Safety and efficacy of high-dose ranimustine (MCNU) containing regimen followed by autologous stem cell transplantation for diffuse large B-cell lymphoma

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Abstract
High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) is widely used as a salvage therapy for relapsed or high-risk diffuse large B-cell lymphoma (DLBCL). To investigate the safety and efficacy of regimens including high-dose MCNU followed by ASCT for DLBCL, we analyzed the data from prospective multicenter trials. Twenty-nine patients were analyzed, and the median follow-up time for survival patients was 70 months. Fifteen patients received MCVC conditioning regimen, and fourteen patients received MEAM regimen. Major toxicities associated with these conditioning regimens included nausea (69%), anorexia (66%), febrile neutropenia (62%), diarrhea (59%), and mucositis (34%). One patient who developed severe sinusoidal obstructive syndrome and acute lung injury died without disease progression, and overall therapy-related mortality at 5 years was 3%. No patient developed therapy-related hematological malignancy. At 5 years, overall survival and progression-free survival in all patients were 82.8 and 58.2%, respectively. The 5-year OS in patients treated by the MCVC and MEAM regimens were 73.3 and 92.9%, respectively. These results suggest that regimens including high-dose MCNU followed by ASCT are feasible and effective for the treatment of relapsed or high-risk DLBCL. Further investigation is needed to evaluate of these regimens.

Keywords DLBCL · MCNU · ASCT

Introduction
High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) has been shown to be an appropriate approach compared with standard salvage therapy in patients with chemo-sensitive relapsed or refractory diffuse large B-cell lymphoma (DLBCL) [1]. To date, various high-dose conditioning regimens have been developed, and nitrosourea-based therapy are commonly used. The safety and efficacy of high-dose carmustine (BCNU) have been well defined in many studies from the western countries [2, 3]; however, BCNU is not yet approved in some countries including Japan. Ranimustine (MCNU) is one of another nitrosourea agent. In some countries, MCNU is being used clinically for cytoreduction of chronic myeloproliferative disorder [4] and used as conditioning regimen followed by ASCT for malignant lymphoma [5, 6]. Though some small studies have shown that an MCNU-based conditioning regimen following ASCT is effective and tolerable for malignant lymphoma, there is very limited information regarding the