Clinical Phenotype, Molecular Architecture, and Survival Follow-Up in NRAS- and KRAS-Mutated Juvenile Myelomonocytic Leukemia

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INTRODUCTION

JMML is a rare pediatric myelodysplastic/myeloproliferative neoplasm driven predominantly by RAS-pathway lesions. The biological and clinical meaning of NRAS- versus KRAS-mutated disease remains incompletely described in single-center practice.

AIM

To describe diagnosis-time phenotype, molecular context, and survival follow-up in children with NRAS- and/or KRAS-mutated JMML, while transparently presenting treatment and HSCT documentation.

METHODS

- Retrospective single-center cohort, November 2010 to September 2022.
- Thirty-four children had classifiable NRAS and/or KRAS alterations.
- NRAS-only and KRAS-only subgroups were compared for diagnosis-time phenotype.
- OS was evaluable in 30.
- Molecular testing evolved from hotspot-focused assays to broader NGS over time.
- HSCT was modeled as a post-diagnostic time-dependent exposure.

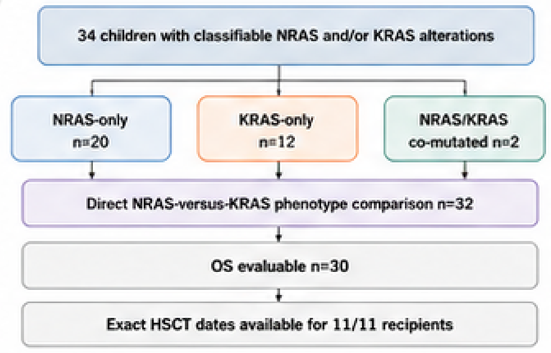
CONCLUSIONS

- KRAS-only JMML showed higher relative monocyte and lymphocyte percentages, while absolute monocyte count was similar to NRAS-only disease.
- NRAS/KRAS subtype alone did not significantly stratify overall survival.
- Molecular co-alteration, methylation, and treatment timing remain important for interpretation.
- The HSCT signal is observational and should not be interpreted as randomized causal evidence.

RESULTS

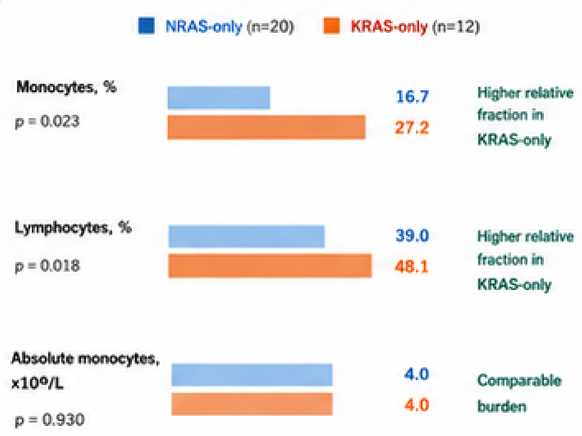
34 patients | 20 NRAS-only | 12 KRAS-only | 2 co-mutated | OS evaluable n=30

Figure 1. Cohort structure & molecular context



Co-mutated cases were retained for cohort description but excluded from the direct *NRAS-versus-KRAS* comparison.

Figure 2. Diagnosis-time phenotype

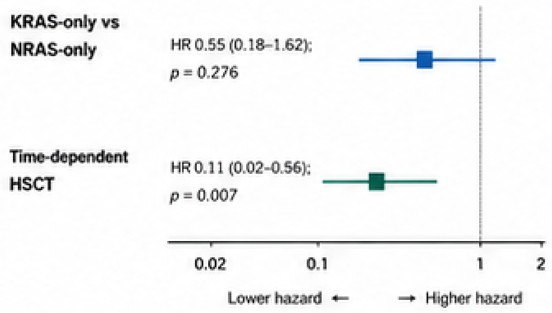


Key interpretation: Relative leukocyte composition differed, whereas absolute monocytic burden did not.

Values are medians; subgroup *p* values are descriptive.

Figure 3. Survival & HSCT treatment context

OS cohort: n = 30 • deaths = 15 • median OS = 13.0 months



Time-aware treatment analysis: HSCT entered the Cox model only after the transplantation date.

HSCT documentation: Exact dates available for all 11 transplant recipients.

The HSCT estimate is an observational treatment-context association; treatment selection and residual confounding preclude causal inference.

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REFERENCES

1. Wintering A, Dvorak CC, Stieglitz E, Loh ML. Blood Adv. 2021;5:4783–4793.
2. Locatelli F, Niemeyer CM. Blood. 2015;125:1083–1090.
3. Stieglitz E, et al. Nat Genet. 2015;47:1326–1333.
4. Locatelli F, et al. Blood. 2005;105:410–419.