

## Risk-stratified therapy for infant ALL

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**Tomizawa D, Miyamura T, Imamura T, Watanabe T, Moriya Saito A, Ogawa A, Takahashi Y, Hirayama M, Taki T, Deguchi T, Hori T, Sanada M, Ohmori S, Haba M, Iguchi A, Arakawa Y, Koga Y, Manabe A, Horibe K, Ishii E, Koh K. A risk-stratified therapy for infants with acute lymphoblastic leukemia: a report from the JPLSG MLL-10 trial. *Blood*. 2020;136(16):1813-1823.**

**1. Your patient is a 5-month-old male infant with newly diagnosed acute lymphoblastic leukemia (ALL) with rearrangement of the KMT2A gene (KMT2A-r). According to findings of the Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG) trial MLL-10 by Tomizawa and colleagues, which of the following statements about the outcomes of infants with higher-risk (HR) KMT2A-r ALL and lower-risk (LR) KMT2A-g ALL is correct?**

- Three-year event-free survival (EFS) was  $66.2\% \pm 5.6\%$  for KMT2A-r ALL (intermediate risk [IR] plus HR);  $93.3\% \pm 6.4\%$  for LR KMT2A-g ALL;  $94.4\% \pm 5.4\%$  for IR KMT2A-g ALL; and  $56.6\% \pm 6.8\%$  for HR KMT2A-g ALL
- For HR patients, 3-year overall survival (OS) was 49%; 5-year OS was 29%
- Chemotherapy for IR/HR patients appeared to be limited by significant toxicities and early deaths
- Of HR cases achieving complete remission (CR), 47% received hematopoietic stem cell transplantation (HSCT) in first complete response, and 27% are alive in CR

**2. According to the findings of the JPLSG trial MLL-10 by Tomizawa and colleagues, which of the following statements about the impact of minimal residual disease (MRD) and other prognostic factors on the outcomes of infants with KMT2A-r ALL and KMT2A-g ALL is correct?**

- Infants with ALL were stratified into 3 risk groups only, according to KMT2A status and age
- Male sex was significantly associated with poor prognosis
- In multivariable analysis, MRD  $\geq 0.01\%$  at the end of early consolidation was significantly associated with poor prognosis
- Three-year and 5-year EFS rates of patients with positive MRD were significantly worse than those of patients with negative MRD only at early time points

**3. According to findings of the JPLSG trial MLL-10 by Tomizawa and colleagues, which of the following statements about clinical implications of the outcomes of infants with KMT2A-r ALL and KMT2A-g ALL is correct?**

- The findings supported conventional therapeutic approaches, including HSCT, in the conventional HR group and infants with residual MRD
- Novel purine nucleoside analogs, epigenetic modifiers, BCL-2 inhibitors, menin inhibitors, and immunotherapies are novel therapeutics expected to be active against infant KMT2A-r ALL
- Outcomes in the MLL-10 trial were similar to those seen in previous Japanese infant ALL trials
- MLL-10 had longer follow-up and larger sample size than the Interfant-06 study