Current Practice and Research in T-cell and NK/T-cell Lymphoma in Japan

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Fewer than 10% of all lymphoma patients in Japan have mature T/NK-cell lymphoid neoplasms. For patients with major subtypes of peripheral T-cell lymphoma (PTCL), including PTCL not otherwise specified, angioimmunoblastic T-cell lymphoma (AITL), and anaplastic large cell lymphoma, the 2024 Japanese Society of Hematology (JSH) guidelines recommend the use of brentuximab vedotin (BV)-CHP for CD30-positive tumors and CHOP-like regimens for CD30-negative tumors as the first-line treatment. A dose-adjusted EPOCH regimen can be considered for patients with AITL based on the results from a phase II study in Japan and a subgroup analysis of the ECHELON-2 trial. The significance of consolidative high-dose chemotherapy with autologous blood stem cell transplantation for patients with PTCL in the first CR is uncertain. The Lymphoma Study Group of the Japan Clinical Oncology Group (JCOG-LSG) is conducting a randomized phase III study (JCOG2210) to answer this clinical question. For patients with relapsed/refractory T-cell and NK/T-cell lymphoma, many therapeutic drugs (mogamulizumab, BV, pralatrexate, forodesine, romidepsin, alectinib, denileukin diftitox, tucidinostat, darinaparsin, and valemetostat) are approved and available in Japan. However, there is still little evidence regarding their usage, and various studies are underway.

A pooled analysis of patients enrolled in JCOG trials revealed that adult T-cell leukemia/lymphoma and extranodal NK/T-cell lymphoma (ENKL) patients had particularly poor prognoses when treated with standard anthracycline-containing chemotherapy, leading to the development of treatments for these lymphomas. During the past decade, the first-line treatment for ENKL in Japan has dramatically changed based on the results of two clinical trials, JCOG0211 and SMILE-P2. The 2024 JSH guidelines recommend the use of RT-2/3DeVIC for patients with newly diagnosed localized nasal ENKL and the use of SMILE or other L-asparaginase-containing chemotherapies for patients with newly diagnosed, advanced-stage ENKL. Two outcome studies, namely, NKEA (2000–2013) and NKEA-Next (2014–2021), were conducted to evaluate the safety and efficacy of these treatments in real-world clinical settings. RT-2/3DeVIC was selected in 79% of patients with localized ENKL. The use of SMILE was associated with favorable survival in patients with advanced-stage ENKL. These studies confirmed the usefulness of these treatments while also clarifying their limitations. The results also served as historical controls for subsequent clinical studies.

In Japan, close collaboration between hematologists and radiation oncologists has been achieved in the development of treatments for localized ENKL. However, among immune checkpoint inhibitors, only atezolizumab was approved for the treatment of ENKL in 2025, and little experience is available with its use. Patients with ENKL in Japan account for less than 1% of all lymphoma patients, which is as low as in Western countries. To fill these gaps, an international observational study (International ENKL project 2025: UMIN000056213) is currently underway.