Upfront Autologous Stem Cell Transplantation for Patients with Primary Central Nervous System Lymphoma Who Received Rituximab and High-dose Methotrexate Treatment

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Background: Primary central nervous system lymphoma (PCNSL) is rare but fatal extranodal non-Hodgkin lymphoma, and most cases are histologically diffuse large B-cell lymphoma (DLBCL). Although the efficacy of rituximab is still less evident in PCNSL due to the blood-brain barrier than systemic DLBCL, rituximab in combination with high-dose methotrexate (HD-MTX) chemotherapy is widely used as the standard front-line treatment for newly diagnosed, treatment-naïve patients with PCNSL. Nevertheless, early or late relapse of PCNSL remains a problem in a substantial number of patients. Thus, the upfront use of autologous stem cell transplantation (auto-SCT) has been recommended as a consolidation treatment (upfront auto-SCT) for PCNSL patients who are eligible for auto-SCT. However, it is still not clear whether upfront auto-SCT could be more beneficial in terms of survival outcome than auto-SCT after salvage chemotherapy (salvage auto-SCT).

Materials and Method: We analyzed the medical data of PCNSL patients (n = 91) who consecutively received rituximab, HD-MTX, vincristine, and prednisolone (R-MVP) as front-line chemotherapy after enrolled into the Samsung Medical Center Prospective Lymphoma Cohort. The aim of this study was to evaluate the role of upfront auto-SCT in patients with PCNSL who received the induction treatment with rituximab and HD-MTX. Thus, the progression-free survival (PFS) and overall survival (OS) were compared between patients undergoing upfront auto-SCT (n = 32) and the remaining patients who did not (n = 59). We also compared the outcome of upfront auto-SCT with that of salvage auto-SCT and analyzed mutation profiles of patients undergoing auto-SCT with targeted sequencing of primary tumor tissue.

Results: Out of 91 patients, forty-one (45.1%) patients were over 65 years old and involved deep sites of brain parenchyma such as periventricular regions, basal ganglia, cerebellum according to the IELSG definition. Although the treatment response to R-MVP was not significantly different between patients with and without upfront auto-SCT, the relapse rate of patients undergoing upfront auto-SCT (7/32, 21.8%) was significantly lower than that of patients who did not (26/59, 44.1%). Accordingly, the PFS of patients who underwent upfront auto-SCT was significantly better than patients without upfront auto-SCT (P=0.032). The OS of upfront auto-SCT also showed a longer outcome although it was not statistically significant (P=0.078). The comparison of upfront and salvage auto-SCT demonstrated benefits in terms of OS and PFS (P<0.01). The analysis of mutation profiles showed patients who had a high mutation burden could achieve long-term survival after upfront auto-SCT. There was no event of transplantation-related mortality in our patients.

Conclusion: Our study demonstrated the benefit of upfront auto-SCT in PCNSL patients who received rituximab and HD-MTX induction treatment in terms of PFS. Thus, upfront auto-SCT could provide a prolonged disease-free period leading to long-term survival in patients who were treated with rituximab-containing HD-MTX chemotherapy. Our results suggest the active use of upfront auto-SCT for PCNSL patients eligible for auto-SCT.

Keywords: Primary central nervous system lymphoma, Autologous stem cell transplantation