

UAMS Clinical Implications of Loss of Bone Marrow Minimal Residual Disease Negativity in Multiple Myeloma



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BACKGROUND

Attainment of MRD negativity in concert with IMWG \geq CR is predictive of superior clinical outcome and is emerging as an optimal therapeutic goal. This study describes the clinical implications of loss of bone marrow MRD negativity or MRD conversion in MM patients in sustained remission.

METHODOLOGY

We identified a cohort of patients with BM MRD assessment done in 2014. 606 MM patients treated on an intensive treatment regimen incorporating multi-agent chemotherapy, novel agents and high dose chemotherapy and autologous stem cell transplantation (ASCT), achieving a sustained \geq VGPR with bone marrow MRD negativity (\geq 2 consecutive reading at least 3 months apart) with comprehensive response assessment with simultaneously PET/CT and MRI DWIBS negativity were included in the analysis. Patients were followed by serial labs, bone marrow assessment and imaging studies including PET/CT and MRI till clinical relapse. Loss of MRD or MRD conversion is defined as detectable minimal residual disease by way of positive flow cytometry assay. Bone marrow (BM) aspirate MRD assessment was done by 8-color next generation flow (NGF, EuroFlow) with a minimal sensitivity of 10^{-5} cells.

MRD conversion occurs in a significant proportion of MM patients (40%) on long-term follow-up and predicts future clinical relapse

Significance of MRD conversion has a temporal relationship from diagnosis and portray inferior clinical outcome particularly within 5 years of diagnosis

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RESULTS

Median age of this cohort is 57.8 with 63% males. Most patients had LR MM with a UAMS GEP70 risk score of \leq 0.66 (92%; 495/538); with no significant difference in MRD conversion between LR vs HR patients: LR - 40%; 199/495 HR - 35%; 15/43 (P=0.52).

At a median follow up of 10 years, 60% (364/606) of patients had sustained MRD negativity, with 40% (242/606) experiencing MRD conversion. Median time to MRD conversion is 6.3 year from diagnosis and 5.7 years from HDC ASCT

A ratio of myeloma to normal plasma cells of $>$ 0.2 correlates with disease relapse (RR 19.65; 95%CI 4.92-78.4) and median time from loss of MRD negativity/MRD conversion to the clinical relapse is 1.1 year.

MRD conversion is associated with increased risk of progression; RR 3.5 (95% CI 2.9-4.4) with p $<$ 0.0001 with MRD negative relapse seen in 3.8% (14/364).

