ELSEVIER

Blood 142 (2023) 3829

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

101.RED CELLS AND ERYTHROPOIESIS, EXCLUDING IRON

Rituximab Plus Bortezomib for Refractory and Relapsed Warm Autoimmune Hemolytic Anemia:a Prospective, Single-Arm, Phase II Trial

Xijuan Lin[1], *Chen Yang*[2], *Junling Zhuang, MDPhD*[3], *Daobin Zhou, MD*[4], *Miao Chen*[5], *Bing Han, MDPhD*[6]

[1] Peking Union Medical College, Beijing, China
[2] Peking Union Medical College Hospital, Beijing, China
[3] Department of Hematology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China
[4] Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China
[5] Peking Union Medical College Hospital,Chinese Academy of Medical Sciences, Beijing, China
[6] Dept. of Hematology, Peking Union Medical College Hospital,Chinese Academy of Medical Sciences&Peking Union Medical College, Beijing, China

Background Treatment of refractory and relapsed warm autoimmune hemolytic anemia (RR wAIHA) is challenging, especially for those who are in emergency with severe anemia and crossmatching incompatibility. Rituximab is now the preferred second-line treatment for RR wAIHA with unsatisfactory onset speed and sustained efficacy. Bortezomib induces apoptosis of plasma cells that produce autoantibodies and has multiple immunoregulatory functions. In this study, we report the results of rituximab plus bortezomib for the treatment of RR wAIHA in a prospective phase 2 trial.
Methods A prospective single arm trial to investigate the activity and safety of the combination of rituximab and bortezomib (RB regimen) in RR wAIHA patients were conducted. Eligible patients were aged 18 years or older, had a diagnosis of primary or secondary wAIHA or EVANS syndrome, refractory or dependent to glucocorticoids. Patients were given a single dose of 500 mg rituximab infusion on day 0 and a subcutaneous injection of 1.3 mg/m ^{2} bortezomib twice a week for two weeks on days 1, 4, 8, and 11. A same course was repeated after 3 months, with response assessment after 3 and 6 months. Patients with response were given rituximab 500mg every three months for 6 cycles. The primary endpoint was overall response rate (ORR) after 6 months; the co-primary endpoint was the days to hemoglobin (HGB) increase >20 g/L and transfusion independence.
Findings Between Sep 2, 2019 and Jan 15, 2023, a total of 33 patients were enrolled, with 27 females (81.8%) and a median age of 56.5[interquartile range (IQR) 42.75 - 65.75]. There were 30 (91%) relapsed patients and 3 (9%) refractory patients, and 20 (60.6%) patients with primary wAIHA and 13 (39.4%) patients with secondary wAIHA. At 6 months, the ORR was 75.8%, with 11.7% of CR. The median days to HGB increase >20 g/L and transfusion independence was 19 days [interquartile range (IQR) 13 - 61.5]. After a median follow-up of 24 months [interquartile range (IQR) 6 - 24], the ORR was 84.8% with 21.2% of CR. 28.6% patients relapsed at a median interval of 12 months [interquartile range (IQR) 5.75 - 19]. 2 patients (6.1%) experienced adverse events grade $\geq$ 3, both of whom experienced severe pulmonary infection. There was a significant reduction in B cell counts ($P = 0.011$), but no significant change in quantitative measurement of serum immunoglubulin G (IgG) ($P = 0.056$), IgA ($P = 0.052$) and IgM ($P = 0.057$) after 6 months treatment. Mann-Whitney analysis showed that patients with a higher amount of B cells before RB regimen treatment were more likely to achieve CR ($P = 0.02$).
Conclusion The combination of rituximab with bortezomib for RR wAIHA patients showed excellent efficacy with rapid responses and safety. The trial was registered at ClinicalTrials.gov as NCT04083014.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Rituxumab is B-cell targeting drug and primarily indicated for the treatment of patients with relapsed or refractory low-grade or follicular, B-cell non-Hodgkin lymphoma. Bortezomib is a first-in-class, potent, selective and reversible proteasome inhibitor approved for the treatment of multiple myeloma (MM) and relapsed/refractory mantle cell lymphoma.

https://doi.org/10.1182/blood-2023-178625