

Reduced-dose lenalidomide and obinutuzumab in Patients with Relapsed/Refractory Waldenström macroglobulinemia

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Abstract

Introduction:

Waldenström macroglobulinemia (WM) is a rare type of lymphoma, with no optimal treatment. All patients will ultimately relapse and the management of relapsed or refractory (RR) disease remains challenging. Lenalidomide is an oral immunomodulatory drug with pleiotropic effects, including direct cytotoxicity, immunomodulation, blockade of angiogenesis, and stimulation of natural killer and T cell. Although some studies had reported the hematological adverse effect in patients treated with lenalidomide, other study showed that lower doses of lenalidomide could be effective with manageable toxicity. Combined lenalidomide with other treatment would achieved higher ORR rate. Therefore, we explore the combining reduced-dose lenalidomide with Obinutuzumab for the treatment of relapse and refractory WM, aiming to evaluate the safety and effect of RRWM patients.

Methods:

The study comprised a 6-month induction phase and a 12-month maintenance phase. During induction, patients received obinutuzumab (1000 mg intravenously on days 1, 8, 15 of cycle 1, and day 1 of cycles 2-6) and lenalidomide (20 mg orally on days 2-22 in 28-day cycles). Those achieving minimal response (MR) or better transitioned to maintenance with lenalidomide (10 mg orally on days 1-21 monthly for 1 year). Patients not achieving MR were withdrawn from the study. primary endpoint was the deep remission rate.

Results:

13 patients were enroll in this enroll in this study and achieved at least one cycle of treatment. All patients had previously received rituximab-based chemotherapy, and nine patients had previously been treated with BTK inhibitor. The median prior lines of therapy were 2 (range, 1-3). The median baseline age was 51 years (range, 45-72). The median baseline hemoglobin was 106 g/L (range, 71-132), and the median baseline IgM was 28.6 g/L (range, 1.03-51.7). One patient had undergone plasmapheresis.

Six of 13 patients completed the entire treatment. Two patients discontinued after completing the induction therapy. Two patients discontinued treatment after one cycle

due to intolerance to lenalidomide, and three patients discontinued after two cycles of treatment for their own reasons; all three of these patients achieved a treatment response, one patient achieved PR and the other two patients achieved MR. The median treatment duration for patients completed induction is 7.34 months (range, 3.0-23.47). For the eight patients who completed induction, two patients achieved VGPR and one patient achieved CR, two patients achieved PR and two patients achieved MR and one patient was SD. The overall response rate and the major response rate were 87.5% and 62.5% . With a median follow-up of 27 months (range, 17-35), median progression-free survival was not reached. The median times to first and best responses were, respectively, 5.3 months (range, 1.63-14.74) and 5.3 months (range, 1.63-17.70).

After treatment, patients showed significant improvement in IgM levels, with the median IgM decreasing from 28.6 g/L (range, 1.03-51.7) to 6.98 g/L (range, 0.66-22.5). One patient suffered mild Hb decreasing after lenalidomide, and then increased. All other patients obtained an increase in hemoglobin. The median hemoglobin increased from 107.5 g/L (range, 72-132) to 140 g/L (range, 120-165). The most frequent adverse events were neutropenia, thrombocytopenia and rash. The adverse event of grade 3 or higher is neutropenia. No infusion-related reactions or immunoglobulin M flare occurred with use of subcutaneous obinutuzumab. There were no deaths associated with treatment.

Conclusion:

Overall, reduced-dose lenalidomide with Obinutuzumab might be effective in RRWM patients with manageable AEs.

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