Phase II clinical study of Zanubrutinib combined with bendamustine and rituximab (ZBR) for time-limited treatment of Waldenstrom macroglobulinemia

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Waldenström macroglobulinemia (WM) is a rare type of lymphoma, with no established optimal treatment. BTK inhibitors and bendamustine-rituximab (BR) are the preferred regimens with promising outcomes. However, whether can we combined these two therapy to achieve deep remission and time-limited course is an interesting question. We conducted a phase 2 clinical trial (NCT05979948) to evaluate the efficacy and safety of combining zanubrutinib, bendamustine and rituximab (ZBR) in newly diagnosed symptomatic patients with WM.n Patients with newly diagnosed symptomatic WM received ZBR for 6 cycles and Zanubrutinib will be given up to 12 months. Up to the last followup, 37 patients were enrolled. The median age was 63 (33-76), with 15 patients (40.5%) being 65 years of age or older. 20 patients completed induction treatment. After induction treatment, 2 patient (10%) achieved CR , 11 patients (55%) achieved VGPR, 6 patients (30%) achieved PR and 1 patient achieved MR. 12 patients completed maintenance therapy and stopped treatment. The overall, major and deep remission rates were 100%, 91.7% and 75%, respectively. Minimal residual disease (MRD) analysis showed that ZBR was effective in removing abnormal cells from the bone marrow. 10 out of 20 (50%) patients obtained MRD negativity by FCM. The most common AE was hematological toxicity. AE (grade ≥3) were neutropenia (30%), infection (25%), thrombocytopenia (15%), rash (10%), fatigue

(5.0%). No IgM rebound occurred in any of the 12 patients who ended treatment and discontinued the drug. In conclusion, the ZBR regimen reached significant deep remission rates in newly diagnosed symptomatic WM patients with manageable adverse events. In addition, it can effectively remove tumor cells and extramedullary masses.