Joint Event on

20th Euro-Global Gastroenterology Conference

23rd World Hematology Congress

July 07-08, 2025

Webinar

J Cancer Sci Ther 2025, Volume 17

USP7 mutations predict adverse long-term outcomes in pediatric T cell acute lymphoblastic leukemia and lymphoma

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Background: USP7 alterations was discovered in pediatric T-cell acute lymphoblastic leukemia (T-ALL). However, the prognostic implication hasn't been reported. This study aimed to investigate the clinical aspects and long-term outcomes of pediatric T-ALL and T-cell lymphoblastic lymphoma (T-LBL) with USP7 mutations.

Methods: 313 pediatric patients with T-ALL/T-LBL were enrolled in study, USP7 catalytic domain mutations as well as NOTCH1 mutations were detected by Sanger sequencing. The correlations between clinical aspects and prognosis with USP7/NOTCH1 were analyzed. Independent prognostic importance of USP7 mutation was evaluated by Cox regression model and nomogram.

Results: Overall, twelve patients with USP7 heterozygous mutations were found including 10 of T-ALL and 2 of T-LBL. USP7 mutations were associated with older age and higher proportion of not remission at day 15 bone marrow morphology evaluation. Patients with USP7 mutation showed significant poorer 5-year event-free survival (EFS) and overall survival (OS) than those wild-type when analyzed in T-ALL alone and T-ALL/LBL together. Moreover, the EFS and OS of patients with USP7mutNOTCH1wt was the worst among four subgroups, while USP7wtNOTCH1mut was the best. USP7 mutations, MRD ≥10-4 pre-consolidation and CNS leukemia were identified as independent adverse prognostic factors for EFS, and the former two were also for OS. USP7 mutational status was validated as the most contributor for prognosis with nomogram and prediction model included USP7 status presented better prediction accuracy.

Conclusions: These findings indicate USP7 mutations identified a subset of T-ALL/LBL patients with adverse outcomes on conventional intensive treatment and might be improved by innovative targeted therapy.

Keywords: T-ALL, T-LBL, pediatrics, clinical study, prognostic factor, molecular diagnosis