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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Health-Related Quality of Life (HRQoL) in Fit, Unfit and Frail Patients Enrolled in Fitness (UK-MRA Myeloma XIV): A Cross Sectional Study

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Introduction
In the UK in 2016-2018, more than 4 in 10 new diagnoses of multiple myeloma (MM) were in people aged at least 75 years old. Transplant-ineligible (TNE) patients are a heterogeneous group that is not well-defined by age, but by the interplay of age, physical function, cognition and comorbidity better defined as 'frailty'. There is little evidence on the effect of frailty on HRQoL in patients with MM. We examined patient-reported outcomes from participants enrolled in the FiTNEss study to understand HRQoL according to frailty group and the contribution of different elements of the International Myeloma Working Group (IMWG) frailty score (FS) to HRQoL.
Methods
FiTNEss (UK-MRA Myeloma XIV, NCT03720041) is a phase III, multi-centre, randomised controlled trial for newly diagnosed TNE MM patients. Patients receive lenalidomide, ixazomib, and dexamethasone induction and maintenance, comparing

frailty score-adjusted up-front dose reductions and standard up-front dosing followed by toxicity dependent reactive dose adjustments.

Frailty was defined using the IMWG FS. It includes age (<75y, 75-80y, >80y), Katz Activity of Daily Living (ADL<=4), Lawton Instrumental Activity of Daily Living (IADL<=5), and the Charlson Comorbidity Index (CCI<=1). The UK-MRA Myeloma Risk Profile (MRP) [1] was scored using age, performance status (PS), ISS and CRP.

HRQoL was measured by EORTC QLQ C30 and MY20 completed at trial entry. We used a one-way ANOVA and two-sample unequal variance t-tests to compare subscales in different frailty groups. We sought minimally important differences that were at least medium size [2], and adjusted p-values using the Bonferonni correction for the 19 subscales (adjusted $P = 0.05/19 = 0.0026$).

Results

Baseline HRQoL was available for 559 trial participants. Median age was 77y (<75y: 183 [32.7%], 75-80y: 248 [44.4%], >80y 128 [22.9%]), 307 (54.9%) were male and 427 (76.2%) ECOG PS0-1. 160 (28.6%) patients were classified as Fit, 182 (32.6%) were Unfit and 217 (38.8%) were Frail according to IMWG FS. 105 (18.8%) patients had CCI <=1, 60 (10.7%) had ADL<=4 and 115 (20.6%) had IADL <=5. 167 (31.0%) patients were classified as low risk, 180 (33.5%) were intermediate risk and 191 (35.5%) were high-risk according to MRP.

Contrasting IMWG fit, unfit and frail patients, significant differences were evident in 7 of 15 C30 subscales (Global Health Status [QL], Physical [PF], Role [RF], Cognitive [CF] and Emotional Functioning [EP], Appetite loss [AP], Dyspnoea [DY]) and 1 of 4 MY20 subscales (Side Effects [MYSE]) (Figure A). The largest differences in subscales were between the Fit/Unfit and Frail groups with only a single nominally different subscale (PF) between Fit and Unfit.

When comparing the frailty score elements, age group and CCI were not significantly different using C30 or MY20 subscales. However, when considering ADL: 11 of 15 C30 (QL, PF, RF. CF, Social Functioning [SF], Fatigue [FA], Pain [PA], AP, Constipation [CO], DY, Financial Problems [FP]) subscales and 2 of 4 MY20 subscales (Disease Symptoms [MYDS], MYSE) were significantly different. Similarly, when considering IADL: 10 of 15 C30 subscales (QL, PF, RF, CF, SF, FA, PA, AP, CO and DY) and 4 of 4 MY20 subscales (MYDS, MYSE, Body Image, Future Perspective Worries) were significantly different (Figure B).

When comparing between MRP risk groups, 10 of 15 C30 subscales (QL, PF, RF, CF, SF, FA, PA, AP, CO and DY) and 2 of 4 MY20 subscales (MYDS, MYSE) were significantly different. Unlike IMWG FS, 5 subscales were nominally significantly different between low and medium risk groups (QL, PF, RF, SF, DY).

Conclusion

The IMWG FS is associated with several domains from EORTC QLQ-C30 and MY20 at baseline with worse function and symptomatology among frail patients. Examining FS elements show that age and comorbidities do not contribute to heterogeneity in HRQoL. However, ADL and IADL are significantly associated with HRQoL. ADL elements may identify components of frailty that are potentially modifiable through supportive care and rehabilitation and could enhance HRQOL and treatment tolerability in older patients.

The MRP risk profile is associated with baseline HRQoL as shown previously and with a number of other subscales as shown here. There is evidence that the MRP can delineate subscales, including QL better than the IMWG FS.

1. Cook G, et al, *The Lancet Haematology*, *6*(3): E154-E166.
2. Cocks K, et al, *Journal of Clinical Oncology*, *29*(1): 89-96.

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OffLabel Disclosure: Ixazomib, in combination with lenalidomide and dexamethasone, is used as induction and maintenance treatment for transplant-ineligible newly diagnosed patients with multiple myeloma.

EORTC-QLQ-C30 and MY20 subscale score means with associated 95% confidence intervals by group.
(A) IMWG Frailty Score: Fit vs Unfit vs Frail.
(B) Lawton Instrumental Activity of Daily Living (IADL): (Yes = IADL<=5 vs No = IADL>6)

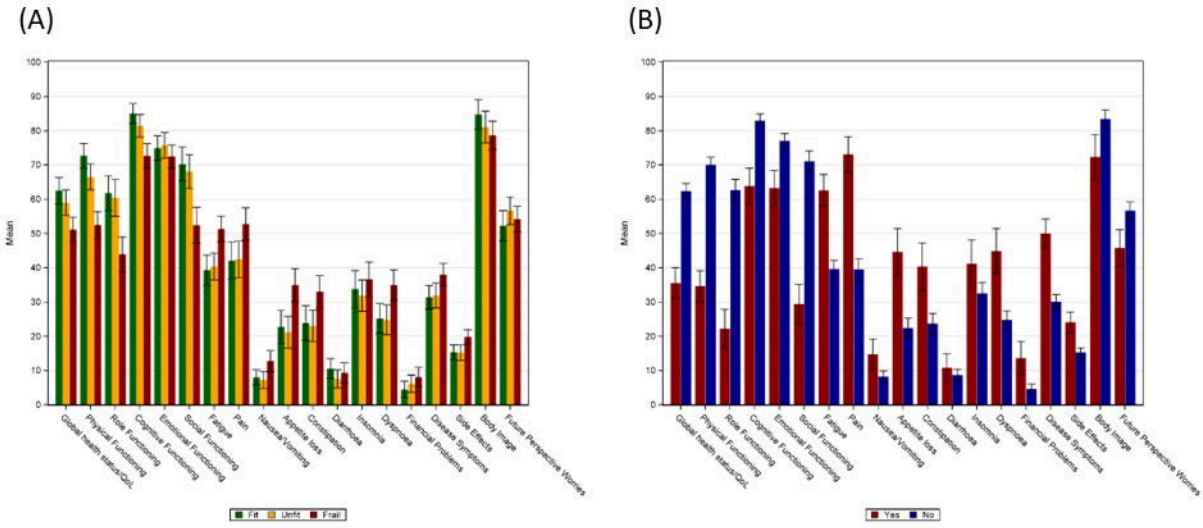

Figure 1

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