			
7.0	0			
10.4	0.03			
8.3	0.08			

CONCLUSIONS

- Despite limitations of this cross-study comparison, including differences in patient populations, patients with RR MM and ≥2 prior therapies had similar HRQoL across studies
- Baseline HRQoL data from HORIZON confirm these patients are representative of the disease burden of other RR MM populations described in the literature
- Healthy adult populations globally have reported EQ-5D mean utility scores from 0.69-0.95 and VAS scores of 71.1-83.7¹⁸
- EQ-5D baseline mean utility scores in HORIZON and RR MM studies reported here are on the low end of this range, from 0.66-0.74
- Baseline health state VAS scores in HORIZON and other RR MM studies are lower than healthy populations at 57.6-63.0, exceeding the 7-point minimally important difference which has been identified as a clinically meaningful impact on HRQoL in cancer¹⁹
- Overall, this analysis indicates that RR MM represents a high burden of disease, including among patients with advanced cancers

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