

2. NEWLY DIAGNOSED MULTIPLE MYELOMA

EARLY TREATMENT RESPONSE EVALUATION WITH WHOLE BODY MAGNETIC RESONANCE IMAGING IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA AND FOCAL LESIONS

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Introduction. Whole-body magnetic resonance imaging (WBMRI) is a highly sensitive technique to detect focal lesions (FL) in patients (pts) with newly diagnosed multiple myeloma (NDMM).

Methods. This prospective study included NDMM pts who underwent WBMRI at diagnosis and two months post treatment initiation. For those with FLs, an Interim MRI-based Response Grade (iMR-RG) was formed. Definite response (DR) was defined as: complete disappearance of the FL or increase of apparent diffusion coefficient (ADC) to $\geq 1.4 \times 10^{-3}$ mm²/s or $\geq 40\%$ increase compared to baseline and disappearance of paramedullary disease (PMD) or extramedullary disease (EMD), if present at baseline. Partial response (PR) included: an increase of ADC to $1.2-1.4 \times 10^{-3}$ mm²/s or $>25\%$ but $<40\%$ increase compared to baseline and a decrease in size of PMD/EMD. Non-response (NR) was characterized by no significant change of ADC compared to baseline and no change in size of PMD. For pts with multiple FLs, response was categorized by the dominant pattern: If most lesions showed DR/PR, cases were labeled definite or partial response dominant, respectively. If most lesions showed NR, the case was classified as "non-response dominant". Definite progression was characterized by new FL(s) or increase in size of the FL(s) or increase in size of the PMD or new PMD/EMD. Bone marrow ADC and fat fraction evaluation was performed in the lower thoracic and lumbar vertebrae and the corresponding mean values were calculated for each pt, as appropriate.

Results. 61 NDMM pts with FLs were included, with a median age of 67.5 years, whereas 40.4% were females. Baseline WBMRI revealed PMD in 17 (18.3%) pts. The median follow-up since the first WBMRI was 6.5 months. Imaging re-

sponses to treatment two months post initiation were as follows: 7 (11.5%) DR, 35 (57.4%) DRD, 16 (26.2%) PRD, 2 (3.3%) NRD and 1 (1.6%). The best hematological responses to first-line treatment were: 3 \geq CR (4.2%), 38 (62.3%) VGPR, 18 (29.5%) PR and 2 (3.3%) MR. Importantly, one PD event was identified before documented hematological progression or clinical deterioration. 13 (76.5%) pts with PMD (76.5%) responded. The depth of imaging response was associated with the depth of hematological response ($p=0.027$). More specifically, DRD WBMRI was associated with VGPR serum (OR=4.26, 95% CI: 1.22-16.07, $p=0.013$). In total, 6 (9.8%) PD events and 4 deaths were recorded. Achieving at least a PRD in WBMRI was linked with significantly superior PFS (HR=0.19, 95% CI: 0.04-0.89, $p=0.035$), while a trend was also observed for OS (HR=0.24, 95% CI: 0.03-2.09, $p=0.197$) and TTP (HR=0.16, 95% CI: 0.02-1.41, $p=0.098$). Similarly, pts achieving at least DRD seemed to have superior PFS (HR=0.33, 95% CI: 0.11-1.02, $p=0.055$) and had significantly superior TTP (HR=0.15, 95% CI: 0.03-0.84, $p=0.031$). In a longitudinal analysis of 48 pts with FLs, median ADC values were 0.42 (0.16-1.00) and 0.48 (0.15-0.71) $\times 10^{-3}$ mm²/s at baseline and second WBMRI, respectively, while median fat fraction values were 43.23% (11.80-72.20%) and 55.20 (22.20-83.80%). Greater decreases in ADC and increases in fat fraction tended to associate with \geq PR ($p=0.089$ and $p=0.097$), and greater Fat Fraction increases with \geq VGPR ($p=0.065$). A greater decrease in ADC was associated with earlier time to best response ($p=0.045$).

Conclusion. The proposed novel criteria for evaluating early treatment response with WBMRI in NDMM seem to have both predictive and prognostic value.