W24: Real World Experience of Bendamustine in Waldenstrom's Macroglobulinaemia (WM): efficacy tempered by toxicity

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Bendamustine is a purine analogue/alkylator hybrid cytotoxic with activity against non-Hodgkin's lymphoma(1). It has been demonstrated in WM to produce significant responses in both first line and relapsed/refractory settings(2). However, significant toxicities including myelosuppression and hypogammaglobinaemia following its use as monotherapy or in combination with an anti-CD20 monoclonal antibody have been shown(3). Owing to the observation of a notable rate of infections during follow up, we undertook a retrospective analysis of patients treated with Bendamustine focussing on myelosuppression and infection-related toxicities.

In total, 21 patients (16 men, 5 women) with WM were commenced on Bendamustine in our cohort between February 2012 and October 2017. Eight patients (38%) received Bendamustine first line and the rest at relapse having had a median of 3 prior lines. Sixteen patients (76%) received it in combination with Rituximab. Thirteen patients (62%) commenced Bendamustine at a dose of 90mg/m^2 and the remainder at 60mg/m^2. Five patients (24%) required a dose reduction of Bendamustine during treatment.

Nine patients (45%) managed to complete 6 cycles, with the remainder completing 1-5 cycles (median 4 cycles). During treatment grade 3 or 4 complications were observed in 15 patients (71%) which included neutropenia (n=9, 43%), anaemia (n=5, 26%) and thrombocytopenia (n=5, 26%). Infection during treatment occurred in 13 patients (62%), with grade 3 or 4 infection in 8 patients (38%).

After completion of treatment, 3 patients with normal pre-treatment immunoglobulin levels developed hypogammaglobulinaemia, of which 2 required immunoglobulin replacement. In the first two years after completion of therapy infection occurred in 10 patients, with grade 3 or 4 infection requiring admission for intravenous antibiotics in 6 patients. Two patients developed shingles in this period.

Overall response rate was 89%, with 2 patients (11%) achieving a complete response, 4 a very good partial response (21%), 8 a partial response (42%), 3 a minor response (16%) and 2 no response (11%). Data on outcomes were incomplete for two patients. Median time to best response was seven months. Median progression free survival was 21 months. Seven of the 19 patients who had outcomes (37%) died within 5 years of treatment. Cause of death was known for 4 patients; 2 died from progressive disease, 1 from infection and 1 from a combination. Median follow up was 11 months.

Outcomes were more favourable for patients treated with Bendamustine at first line compared to relapse, with 71% of patients treated at first line completing 6 cycles compared

to 31% of patients at relapse. Rates of grade 3 or 4 complications during therapy were lower in the former group (57% vs 92%). Responses were also better in the former group, with 100% overall response rate compared to 83% treated at relapse.

Overall Bendamustine use in our centre was associated with high rates of grade 3 or 4 complications, especially infection, and a large proportion of patients failed to complete therapy as intended. This was particularly the case for patients treated at relapse, who were often heavily pre-treated.

1. Leoni LM, Bailey B, Reifert J, Bendall HH, Zeller RW, Corbeil J, et al. Bendamustine (Treanda) displays a distinct pattern of cytotoxicity and unique mechanistic features compared with other alkylating agents. Clin Cancer Res [Internet]. 2008 Jan 1 [cited 2018 Jun 18];14(1):309–17. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18172283
2. Treon SP, Hanzis C, Tripsas C, Ioakimidis L, Patterson CJ, Manning RJ, et al. Bendamustine Therapy in Patients With Relapsed or Refractory Waldenström's Macroglobulinemia. Clin Lymphoma Myeloma Leuk [Internet]. 2011 Feb [cited 2018 Jun 18];11(1):133–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21454214
3. Gafter-Gvili A, Polliack A. Bendamustine associated immune suppression and infections during therapy of hematological malignancies. Leuk Lymphoma [Internet]. 2016 Mar 3 [cited 2018 Jun 18];57(3):512–9. Available from: http://www.tandfonline.com/doi/full/10.3109/10428194.2015.1110748