Abstract #150479

Residual Monoclonal Free Light Chain Positivity By Mass Spectrometry Identifies Patients at Increased Risk of Early Relapse Following First-Line Anti-Myeloma Treatment

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Introduction

Bone marrow based minimal residual disease (MRD) assessments provide greater sensitivity for residual disease detection compared to the standard serological techniques and MRD negativity is associated with improved progression-free survival (PFS). However, the frequency at which MRD can be assessed is limited by the invasive nature and cost of the current assays. These assays may also give false negative results due to the heterogeneous nature of marrow involvement in multiple myeloma and extramedullary disease. Mass spectrometry (MS) methodologies are emerging as a more sensitive way of monitoring monoclonal proteins in the peripheral blood. In this study we assessed the prognostic impact of detectable residual monoclonal FLC by matrix-assisted laser desorption ionisation-time of flight (MALDI-TOF) MS in patients with transplant-eligible newly diagnosed multiple myeloma.

Methods

Patients treated with carfilzomib, lenalidomide, cyclophosphamide and dexamethasone followed by autologous stem cell transplantation (ASCT) and randomisation between lenalidomide maintenance versus observation in the Myeloma XI trial were included in this study. Patients with no residual serum for MS testing from baseline or post cycle one of induction chemotherapy were excluded as a baseline sample was required to establish the isotype and mass-to-charge ratio of the monoclonal FLC. 293 patients were included in this study: 58.4% (171/293) had an IgG monoclonal protein; 23.9% (70/293) had an IgA monoclonal protein;16.4% (48/293) had a FLC only monoclonal protein; 1.0% (3/293) had an IgD monoclonal protein and 0.3% (1/293) had non-secretory myeloma. MS analysis was performed on all available samples from post-induction (n=219), day+100 post ASCT (n=189) and post maintenance randomisation (n=137). Serum samples underwent immunoprecipitation with antisera specific for kappa and lambda FLC conjugated to magnetic microparticles, FLC were eluted and the spectra were acquired by MALDI-TOF MS. Progression free survival (PFS) analysis was performed with SPSS 27.0.1.0 using the Kaplan-Meier method. The log-rank test was used to assess the statistical significance of differences between survival curves. Median follow-up was calculated using the reverse Kaplan-Meier method.

Results

At all three time points MS positivity was associated with shorter PFS: 43.9 months v. not reached (NR) p<0.001 post induction; 45.3 months v. NR p<0.001 at day+100 post ASCT; and 44.1 months v. NR p<0.001 post maintenance randomisation. Post induction 91/219 (41.6%) patients were in CR/sCR and 31/91 (34.1%) had residual monoclonal FLC detectable by MS. Patients in CR/sCR with residual monoclonal FLC detectable by MS post induction had a trend towards shorter PFS compared to MS negative patients (51.1 months v. not reached, p=0.097). At day+100 post ASCT 113/189 (59.8%) were in CR/sCR and 30/113 (26.5%) had residual monoclonal FLC detectable by MS. After a median follow-up of 46.9 months, MS negativity was associated with improved PFS in patients in CR/sCR (p=0.027); 12/30 (40%) MS positive patients have progressed versus 18/83 (21.7%) MS negative patients. Post maintenance randomisation 75/137 (54.7%) of patients were in CR/sCR and 12/75 of these patients (16%) were positive by MS. MS positive patients in CR/sCR had a shorter PFS compared to MS negative patients in CR/sCR (47.1 months v NR, p=0.017).

47 patients had bone marrow MRD (8 colour panel with a sensitivity of 4×10^{-5}) results from post maintenance randomisation: 35 (74.5%) were MRD negative and 12 (25.5%) were MRD positive. 6/35 (17.1%) patients who were MRD negative had residual monoclonal FLC detectable by MS. After a median follow-up of 42.2 months MS positivity in MRD negative patients was associated with shorter PFS; 2/6 (33.3%) MRD negative MS positive patients had progressed versus 2/29 (6.9%) MRD negative MS negative patients (p=0.001). The relapses in the MS positive patients occurred earlier (at 18.8 and 31.0 months) than those observed in the double negative patients (at 43.8 and 51.3 months).

Conclusions

MS provided additional sensitivity for residual disease detection in patients in CR and positivity was associated with reduced PFS. MS also added additional prognostic information for patients who were MRD negative during maintenance with residual positivity being associated with an increased risk of early relapse.

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Yes

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Sanofi	Honoraria and Membership on an entity's Board of Directors or advisory committees

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amgen	Consultancy, Honoraria and Speakers Bureau
takeda	Consultancy, Honoraria, Research Funding and Speakers Bureau
GSK	Consultancy, Honoraria and Speakers Bureau
J and J	Consultancy, Honoraria and Speakers Bureau
oncopeptides	Consultancy
Sanofi	Honoraria and Speakers Bureau

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