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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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First time submitting an abstract to the ASH annual meeting? No

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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 (RRMM) and prior lines of therapy (Vogl et al. *Leuk Lymphoma*. 2009). There are limited treatment options for late-stage RRMM refractory to pomalidomide (pom) and/or daratumumab (dara). Treatment goals for these late-stage patients should include extending OS but also preserving health-related quality of life (HRQOL) and managing disease-related symptoms (Jordan et al. *Support Care Cancer*. 2014).

Melflufen is a lipophilic peptide-conjugated alkylator that rapidly delivers a highly cytotoxic payload into myeloma cells through peptidase activity. Melflufen is taken up by myeloma cells and immediately cleaved by peptidases into hydrophilic alkylator payloads that induce irreversible DNA damage and apoptosis. In phase 2 HORIZON, melflufen + dexamethasone (dex) has demonstrated encouraging efficacy in patients with RRMM refractory to dara and/or pom (overall response rate [ORR], 30%; median progression-free survival, 4 months; median OS, 10 months) and was well tolerated, with infrequent nonhematologic adverse events (AEs) and low rates of discontinuation due to AEs (Richardson et al. EHA 2019; Abstract S1605). This analysis examines baseline HRQOL in the HORIZON study as well as other published studies in RRMM and other advanced cancers, to help characterize the burden of relapsed/refractory disease.

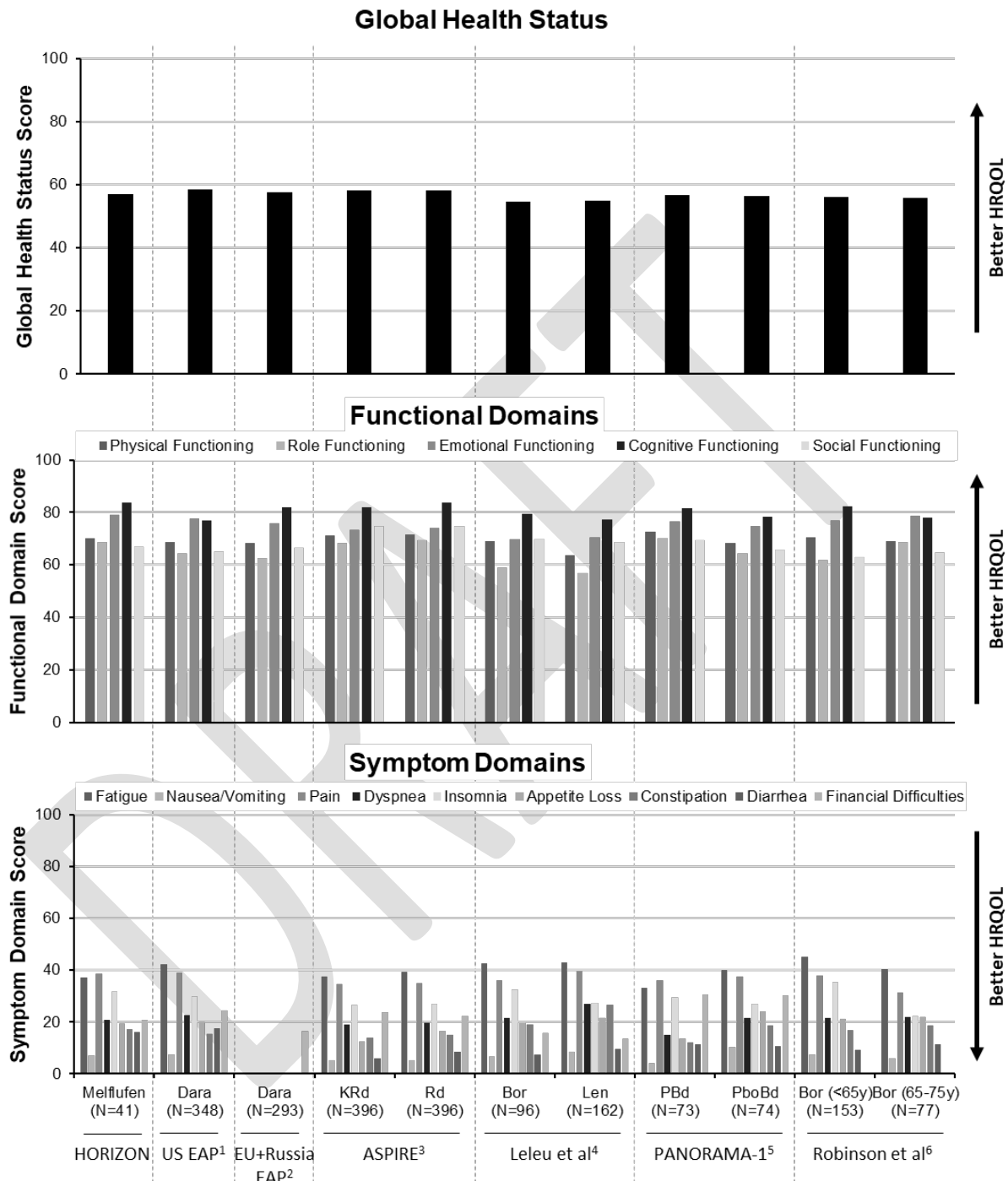
Methods: In HORIZON, patients with RRMM must have received ≥ 2 prior lines, been exposed to an IMiD and PI, and be refractory to pom and/or dara. HRQOL, a secondary endpoint, was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) and the EuroQol 5 Dimension-3 Level (EQ-5D-3L) questionnaire. Questionnaires were administered at baseline and at intervals, through study completion. A literature search was conducted to identify other studies of baseline HRQOL in comparable patient populations with RRMM and other advanced cancers.

Results: As of data cutoff (20 June 2019), 41 patients on HORIZON had baseline HRQOL data: median age, 66 y (46-84); median time since diagnosis, 5.7 y (2-17), 22% International Staging System stage 3 disease, 74% (n=27 evaluable) high-risk cytogenetics at study entry. Additionally, 6 studies with baseline EORTC QLQ-C30 HRQOL data, representing 2068 patients with RRMM with at least 2 prior lines, were identified in the literature, including 2 analyses of dara expanded access programs (EAPs) and the ASPIRE and PANORAMA phase 3 clinical trials (Figure). In HORIZON, QLQ-C30 baseline Global Health Status score was 57.1 (scale 0-100). This was relatively comparable to other RRMM studies (range, 54.8-58.6). QLQ-C30 Functional Domain and Symptom Domain scores were also comparable across HORIZON and other RRMM studies. In HORIZON, EQ-5D baseline mean utility score was 0.74 (scale 0-1) and baseline health state visual analog score (VAS) was 60.54 (scale 0-100). These were similar to EQ-5D baseline mean utility scores of 0.75 and 0.66 and VAS of 63.06 and 57.59 reported in the US and EU + Russia dara EAP analyses, respectively, indicating similar baseline HRQOL across these populations.

To contextualize the disease burden in RRMM, reports of HRQOL in other advanced cancers were identified in the literature. In a study of 534 patients with advanced cancer of the bladder, brain, breast, colon/rectum, head/neck, hepatobiliary tract/pancreas, kidney, lung, lymphoma, ovary, or prostate, EQ-5D mean utility scores ranged from 0.74-0.83 and mean VAS ranged from 61.8-72.0 (Pickard et al. *Clin Ther.* 2016). Despite limitations of cross-study comparisons, this suggests patients with RRMM have a similar, or potentially higher, disease burden as those with other advanced cancers.

Conclusion: Despite differences in patient populations and prior lines of therapy across published studies, patients with RRMM and ≥ 2 prior therapies had remarkably similar HRQOL. Baseline HRQOL data from HORIZON confirm these patients are representative of the disease burden of other RRMM populations described in the literature. Overall, this comparison indicates that RRMM represents a high burden of disease among patients with advanced cancers.

Figure. Baseline EORTC QLQ-C30 HRQOL in HORIZON and RRMM studies. For all 3 graphs, studies are indicated on x-axis of bottom figure.



Bor, bortezomib; Dara, daratumumab; EAP, expanded access program; HRQOL, health-related quality of life; KRd, carfilzomib + lenalidomide + low-dose dexamethasone; Len, lenalidomide; PBd, panobinostat + bortezomib + low-dose dexamethasone; Pbo, placebo + bortezomib + low-dose dexamethasone; Rd, lenalidomide + low-dose dexamethasone. 1. Chari A, et al. *Blood*. 128;Abstract 2133. 2. Cook G, et al. EHA 2019. Abstract PS1425. 3. Stewart AK, et al. *J Clin Oncol*. 2016;34:3921-3930. 4. Leleu X, et al. *Blood Cancer J*. 2017;7:e543. 5. Richardson PG, et al. *Br J Haematol*. 2018;181:628-636. 6. Robinson D Jr, et al. *Br J Haematol*. 2016;174:368-381.