The MM Hub were delighted to attend the 4th World Congress on Controversies in Multiple Myeloma (COMy) held in Paris, France, from 3–5 May 2018. On Thursday 3 May, the second session of the congress took place and was entitled: ‘Organ damage and practical considerations’. The session was moderated by Nikhil Munshi, from the Dana Farber Cancer Institute, Harvard Medical School, Boston and Heinz Ludwig, from the Wilhelminen Cancer Research Institute, Vienna, Austria. Dr Rachid Baz, from the Moffitt Cancer Center and Research Institute, Tampa, US, gave the final talk of this session with the title: ‘Quality of life considerations in myeloma’.

Dr Baz began with a case study which raised the question of the use of quality of life (QoL) data to determine therapeutic strategies. A 69-year-old man was diagnosed with international staging system (ISS) I with standard risk multiple myeloma (MM) in 2014 and was given a combination of lenalidomide, bortezomib, and dexamethasone (RVD) and high dose melphalan, along with a stem cell transplant in 2015. Due to the unwanted side-effects of diarrhea and fatigue, affecting QoL, the patient chose to discontinue maintenance therapy after two years while in complete remission (CR). Following this pause in therapy, biochemical tests revealed an increase in serum M protein suggesting disease progression, although the patient remained asymptomatic except for occasional neuropathy.

A major feature driving the decision to stop therapy was the geographical distance from the treatment center, and as a consequence, the patient requested an oral regimen, though was conscious he did not wish to compromise efficacy. Dr Baz raised the question as to whether QoL data should be used to determine when to start therapy following biochemical relapse, and if QoL can also help to determine the optimal systematic therapy.

Dr Baz then turned to the definition of QoL, raising the question: “Everyone wants it, but what is it?”, and explained that definitions appear to differ vastly, or are avoided altogether. One definition included the description: ‘It appears to be a broad-ranging concept affected in a complex way by the person’s physical health, psychological state, level of independence, social relationships, and their relationship to salient features of their environment’. There is certainly no unified scale and in general, QoL is accepted to be a subjective measure.

Instead, health-related quality of life (HRQL), which is one measure of QoL, may be a more reliable measurement. Dr Baz described HRQL as “a concept that involves those aspects of QoL or function, which is influenced by health status and is based on dimensions (i.e. physical, psychological and social aspects) which can be measured”. He explained that QoL is particularly relevant in MM because the disease is considered incurable and generally affects the frail and the elderly, who are often more affected by drug toxicities, and the increasing cost of care adds a socioeconomic burden.

Further acronyms were then defined, including patient self-reported outcomes (PRO) which come without interpretation from a caregiver, the Global health score – one of the EORTC QLQ0C30 measures, and the minimal important difference (MID) – a measure of the smallest clinically meaningful change perceived by a patient, and finally the Mixed model...
analysis (MMA) – a statistical method to analyze HRQL longitudinally while preserving power and accounting for missing variables. He explained that what is important with this kind of assessment is the ability to link it to a clinically meaningful outcome.

Dr Baz then described a study in which both clinicians and patients were asked to rank various factors in terms of importance, and it was interesting to see that clinicians and patients viewed these factors differently. The clinicians’ top rankings were: pain, fatigue, being easily tired and emotional ups and downs, whereas the patients’ highest ranking factors were: sexual function, uncertainty about health, fatigue, and weight gain. Dr Baz suggested that this was perhaps in part due to both parties perhaps not wanting to talk about sensitive issues, but importantly highlights the need for clinicians to better understand the things that matter most to their patients.

Two tools for measuring HRQL: MDASI-MM HRQL and EORTC QLQ-MY20, were then described, with the lack of emotional, psychological, and socioeconomic components emphasized, as the majority of components were predominantly focussed on symptoms. The Myeloma Patient Outcome Scale (MyPOS) was developed in the UK and uses a module of the Palliative care Outcome Scale (POS) that is enriched with myeloma-specific concerns. It was validated in the UK with 238 patients who completed the questionnaire every 2 months, five times. The questionnaire displayed three categories or scales which included both symptoms and emotional functioning and placed an emphasis on a healthcare support subscale.

Several randomized clinical trials (RCTs) which used HRQL as an endpoint in newly diagnosed (ND) MM patients were then detailed. The HOVON study, comparing melphalan/prednisone (MP) versus MP plus thalidomide (MPT), led to an improvement in global health score (GHS), whereas both the VISTA and UPFRONT studies led to a transient deterioration in GHS, followed by stabilization. The MM-015 and the FIRST study found overall improved HRQL from baseline. The impact of transplant on HRQL was also presented, with a number of studies recording a decreased score during transplant, followed by an improvement within 1 or 2 months post-transplant. Another study showed a better HRQL (less fatigue) in the transplant arm in comparison to patients who were treated with melphalan/prednisone (MP). Interestingly, outpatient versus inpatient transplant resulted in better social well-being but worse physical well-being.

The impact of maintenance therapy on HRQL was investigated in a retrospective study (MM-015). Using the MM database analysis, 238 MM patients were identified as having had any type maintenance, 167 patients received lenalidomide maintenance and 138 patients had no maintenance therapy. Five EQ-5D questionnaires were completed per patient on each arm. No significant differences were observed in EQSD, FACT MM or BPI score for any of the three groups, but a decline in FACT-MM score was identified at the time of progression. However, female gender, advanced age, and progressive disease negatively affected HRQL, and HRQL was associated with a very good partial response (VGPR) or better. In the relapsed setting, several studies were outlined with a common theme being a prolonged time to deterioration in terms of HRQL domains in the treatment arm.

Other factors impacting HRQL in MM were then described. Living with MM appears to affect the GHS linearly, with one point decrease on the GHS for each additional year. MM patients receiving any type of therapy within 30 days was associated with a 9.5 point decrease in GHS in comparison to controls. The first treatment-free interval (TFI) was associated with a better HRQL in comparison to other treatment phases and a longer TFI correlated with a better HRQL. Patients with moderate to severe symptoms had a decrease of 12–19 points, respectively. Dr Baz explained that trial comparisons are limited due to the differences observed in the study population, design and methodology used for HRQL analysis.

It was concluded that there is a lack of HRQL data outside of clinical trials, as well as limited data concerning the impact of socio-economic factors on QoL in comparison to the impact of symptoms reporting. In general, HRQL mirrors the course of the disease, worsening with disease progression and improving with therapy. Consequently, there is a strong rationale...
for the incorporation of HRQL assessments into RCTs, although current HRQL measurement tools are inadequate as socioeconomic and psychological factors are not well-assessed. Dr Baz suggested that future studies should include the assessment of HRQL in the 'real world' as the impact of financial burdens and other social factors may be more prominent.

References

1. Rachid Baz. Quality of life considerations in myeloma. 4th World Congress on Controversies in Multiple Myeloma, 3–5 May 2018.