Lack of correlation between emergence of an abnormal protein band or of oligoclonal bands and survival in patients with multiple myeloma achieving complete remission following autologous stem cell transplantation

Larrea *et al.* recently reported that patients with multiple myeloma (MM) who achieve complete remission (CR) after induction chemotherapy with novel agents (glucocorticoids with bortezomib, lenalidomide, thalidomide, or bortezomib with thalidomide) are more likely to have the emergence of oligoclonal bands in peripheral blood. While only 11% of patients who received conventional chemotherapy developed oligoclonal bands, 60% of patients on novel agents developed oligoclonal bands.[1] The relevance of emergence of an abnormal protein band or of oligoclonal bands in patients with MM in CR stems from the studies which associate a favorable outcome and prolonged survival for such patients with MM in whom the oligoclonal bands emerged after autologous stem cell transplantation (ASCT).[2-4] The emergence of an abnormal protein band or oligoclonal bands, which can be seen in up to 70% of patients, is said to be due to recovery of B-cell function after myeloablative therapy and to represent a more durable immune reconstitution.[2-4] At the Hammersmith Hospital, we have a large cohort of MM patients who have received ASCT as the backbone of their treatment.

We evaluated serum electrophoresis and immunofixation results from 38 patients with MM in CR following ASCT performed between March 1996 and February 2010. These patients represent 11% (38 of 354) of our cohort with MM, who have received ASCT. The European Group for Blood and Marrow Transplantation criteria have been used to assess disease response and in defining CR in these patients. An abnormal protein band or oligoclonal bands were defined as the presence of serum immune-electrophoresis spike(s) different either in heavy and/or light chains or in its migration pattern from the original myeloma protein identified in that particular patient. The 38 patients included 21 males and 17 females in an age range of 26 to 68 years (median age 57 years).

Among the 38 patients, 19 (50%) had abnormal protein band or oligoclonal bands that emerged an average of 14 months (range 1-74 months, median 4 months) after the first ASCT, and the band(s) persisted for an average of 20 months (range 1 to at least 59 months, median 17 months). In 7 cases, the patient went on to have further transplant(s) (9 autologous and 2 allogenic). Both the patients in whom abnormal protein bands appeared after a gap of five years from the first ASCT (74 months and 67 months) have had subsequent ASCTs and the abnormal protein band appeared at four months and one month after the second ASCT. The mean age of patients with and without the emergence of an abnormal protein band or oligoclonal bands were 55 and 56 years, respectively. Among the 19 patients, 13 had an abnormal protein band (8 IgG lambda, 4 IgG kappa and 1 IgA kappa), and 6 had oligoclonal bands (6 IgG lambda, 4 IgG kappa and 2 IgA). Twenty-two of the 38 patients (58%) relapsed and/or died of disease. This included 11 of 19 patients with oligoclonal bands and 11 of 19 patients without oligoclonal bands. In patients with and without oligoclonal bands, the 5-year overall survival from the first ASCT (76±21% *vs.* 83±18%; P=0.673) and the 5-year relapse free survival from the first ASCT (37±23% *vs.* 56±25%; P=0.985) did not show any significant difference on log rank analysis.

In our cohort of MM patients who had undergone ASCT and achieved CR, we were unable to document any prognostic relevance of the emergence of an abnormal protein band or oligoclonal bands in the serum / peripheral blood. Zent *et al.* have previously shown that in patients with MM receiving ASCT emergence of an abnormal protein band or oligoclonal bands correlates with higher CR rates and with a favorable event-free and overall survival.[2] However, whether the emergence of an abnormal protein band or of oligoclonal bands in patients achieving CR following ASCT for MM translates to improved survival has yet to be established.

Elizabeth Byrne,[1] Chrissy Giles,[2] Joanne Andrews,[3] Amin Rahemtulla,[2] and Kikkeri N. Naresh[1]

[1]Departments of Histopathology, [2]Haematology and [3]Biochemistry; Hammersmith Hospital Campus, Imperial College & Imperial College Healthcare NHS Trust, London UK

Correspondence: Kikkeri N Naresh, Haematopathologist, Department of Histopathology, Hammersmith Hospital Campus, Imperial College Healthcare NHS Trust and Imperial College, Du Cane Road, London W12 0HS, UK.
E-mail: k.naresh@imperial.ac.uk

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