

Updated Analysis of Half-Dose CHOP Combined with Rituximab as Primary Therapy for Symptomatic Waldenström Macroglobulinemia: Single Institutional Experience in Japan

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Introduction

Epidemiological treatment patterns for Waldenström Macroglobulinemia (WM) vary among countries. Recent reports from the US suggested that bendamustine and proteasome inhibitor containing-regimens are recently used more often than alkylating agent-containing regimens (*Oncologist. 2016; 21: 1377, Blood 2017 130: 348*). However, according to reports from European countries and Japan, alkylating agent-containing regimens, including R-CHOP therapy, remain popular (*Blood 2015. 126: 2096, IJH 2017; 106: 681*). Furthermore, alkylating agent-containing regimens were found to be more cost effective (*Blood 2017 130: 348*). As standard dose R-CHOP therapy is accompanied by severe myelosuppression and WM patients are generally elderly, we performed half-dose R-CHOP therapy (R-half CHOP) as the primary therapy (*9th IWWM #46, Blood Research (in press)*). We herein report the updated analysis of R-half CHOP for untreated WM.

Patients and Methods

Twenty-five untreated symptomatic WM patients who received R-half CHOP as their primary therapy between April 2011 and April 2018 were enrolled in this study. The diagnostic criteria for WM were according to the 2nd International Workshop on WM. Responses, time to response, PFS, OS, and toxicities were analyzed.

Results

Of the 25 patients analyzed, the median age was 70 years (range: 50-85). The median Hb level was 9.1 g/dL (5.3-14.3) and the median M-protein level was 2.13 g/dL (0.66-6.6). Seven patients had hyperviscosity syndrome (28%) and underwent plasma exchange prior to chemotherapy. According to the IPSSWM, 3 (12%), 12 (48%), and 10 (40%) patients were

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classified as low-, intermediate-, and high-risk, respectively.

After completing R-half CHOP, 2 (8%) achieved CR, 1 (4%) achieved VGPR, 12 (48%) achieved PR, 6 (24%) achieved MR, and 4 (16%) achieved SD; therefore, the overall response rate (ORR) and the major response rate (MRR) were 84% and 60%, respectively. The median times to a response and to the best response were 5.7 and 9.7 weeks, respectively.

Grade 3/4 leukocytopenia was observed in 8 patients (33%), neutropenia in 9 (38%), and reduced hemoglobin in 5 (21%). Grade 1 PN was observed in 5 patients (21%).

The 2-year PFS, 3-year PFS, and 3-year OS were 72%, 64%, and 96%, respectively.

During the median follow-up of 37.7 months (range: 12-83.2), 9 patients developed refractory disease or progression. All patients started bendamustine-containing regimens as 2nd-line therapy, and 8 responded; 2 achieved VGPR, 6 achieved PR, and 1 achieved SD (ORR/MRR 89%). The median times to a response and to the best response were 4.4 and 13.6 weeks, respectively. The median second PFS was 39 months.

Grade 3/4 leukocytopenia was noted in 4 patients (44%), neutropenia in 4 (44%), and lymphopenia in 9 (100%), but reduced hemoglobin was not observed. Grade 1 angialgia was noted in 2 patients.

Three patients received 3rd-line therapy. Two of the 3 received bortezomib-containing regimens. During the follow-up, 3 patients died due to traumatic subarachnoid hemorrhage, Bing-Neel syndrome, and suicide, respectively.

Conclusion

The present study revealed that R-half CHOP as primary therapy was effective and well-tolerated. Therefore, this regimen may be considered as one primary therapy treatment option for WM.