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# P885 PROSPECTIVE ASSESSMENT OF MYELOMA TUMOUR BURDEN AND BONE DISEASE USING DW-MRI AND EXPLORATORY BONE BIOMARKERS

**Topic:** 14. Myeloma and other monoclonal gammopathies - Clinical

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**Background:**

Key clinical priorities for multiple myeloma (MM) are to reduce tumour burden and complications, of which lytic bone disease is the major cause of morbidity. To guide treatment, there is a pressing need for biomarkers that can accurately quantify MM tumour burden and associated bone disease. To this end, Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) and bone turnover markers are promising radiological and serum metrics, respectively, although their clinical value in prospective assessment is unclear.

**Aims:**

LOOMIS was a single-centre observational cohort study that evaluated the relative merits of DW-MRI and bone turnover markers in prospectively assessing tumour burden and bone disease when added to standard clinical assessment, in patients with MM and monoclonal gammopathy of undetermined significance (MGUS).

**Methods:**

A total of 67 patients were enrolled (14 newly diagnosed MM, 12 relapsed MM, 15 smouldering MM, 14 MGUS and 12 healthy volunteers) between March 2018 and March 2020. At baseline (and 6-month follow-up for MM/MGUS), participants had a DW-MRI scan and serum measurements of established (P1NP, CTX-1, ALP) and exploratory (DKK1, sclerostin, RANKL:OPG ratio) bone turnover markers. MM/MGUS patients additionally had standard myeloma bloods and Dual-Energy X-ray Absorptiometry (DXA) at each visit, as correlates of tumour burden and bone loss. DW-MRI scans were double reported by expert Radiologists for Apparent Diffusion Coefficient (ADC) measurements of lytic bone lesion(s), and Myeloma Response Assessment and Diagnosis System (MY-RADS) Response Assessment Category (RAC) scoring. Patients were classified by International Myeloma Working Group (IMWG) response criteria as a clinical correlate of therapy response.

**Results:**

On assessment of baseline tumour burden, there was no correlation between single lesion DW-MRI ADC and serum paraprotein [$p>0.05$]; however, there was moderate positive correlation between serum DKK1 and serum paraprotein [$r=0.39$, $p=0.04$]. At follow-up, radiological MY-RADS RAC scoring correlated with conventional IMWG response criteria [$p=0.015$]; additionally, longitudinal relative change in serum DKK1 differed between IMWG-defined therapy responders (37% decrease) and non-responders (15% increase) [$p<0.01$]. On baseline assessment of bone loss, there was moderate positive correlation between serum sclerostin and DXA bone mineral density at femoral neck [$r=0.40$,

*p<0.01*] and lumbar spine [*r=0.54, p<0.001*]. At follow-up, there was a moderate negative correlation between longitudinal % change in the RANKL:OPG ratio and % change in DXA bone mineral density at femoral neck [*r= -0.45, p<0.01*].

**Summary/Conclusion:**

Our prospective trial validates DW-MRI-based MY-RADS RAC scoring as a qualitative radiological tool to assess therapy response. Whilst previous work has supported single lytic lesion ADC measurements as a correlate of tumour volume, we did not find this; small sample size and prior chemotherapy in our study may have limited our ability to detect this. In comparison, serum bone turnover markers such as DKK1 may provide a more global measure to quantify myeloma burden both at baseline diagnosis and longitudinally with therapy. Additionally, our data highlight serum sclerostin and RANKL:OPG ratio as potential biomarkers to assess and monitor bone loss. Overall, our study highlights emerging radiological and serum biomarkers of tumour burden and associated bone loss in MM and MGUS, which merit further exploration alongside uniformly treated cohorts, to better understand their clinical utility.