# Abstract: P1352

## Title: CDKN2A/B GENE DELETION AS AN INDEPENDENT PROGNOSTIC FACTOR IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA RECEIVING ALLOGENEIC STEM CELL TRANSPLANTATION

**Abstract Type: Poster Presentation**

**Topic: Stem cell transplantation - Clinical**

**Background:**

Allogeneic hematopoietic stem cell transplantation (HSCT) is an established potentially curative therapy for high risk pediatric Acute Lymphoblastic Leukemia (ALL). Outcome after HSCT is a result of various patient- and transplant related parameters. CDKN2A/2B gene deletions have been investigated as a prognostic factor for chemosensitivity and disease course, but their role barely in transplantation outcome remains largely unknown.

**Aims:**

To investigate the impact of CDKN2A/B deletions on leukemia-free survival (LFS), relapse and overall survival (OS) after HSCT for children with ALL.

**Methods:**

Pediatric patients with ALL transplanted in our Unit from 1/1/2002 till 31/03/2023 were included in the study. CDKN2A/B gene deletions were evaluated with conventional cytogenetics and/or fluorescence in situ hybridization at diagnosis or last relapse and results were correlated with LFS, relapse and OS. Probabilities of OS and EFS were calculated using Kaplan–Meier method and cumulative incidence (CI) of relapse using CI of competing events and Gray test. Cox proportional-hazard regression model was used for multivariate analysis.

**Results:**

219 patients (73 girls) were included, with median age at transplant 9.2 years (0,5–18,5). Flow cytometry immunophenotype was B-ALL for 162 and T-ALL for 55 patients. 129/219 patients were transplanted in CR1, 71/219 in CR2 and 19/219 in CR3/refractory disease. Patients received PBSC (73/219), marrow (138/219) or CB (8/219) from matched unrelated (n=129), matched sibling (n=75) and haploidentical donors (n=15). Preparative conditioning regimen was TBI-based or busulfan-based in 60 and 159 children respectively. 50/219 (22%) patients harbored CDKN2A/B gene deletion. Median follow up was 41.3 months. Probabilities of LFS and OS were 52% and 60% respectively. CI of relapse was 31.6%. LFS of patients with CDKN2A/2B deletion was significantly inferior compared to patients without the deletion, 35% versus 57%, p=0.007. No other parameter, i.e. age, immunophenotype, high-risk cytogenetics i.e.t(9;22), MLL rearrangement, t(1;19), del(6), hypodiploid ALL, iAMP21, -7 and delIKAROS, disease state at transplant, donor and type of conditioning, was statistically significant in the univariate analysis. In the multivariate analysis that included all formerly mentioned parameters, CDKN2A/B deletion remained an independent adverse prognostic factor for EFS, HR 1.77(95%CI1.12–32.7), along with T immunophenotype, HR=1.89(95%CI1.1-3) and HSCT in >CR1, HR=1.79(95%CI1.1-2.9). Accordingly, relapse rate was significantly higher for patients with CDKN2A/2B deletion, 50.5% vs 26.1%, p=0.005. Relapse was also higher for patients of the high-risk cytogenetics subgroup (41% vs 25, 4%,p=0,013) and for patients aged <10 years (39% vs 21%,p=0.006). In the multivariate analysis CDKN2A deletion and age<10 years were independent negative prognostic markers, with HR 2.1(1.2-3.5) and 1.9(1.03-3.5) respectively.

OS did not correlate with CDKN2A/B deletion status and was higher for patients transplanted in CR1 and patients with B-ALL, HR=2.42(1.4-4.8) and 2.32(1.36-3.9) respectively in the multivariate analysis.

**Summary/Conclusion:**

Our study correlates CDKN2A/B gene deletion with LFS and relapse after HSCT for pediatric ALL. Potential use

of this genetic alteration as a prognostic factor for HSCT, suggesting additional therapeutic approaches, such as cellular therapy post-transplant or targeted agents against CDK4/6 complexes may be useful, in order to reduce probability of relapse.

**Keywords:** ALL, Chromosomal abnormality, allo BMT