W2: Treatment of IgM-associated immunoglobulin light chain amyloidosis with Bendamustine-Rituximab

Richa Manwani[1], Sajitha Sachchithanantham[1], Shameem Mahmood[1], Darren Foard[1], Faye Sharpley[1], Tamer Rezk[1], Thirusha Lane[1], Cristina Quarta[1], Marianna Fontana[1], Helen J Lachmann[1], Julian D Gillmore[1] Carol Whelan[1], Philip N Hawkins[1] and Ashutosh D Wechalekar[1*]

[1] National Amyloidosis Centre, University College London (Royal Free Campus), Rowland Hill Street, London

Background

IgM-associated AL amyloidosis (IgM-AL) is rare, accounting for 5-7% of patients with AL amyloidosis. There is a paucity of data on optimal therapy in IgM-AL and outcomes are generally poor, with few complete responses. Bendamustine, which has features of both an alkylating agent and purine analog, is increasingly used alongside rituximab in the treatment of non-Hodgkin lymphoma. There have been no studies to date focusing on the use of bendamustine-rituximab (BR) in upfront or relapsed/refractory IgM AL. We sought to assess the efficacy of BR in treatment-naïve and relapsed/refractory IgM-AL.

Methods

27 patients with AL treated with BR from 2011-2017 were included; 22 received BR as first-line therapy and five as second-line. 25 had a serum IgM M-protein. Of the remaining two, one had a serum IgG M-protein and the other had both a lambda and IgG M-protein; both were treated with BR first-line and both had bone marrow infiltration with lymphoplasmacytic lymphoma. Primary outcome variables were haematological and organ responses, overall survival (OS) and time-to-next-treatment (TNT).

Results

Median age was 70 years (range 56-86). The number of patients with Mayo Stage I, II and III disease was: 9 (33%), 12 (45%) and 6 (22%). The number of patients with cardiac, renal, liver, peripheral nerve, autonomic nerve, soft tissue and lymph node involvement was: 17 (63%), 17 (63%), 6 (22%), 6 (22%), 4(15%), 2(7%) and 13 (48%), respectively. The median NT-proBNP was 978ng/L (42-5708ng/L). Median M-protein was 11.5g/L (1-30g/L); 19 had a serum free light chain excess and median dFLC was 59.8mg/L (range 2.2-856mg/L). 21 patients had available bone marrow data: 3 normal, 1 plasma cell infiltrate, 14 lymphoplasmacytic lymphoma, and 3 NHL not specifically classified. Five were treated second-line for refractory disease; previous therapy included bortezomib-cyclophosphamide-dexamethasone (2 patients), rituximab-cyclophosphamide-dexamethasone (1 patient); median number of previous cycles was 6 (4-8). Patients received a median of 5 cycles of BR (1-8).

ITT haematological responses (AL response criteria) were: complete response 3 (11%), very good partial response (VGPR) 10 (37%), partial response (PR) 3 (11%), non-response (NR) 11 (41%, including 6 deaths). In the second-line group, 3 (60%) achieved VGPR and 2 were non-responders (including 1 death). 18% of patients with cardiac involvement achieved a cardiac response, and 18% with renal involvement achieved a renal response. Median follow up was 18 months (range 3-55). Median OS was not reached. Three patients progressed to next treatment and median TNT was not reached with 88% and 79% of evaluable patients in a haematological response at 1 and 3 years, respectively. Median OS was not reached in patients who achieved VGPR/better, compared to 9 months in patients who did not.

Conclusion

The treatment approach in IgM-AL has been historically heterogenous due to scant data and poor haematological responses. Data from this small retrospective study demonstrate an excellent overall response rate (ITT) of 59% in patients treated with BR, much better than previously reported and with a higher proportion achieving VGPR/better. This study suggests that first-line BR may be the treatment of choice in IgM-AL.

Figure 1. Overall survival (OS) and time-to-next-treatment (TNT).

A) This shows the overall survival (OS) on an ITT basis and evaluable time-to-next-treatment (TNT). Median OS and median TNT were not reached. OS at 1 year and 3 years was 65% and 56%. At 1 and 3 years, only 88% and 79% of evaluable patients needed further treatment. B) Median OS was not reached in those patients who achieved a very good partial response (VGPR) or better with 92% alive at 2 years; median OS was 9 months in patients who did not achieve a VGPR.