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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Survival and CNS Relapse in Patients with CD5-Positive Diffuse Large B-Cell Lymphoma: A Multi-Institutional Observational Study in Japan

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Background: CD5-positive diffuse large B-cell lymphoma (CD5+ DLBCL) is usually characterized by activated B-cell type, poor prognosis, and frequent central nervous system (CNS) relapse. A sandwich therapy of dose-adjusted (DA)-EPOCH-R combined with high-dose methotrexate (HD-MTX) (DA-EPOCH-R/HD-MTX) showed excellent efficacy in a phase II study for newly diagnosed stage II-IV CD5+ DLBCL, including 2-year (yr) overall survival (OS), progression-free survival (PFS), and CNS relapse rates of 89%, 79%, and 9%, respectively (Miyazaki K, et al. Haematologica, 2020). It has been introduced in practice in Japan; however, the current status of treatment and the prognosis in patients with CD5+ DLBCL are unclear.
Methods: We retrospectively analyzed the prognosis and CNS relapse rate of consecutive patients with untreated CD5+ DLBCL who were diagnosed at 30 hospitals in Japan from January 2016 to December 2021. Patients who were diagnosed with double-/triple-hit lymphoma, those with CNS involvement at diagnosis, and those who had not received any anthracycline-containing chemotherapy with rituximab (R-chemo) were excluded. We identified risk factors for OS using Cox proportional hazards method. The outcomes in the stage II-IV patients who received DA-EPOCH-R/HD-MTX were compared with those of the phase II study. To evaluate the efficacy of CNS prophylaxis, we divided patients into four groups: HD-MTX alone, intrathecal administration of MTX alone (IT MTX), both HD-MTX and IT MTX (HD/IT MTX), and no CNS prophylaxis.
Results: Among the413 enrolled patients, 20 were excluded due to ineligible diagnosis or insufficient clinical information, 18 had CNS involvement at diagnosis, and 27 did not receive R-chemo. As a result, 348 patients were eligible and showed the following features: median age, 71 yrs (range, 23-92); male sex, 54%; stage II-IV, 90%; stage III or IV, 73%; ECOG performance status (PS) $>$ 1, 30%; $>$ 1 extranodal site, 42%; elevated serum lactate dehydrogenase (sLDH) level, 71%; high-intermediate or high International Prognostic Index (IPI), 63%; high CNS-IPI, 41%; and B symptoms, 29%. According to Hans's criteria, the nongerminal center B-cell type accounted for 67% of the 276 cases examined. Among the 348 patients, 62 (18%) received DA-EPOCH-R/HD-MTX, and 286 (82%) were treated with other R-chemo, such as R-CHOP (n = 254). The median age was 63.5 yrs (range, 29-75) in the DA-EPOCH-R/HD-MTX group and 72 yrs (range, 23-92) in the other R-chemo group. The DA-EPOCH-R/HD-MTX group included significantly more patients aged $\leq$ 60 yrs ($P < 0.001$), although it tended to have more patients with ECOG PS $>$ 1 than the other R-chemo group ($P = 0.069$). Patients who received IT MTX made up 16% of the DA-EPOCH-R/HD-MTX group and 31% in the other R-chemo group. HD-MTX was used in 100% of patients in the DA-EPOCH-R/HD-MTX group and 17% of patients in the other R-chemo group. Details of CNS prophylaxis were HD-MTX alone in 84 patients (24%), IT MTX alone in 70 (20%), both HD/IT MTX in 28 (8%), and no CNS prophylaxis in 166 (48%).
At a median follow-up of 43 months, the 2-yr OS, PFS, and CNS relapse rates of patients with stage II-IV disease in the DA-EPOCH-R/HD-MTX group were 87% (95% CI, 73-94%), 78% (95% CI, 63-87%), and 7.3% (95% CI, 2.8-18.2%), respectively. There were no significant differences in OS or PFS between stage I and stage II-IV patients in the DA-EPOCH-R/HD-MTX group. In all 348 patients with stage I-IV, both the OS ($P = 0.044$) and PFS ($P = 0.043$) in the DA-EPOCH-R/HD-MTX group were longer than those in the other R-chemo group. The 2-yr OS in these groups were 89% and 78%, and their 2-yr PFS were 78% and 64%, respectively. Multivariate analysis identified elevated sLDH ($P = 0.005$), $>$ 1 extranodal involvement ($P < 0.001$), no IT MTX ($P = 0.005$), and no DA-EPOCH-R/HD-MTX ($P = 0.005$) as independent risk factors for OS. The 2-yr CNS relapse rate was 6.5% in the DA-EPOCH-R/HD-MTX group (n = 4) and 10.0% in the other R-chemo group. There were no significant differences in the CNS relapse rate between the two groups ($P = 0.54$). The 2-yr CNS relapse rates of HD-MTX, IT MTX alone, both HD/IT MTX, and no prophylaxis were 9.8%, 9.1%, 3.7% (n = 1), and 10.3%, respectively.
Conclusions: Our results confirmed favorable survival in the phase II study of DA-EPOCH-R/HD-MTX in clinical settings. DA-EPOCH-R/HD-MTX and IT MTX were associated with longer OS of patients with CD5+ DLBCL in our study cohort, warranting further investigation.

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