Characteristics and outcomes of IgM associated systemic AL amyloidosis –analysis of a prospective study (ALChemy study)

Ashutosh Wechalekar, Darren Foard, Lisa Rannigan, Thirusha Lane, Sajitha Sachachtanatham, Shameem Mahmood, Rabya Sayed, Ketna Patel, Carol Whelan, Helen Lachmann, Philip Hawkins and Julian Gillmore

From: National Amyloidosis Centre, University College London Medical School, London

IgM associated AL amyloidosis, secondary to underlying Waldenstrom's macroglobulinaemia (WM), is rare. There are no prospective studies in IgM associated AL amyloidosis. ALChemy is one of the largest prospectively followed up patient cohorts in systemic AL amyloidosis. Out of a total of 714 patients with systemic AL amyloidosis recruited in the ALChemy study from September 2009 to December 2013, IgM associated AL amyloidosis with an underlying WM accounted for 44 (6.1%) of cases. The characteristics and outcomes of these patients are presented here. All patients had a detailed baseline assessment. Data on treatment, response to treatment and toxicity was collected monthly. After completing treatment, all patients had protocolized assessments every six months. Heart was involved in 41%, kidneys in 70%, liver in 20%, peripheral neuropathy 18% and autonomic neuropathy 13%. The Mayo disease stage was: stage I – 12 (27%); stage II - 21 (47%); stage III – 11 (25%). The median NT-proBNP was 3974 ng/L and only two patients had NT-proBNP >8500 ng/L (a marker of very poor prognosis). Median difference in involved and uninvolved serum free light chain (dFLC) was 123 mg/L and 43% had an IgM monoclonal protein >10g/L. Median overall survival (OS) was not reached. The estimated survival at 6, 12 and 36 months was 73%, 63% and 59% respectively. All patients with Mayo stage I disease are live, median OS stage II and III 36 months and 5.2 months respectively with only one patients with stage III disease alive at 12 months. dFLC at presentation has no impact on outcomes. Treatments were: Rituximab containing regime 59%, bortezomib based 25%, R-CHOP/R-CVP 11%, R-cyclo-Dex (R-CD) 25%., thalidomide based 15% and Benbdamustine-R 7%. On an intention to treat basis, 41% achieved a ≥ partial haematological response (PR) with a complete response (CR) in 9% and dFLC-VGPR in 11%. Of the evaluable patients, 54% achieved a PR or greater. 81% of those treated with a bortezomib based combination responded on an intent to treat basis. All patients who achieved a CR were treated with bortezomib as were 3 patients who achieved a VGPR (two other VGPR's – one with CTD and R-CD respectively). There were no deaths in patients achieving a CR/VGPR. 60% received at least 4 cycles of treatment and only 26% received >4 cycles. 43% experienced ≥ grade 3 and 14% patients reported ≥grade 3 toxicity in more than one cycle. In summary, the prospective series shows that outcomes of Mayo stage III patients with IgM associated AL amyloidosis is very poor. Standard prognostic markers from non-IgM AL amyloidosis like dFLC are not useful in IgM associated AL. Responses to treatment are still unsatisfactory but bortezomib based regimes show promise. Patients with early stage disease and those achieving a CR/VGPR have excellent long term outcomes.