CAR T-cell Therapy in Primary and Secondary CNS Lymphomas in Korea

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Primary central nervous system lymphoma (PCNSL) is a rare extranodal non-Hodgkin lymphoma confined to the brain, spinal cord, leptomeninges, or eyes, accounting for less than 1% of all lymphomas. The incidence is increasing, particularly in elderly patients. Despite high-dose methotrexate, prognosis remains poor with 5-year survival rates of 22-40%. Approximately 30-60% of patients achieving complete remission relapse within 1-2 years, and the prognosis of these patients is extremely poor with median survival of less than 6 months.

Patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) with secondary CNS involvement also have dismal prognosis, with a median overall survival of approximately 3 months. No standard treatment exists for relapsed/refractory PCNSL or secondary CNS lymphoma. Available salvage regimens such as ICE (ifosfamide, carboplatin, and etoposide), lenalidomide, or ibrutinib show limited efficacy with an overall response rate of 30-50%, and median progression-free survival of 2-5 months.

Recently, anti-CD19 CAR T-cell therapies have transformed B-cell lymphoma treatment. In patients with systemic DLBCL, these agents achieve approximately 40% cure rates in third-line or beyond settings, compared to 10% cure rates with conventional therapies. In addition, recent phase 3 trials demonstrated that CD19 CAR T-cell therapies significantly improved survival outcomes compared to high-dose chemotherapy with autologous stem cell transplantion in second-line settings.

Recent clinical data support the efficacy of CAR T-cell therapy in CNS lymphomas. A phase 1/2 study of tisagenlecleucel in relapsed/refractory PCNSL demonstrated encouraging response rates with acceptable safety profile. Real-world evidence from large multicenter studies confirmed these findings, showing durable remissions in both primary and secondary CNS lymphomas. Survival curves showed plateau after 1 year, suggesting approximately 40% of patients may achieve cure.

CAR T-cell therapy has emerged as an important treatment option for relapsed/refractory primary and secondary CNS lymphomas. It offers potential for durable remissions and cure in a disease setting with historically dismal outcomes.