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POSTER ABSTRACTS

617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Integrated Analysis of *KIT* Exon 17 Mutations and Flow-MRD Refines Risk Stratification in Pediatric Acute Myeloid Leukemia with *RUNX1*:: *RUNX1T1*

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INTRODUCTION: Pediatric acute myeloid leukemia (AML) with *RUNX1*:: *RUNX1T1* is considered a favorable risk group, with a high probability of event-free survival (EFS) in recent clinical trials. However, 20-30% of patients still experience relapse within three years and some patients have poor outcome. Several prognostic factors, including secondary genetic abnormalities and treatment response, have been previously reported. Flow cytometry-based measurable residual disease (flow-MRD) has been suggested as a poor prognostic factor in AML with *RUNX1*:: *RUNX1T1*. Additionally, *KIT* mutations, particularly mutations of exon 17, have been associated with poor EFS in both adult and pediatric patients. However, the combined impact of *KIT* exon 17 mutations and flow-MRD on prognosis has not been thoroughly investigated. This study aims to evaluate the clinical and genetic features of pediatric patients with *RUNX1*:: *RUNX1T1*-positive AML enrolled in the Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG) AML-12 trial and determine if integrated analysis of flow-MRD and *KIT* exon 17 mutations can improve risk stratification.
METHOD: A total of 101 pediatric AML patients with *RUNX1*:: *RUNX1T1* were enrolled in the study. The patients were treated in the JPLSG AML-12 trial, and their clinical and genetic characteristics were analyzed. Targeted capture sequencing was performed on bone marrow samples obtained at diagnosis. The custom gene panel was designed for mutation profiling of pediatric AML, including 504 genes. Flow-MRD was centrally monitored at the end of induction 1 (EOI1) and the end of induction 2 but was not used to guide subsequent therapies. Leukemia-associated immunophenotypes were identified in diagnostic specimens and marker combinations that allowed detection of leukemia with a sensitivity of at least 0.1% were applied to subsequent samples.
RESULTS: Patients with *KIT* exon 17 mutations had a higher white blood cell count at diagnosis and a significantly higher rate of MRD positivity (≥0.1%) at EOI1 compared to patients without *KIT* exon 17 mutations. Immunophenotypic analysis

showed no significant differences in CD117 or CD33 expression between patients with and without *KIT* exon 17 mutations; whereas CD19 expression was observed less frequently and, although not significantly, CD56 expression was observed more frequently in the patients with KIT exon 17 mutations. The genetic landscape analysis revealed that *KIT* mutations were the most common and tended to coexist with *ARID1B* mutations, while *NRAS* mutations were mutually exclusive. The 5-year EFS and overall survival (OS) for the entire cohort were 67.3% and 82.7%, respectively. Negative MRD at EOI1 was associated with significantly superior 5-year EFS and OS (71.6% and 85.9%) compared to positive MRD (12.5% and 37.5%)($p<0.01$). Patients with *KIT* exon 17 mutations had significantly inferior 5-year EFS and OS (46.9% and 62.2%) compared to those without *KIT* exon 17 mutations (76.8% and 92.4%) ($p<0.01$). Furthermore, we evaluated a prognostic impact of MRD within the *KIT* exon 17 mutated and non-mutated cases. As for the non-mutated cases, the 5-year OS in the patients with negative MRD was 92.2%. Among the *KIT*-mutated cases, the 5-year OS in the patients with negative and positive MRD was 68.0% and 33.3%, respectively.

CONCLUSION: Patients with both non-mutated *KIT* exon 17 and negative MRD have the best prognosis, while positive MRD and *KIT* exon 17 mutations are associated with poorer outcomes. These findings indicated that integrated analysis of flow-MRD and *KIT* exon 17 status enables optimal risk assignment strategies in pediatric AML with *RUNX1*:: *RUNX1T1*.

Disclosures Kato: *Amgen:* Honoraria; *Novartis:* Honoraria; *Chugai:* Honoraria.

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Figure. EFS and OS in status of flow-MRD and KIT exon 17 mutations

	No. patients	5yr-EFS	95% CI
KIT WT and MRD<0.1%	55	80%	: 70.1–91.3%
KIT MT and MRD<0.1%	19	47.4%	29.5–76.1%
KIT WT and MRD≥0.1%	2	NA	NA
KIT MT and MRD≥0.1%	6	16.7%	2.8–99.7%

	No. patients	5yr-OS	95% CI
KIT WT and MRD<0.1%	55	92.2%	85.1–99.9%
KIT MT and MRD<0.1%	19	68.0%	49.8–92.8%
KIT WT and MRD≥0.1%	2	NA	NA
KIT MT and MRD≥0.1%	6	33.3%	10.8–100%

Figure 1