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Outcomes of hematopoietic stem-cell transplantation in infants with *KMT2A*-rearranged acute lymphoblastic leukemia in first remission: a systematic review and single-arm meta-analysis

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ABSTRACT

Infants with acute lymphoblastic leukemia (ALL) frequently experience poor outcomes, with *KMT2A* gene rearrangements (*KMT2A*-r) serving as the most significant adverse prognostic factor. Allogeneic hematopoietic stem cell transplantation (HSCT) in first complete remission (CR1) has been utilized to improve survival, yet its definitive role remains a subject of intense debate. This systematic review and meta-analysis aimed to evaluate survival outcomes of HSCT in infants with *KMT2A*-r ALL in CR1. We systematically searched PubMed, Embase, and the Cochrane Library for randomized and observational studies reporting survival outcomes for infants with *KMT2A*-r ALL undergoing HSCT in CR1. Survival data were synthesized using parametric modeling (Weibull distribution) to estimate pooled outcomes. Mean survival across 1,000 iterations per study was calculated with 95%CI. Heterogeneity was assessed using I^2 statistics. All analyses were performed using R software (version 4.1.3). Seven studies comprising 371 patients were included. The pooled analysis demonstrated a 4-year overall survival (OS) of 65% (95%CI 58.7-72.1), a 4-year disease-free survival of 57.5% (95%CI 51.8-64.3), and a 3-year event-free survival (EFS) of 53.2% (95%CI 41.5-66.1). Our findings suggest that HSCT in CR1 is a viable therapeutic strategy for selected high-risk infants with *KMT2A*-r ALL, showing improved survival compared to historical benchmarks. While novel and safer therapies are currently under investigation, HSCT remains a reasonable option. Clinical decisions should carefully balance the curative potential of transplantation against the risk of severe treatment-related toxicities and long-term sequelae.

Keywords: Acute lymphoblastic leukemia (ALL); Infant; Stem cell transplantation (HSCT); *KMT2A*.

INTRODUCTION

Although current survival rates exceed 90% for most pediatric acute lymphoblastic leukemia (ALL) cases,[1] managing ALL in infants (diagnosed within the first year of life) remains a significant challenge. Infant ALL accounts for 2.5% to 5% of pediatric cases and exhibits distinct biological, clinical, and prognostic features compared to older children.[2] Approximately 75% of infant ALL cases harbor rearrangements of the *KMT2A*

gene (formerly *MLL*), located at chromosome band 11q23.[3] In contrast, this cytogenetic abnormality occurs in only 1% to 2% of older children with ALL.[4] While survival outcomes for older children and infants with *KMT2A*-germline ALL have improved over recent decades, outcomes for infants with *KMT2A* gene rearrangements (*KMT2A*-r) ALL remain poor.[5]

KMT2A-r is the most significant adverse prognostic factor,[6] often compounded by young age, high white blood cell count, and poor prednisone response.[7] Most infants with *KMT2A*-r ALL present with hyperleukocytosis, hepatosplenomegaly, and central nervous system involvement.[6,8,9] Their leukemic cells typically exhibit a pro-B-cell phenotype lacking CD10 expression.[10] Given the dismal prognosis in this population, various treatment strategies have been explored, with allogeneic hematopoietic stem cell transplantation (HSCT) being a primary focus.[6,11] Current evidence suggests that if HSCT is indicated, it should be implemented during the first complete remission (CR1), as survival rates drop significantly when administered in subsequent remissions.[8,12-14]

However, the efficacy and safety of HSCT in CR1 for infants with *KMT2A*-r ALL remain subjects of intense debate, particularly regarding treatment-related toxicities, long-term morbidity, and transplant-related mortality in this vulnerable age group.[15-17] Recent narrative reviews[6,9,11,15,18,19] and the 2020 National Comprehensive Cancer Network clinical practice guidelines[20] emphasize the ongoing controversy surrounding the role of HSCT. Given the rarity of infant ALL and the lack of robust, aggregated data on HSCT outcomes specifically for the *KMT2A*-r subset, this study aims to systematically investigate the impact of HSCT on survival outcomes in these patients

METHODS

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and the Cochrane Collaboration recommendations. The protocol was prospectively registered in the International Prospective Register of Systematic Reviews in December 2023 (registration number: CRD42023494213).

Eligibility criteria

Studies were included if they met the following criteria: 1) randomized or non-randomized clinical studies; 2) involved infants (diagnosed at < 1 year of age) with ALL and *KMT2A* rearrangements; 3) included patients who underwent HSCT in CR1; and 4) were published within the last 20 years to account for contemporary advances in HSCT conditioning regimens and supportive care.

Studies were excluded if they 1) were not published in English; 2) were abstracts, conference presentations, or case reports; or 3) were duplicate publications with overlapping cohorts. In cases of multiple reports from the same study population, only the most comprehensive or recent publication was selected.

Search strategy and data extraction

We systematically searched PubMed, Embase, and the Cochrane Library from inception to December 21, 2023. The search strategy utilized terms including "infant," "leukemia," and "stem cell transplantation," along with relevant MeSH terms and synonyms. Search results were managed using Zotero (version 6.0.22). Two reviewers (BLF and AMS) independently screened titles and abstracts. Potentially eligible articles underwent full-text assessment by the same reviewers. Discrepancies were resolved through consensus.

Endpoints

The primary outcomes of interest were overall survival (OS) and event-free survival (EFS). EFS was defined as the time from HSCT to the first event, including relapse, lineage switch to AML, secondary malignancy, or death from any cause. Disease-free survival (DFS) was also analyzed and defined as the time from CR1 achievement to first failure (relapse or death).

Data synthesis and analysis

To enable meta-analysis, raw survival data or Kaplan-Meier (KM) curves were prioritized. For studies where only point-estimate survival values were reported, we applied parametric modeling using the Weibull distribution to estimate survival trajectories.

For studies that provided KM curves, we extracted survival data from the published curves and fitted Weibull survival functions by nonlinear modeling to estimate the distribution parameters: the scale (lambda) and the shape (k). After estimating parameters for all studies with available curves, we computed the mean k across those studies. For studies without curves but with time-point survival values, we combined this mean k with the reported survival probabilities to back-calculate the corresponding lambda and simulate the missing survival trajectories. These reconstructed trajectories were then used to estimate survival over time and to derive the number of patients at risk.

Survival values were estimated for five distinct time periods (1 to 5 years), along with the number of patients at risk. These data formed the basis for calculating the average survival curve, following the methodology described by Combescure et al.[21] Since this approach involves data simulation, we performed 1,000 iterations per study to minimize the effects of random noise. The mean survival across these iterations was then calculated, along with its corresponding 95%CI.

Graphs were generated to illustrate the individually modelled survival curves for each study and the estimated average survival curve. Additionally, heterogeneity was assessed using Q, H^2, and I^2 statistics, which quantify variability among the included studies. All statistical analyses were conducted using R software, version 4.1.3 (R Core Team, 2022).

Risk of bias assessment

The methodological quality and risk of bias of the included studies were independently assessed by two reviewers. We utilized the Joanna Briggs Institute JBI Critical Appraisal Checklist for Case Series[22] for retrospective studies without a comparator group and the ROBINS-I tool[23] for non-randomized intervention studies.

Ethics statement

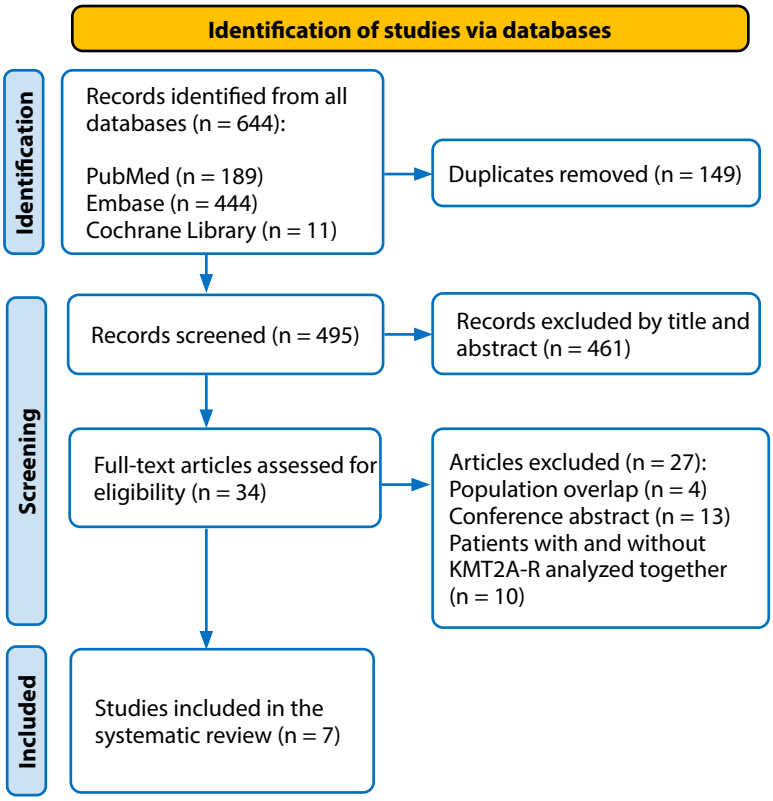
This study is a systematic review and meta-analysis of previously published, aggregate data and did not involve human participants or access to identifiable private information. Institutional review board approval and informed consent were not required.

RESULTS

Study selection and characteristics

The initial literature search yielded 644 records (Fig. 1). After removing duplicates and screening titles and abstracts, 34 articles were selected for full-text review. The majority of these studies addressed infant ALL as a whole, without providing specific subgroup analyses for the *KMT2A*-r population. Given the distinct biological behavior and prognosis of these subsets, studies with mixed populations lacking stratified data were excluded. Furthermore, several studies involved overlapping cohorts,[24,25-28] in which case only the most comprehensive or updated dataset was included.

Ultimately, seven studies comprising 371 patients met the eligibility criteria. Of these, three were retrospective, and four were prospective. Detailed study characteristics are provided in Table 1. For studies providing empirical KM curves, the modeled survival functions demonstrated a strong fit to the original data, with a calculated mean shape parameter (k) of 0.28.



Source: Elaborated by the authors.

Figure 1. PRISMA flowchart.

Table 1. Baseline characteristics of included studies.

Study group	Study protocol	Study design	n (CR1 KMT2Ar held for HSCT)	HSCT indication	Conditioning regimen	Follow-up, years
COG[29]	Children's Cancer Group 1953; Pediatric Oncology Group 9407	Prospective trial (1996-2000)	53	KMT2A-r with a suitable donor; the principal investigator agreed with HSCT option	Included cytarabine, CY, and TBI	10
JSHCT[27]	Japan Society for Hematopoietic Cell Transplantation (multiple trials)	Retrospective (1996-2011)	132	Not reported	Bu or TBI	4.9
Interfant[13]	Interfant-99	Randomized chemotherapy protocol; HSCT not randomized (1999-2006)	37	Poor prednisone response; HSCT after completion of reinduction therapy	Etoposide, Bu, and CY	5
Single institution[8]	Institutional; protocols varied by referring institution	Retrospective (1982-2003)	14	Not reported	CY with TBI or Bu	7
Interfant[7]	Interfant-06	Randomized chemotherapy protocol; HSCT not randomized (2006-2016)	76	High-risk (KMT2A-r with age < 6 months and WBC ≥ 300 × 10^9/L or poor prednisone response); medium-risk with MRD ≥ 10^-4	Bu + CY + melphalan or Bu + treosulfan + fludarabine + thiotepa	5.3
Single institution[12]	Pediatric Oncology Group 9407 or 9107	Retrospective (1992-2005)	16	Not reported	TBI/etoposide + CY	4.7
JPLSG[32]	MLL-10	Prospective trial (2011-2015)	43	KMT2A-r and either age < 180 days at diagnosis or CNS3 in CR1	Bu with etoposide and CY	5.7

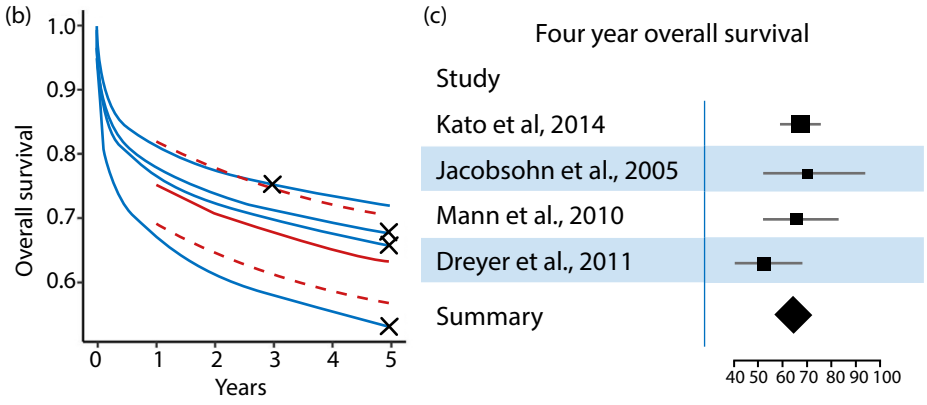
Bu: busulfan; CY: cyclophosphamide; CNS3: > 5 WBC/μL with blasts in cerebrospinal fluid; TBI: total body irradiation. In Interfant-99/06, chemotherapy regimens were randomized, but HSCT allocation was not; therefore, analyses regarding HSCT were considered non-randomized. Source: Elaborated by the authors.

Overall survival

Four studies provided OS data. The pooled 4-year OS was 65% (95%CI 58.7-72.1) (Fig. 2).

(a)

Years	OS (95% C.I.)
1	75.3% (69.1% ; 81.7%)
2	70.7% (64.3% ; 77.6%)
3	67.5% (61.1% ; 74.5%)
4	65% (58.7% ; 72.1%)
5	63.1% (56.7% ; 69.8%)



Source: Elaborated by the authors.

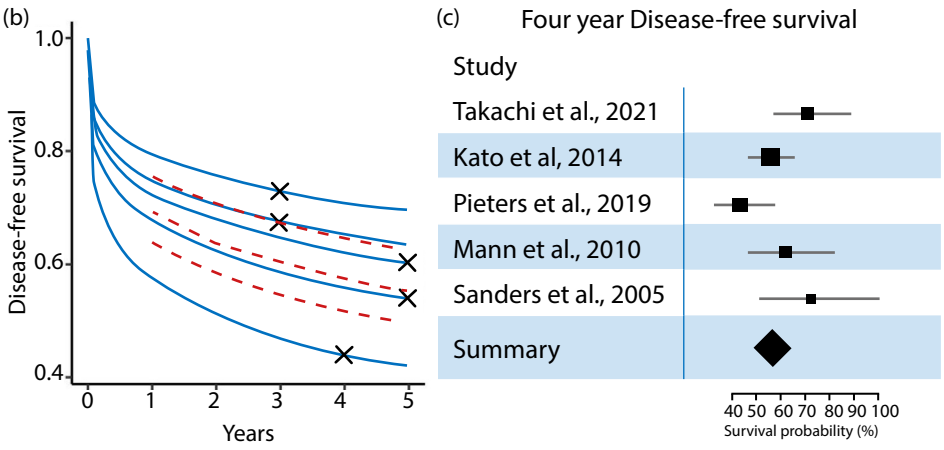
Figure 2. a) OS by year. b) OS curves. Gray lines represent the control curves for individual studies. Red lines represent the summary curve with 95%CIs (dashed red lines). The symbol X represents Q = 13.83 (p = 0.003); H^2 = 0.86; I^2 = 5.13%. c). Forest plot representing 4-year OS.

Disease-free survival

Five studies reported DFS. The pooled 4-year DFS was 57.5% (95%CI 51.8-64.3) (Fig. 3).

(a)

Years	DFS (95% C.I.)
1	69.1% (63.8% ; 75.5%)
2	63.6% (58.3% ; 70.5%)
3	60.2% (54.7% ; 67.1%)
4	57.5% (51.8% ; 64.3%)
5	55.2% (49.6% ; 62.4%)



Source: Elaborated by the authors.

Figure 3. A) DFS by year. B) DFS curves. Gray lines represent the control curves for individual studies. Red lines represent the summary curve with 95%CIs (dashed red lines). The symbol X represents Q = 20.67 (p = 0.001); H^2 = 1.03; I^2 = 9.90%. C) Forest plot representing 4-year DFS.

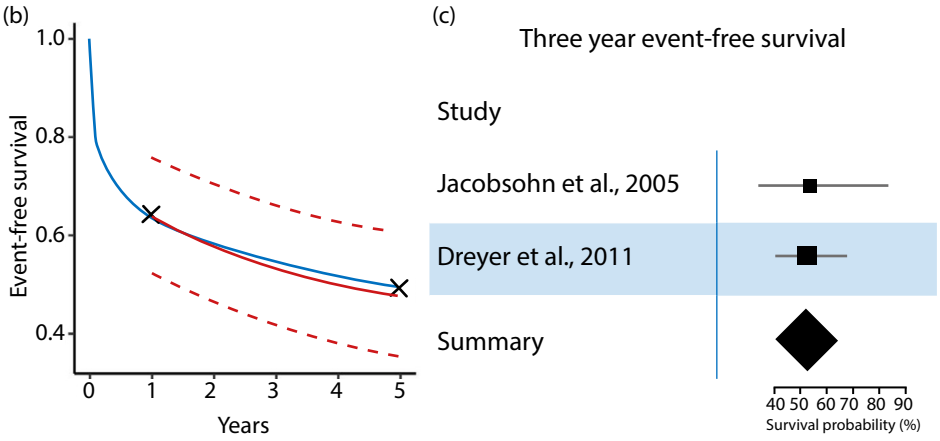
Event-free survival

Two studies reported outcomes as EFS. The pooled 3-year EFS was 53.2% (95%CI 41.5-66.1) (Fig. 4).

represent the control curves for individual studies. Red lines represent the summary curve with 95%CIs (dashed red lines). The symbol X represents Q = 3.22 (p = 0.073); H^2 = 0.40; I^2 = 0.37. C) Forest plot representing 3-year EFS.

(a)

Years	EFS (95% C.I.)
1	63.4% (52.1% ; 75.7%)
2	57.3% (46.0% ; 70.0%)
3	53.2% (41.5% ; 66.1%)
4	50.1% (37.8% ; 62.6%)
5	47.2% (35.1% ; 60.3%)



Source: Elaborated by the authors.

Figure 4. A) EFS by year. B) EFS curves. Gray lines

Methodological quality and risk of bias

The individual study appraisals are detailed in Tables 2 and 3. The primary sources of bias identified were: 1) lack of stratification for additional prognostic factors; 2) pooled analyses of heterogeneous treatment protocols without detailed descriptions of conditioning regimens or specific HSCT indications; and 3) potential selection bias, as patient referral for HSCT was often at the discretion of the principal investigator rather than strictly randomized.

Table 2. Risk of bias summary for non-randomized studies (ROBINS-I).

Study	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias judgement
Dreyer[29]*	Serious	Low	Low	Moderate	Low	Low	Low	Serious
Takachi[32]	Low	Low	Low	Low	Low	Low	Low	Low
Pieters[7]	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Mann[13]*	Serious	Low	Moderate	Low	Low	Low	Low	Serious

Risk of bias domains were evaluated for each study and categorized as low (green), moderate (yellow), or serious (orange). *These studies randomly assigned participants to different chemotherapy protocols, but not to receive HSCT. Therefore, for this review, they were evaluated as non-randomized studies. Source: Elaborated by the authors.

Table 3. Risk of bias for retrospective studies without a comparison group.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Overall appraisal
Kato[27]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Jacobsohn[12]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Sanders[8]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include

The assessment was performed using the JBI Critical Appraisal Checklist for Case Series. Q1 through Q10 correspond to the specific domains evaluated by the tool. The overall appraisal indicates that all listed studies met the methodological quality criteria for inclusion in the synthesis. Source: Elaborated by the authors.

DISCUSSION

In this systematic review and meta-analysis, we evaluated survival outcomes in infants with *KMT2A*-r ALL who underwent HSCT in CR1. Analyzing data from seven studies comprising 371 patients, we found a pooled 4-year OS of 65% (95%CI 58.772.1), a 4-year DFS of 57.5% (95%CI 51.8-64.3), and a 3-year EFS of 53.2% (95%CI 41.5-66.1). Compared to historical cohorts,[17] these results suggest a notable improvement in survival over the past two decades, likely reflecting advances in conditioning regimens, HLA-typing, and supportive care.

The role of HSCT in infant ALL remains one of the most contentious topics in pediatric oncology.[18] The divergence in clinical protocols is striking: while some studies reported no significant survival benefit for HSCT in CR1,[29-31] leading to its exclusion from recent COG protocols, others have demonstrated favorable outcomes.[8,12,14,27,28,32] Our findings align more closely with the latter, supporting the potential benefit of HSCT in this high-risk population. However, risk stratification remains the "Achilles' heel" of these comparisons. For instance, the Interfant-99 Study[13] identified a benefit restricted to a very high-risk (VHR) subgroup, whereas the Japanese MLL-10 trial[32] recently narrowed its HSCT indications due to concerns over long-term toxicities. Our pooled analysis, by including both high- and intermediate-risk patients, provides a broader "real-world" benchmark of what HSCT achieves today.

A primary limitation of this study is the inability to perform a direct comparative meta-analysis between HSCT and chemotherapy alone, as only two identified studies[13,29] provided such data with conflicting results. The Interfant-99 trial showed a stark survival advantage for HSCT in VHR infants (5-year OS 66% vs. 19.3%; $p = 0.001$), while the combined CCG-1953/POG-9407 analysis[29] found no such benefit. These discrepancies may be attributed to small sample sizes and significant protocol deviations, which underscore the difficulty of conducting rigorous trials in such a rare disease.

Furthermore, data scarcity precluded subgroup analyses on critical prognostic factors such as minimal residual disease (MRD) status, *KMT2A* fusion partners, or specific conditioning regimens. The prognostic weight of these variables remains debated; while Kato et al.[27] and Dreyer et al.[29] found limited associations, the Interfant group continues to highlight their significance in risk-tailored therapy. Additionally, our "as-treated" analysis approach, necessitated by the inclusion of observational data, may introduce selection bias by excluding patients who were intended for HSCT but relapsed or died before reaching the procedure.

Despite these constraints, this is the first systematic review and meta-analysis to focus exclusively on the *KMT2A*-r infant population. As we move toward an era of precision medicine, the landscape of infant ALL is shifting. The emergence of menin inhibitors, blinatumomab, and CAR-T cell therapies may soon redefine the indications for HSCT. The ongoing Interfant-21 study (NCT05327894) exemplifies this transition, utilizing blinatumomab as a bridge to HSCT for those remaining MRD-positive.

CONCLUSION

In conclusion, HSCT in CR1 for infants with *KMT2A*-r ALL is associated with a 4-year OS of 65%. While survival remains inferior to older pediatric ALL subsets, these results represent a significant historical improvement. HSCT remains a viable and reasonable strategy for selected high-risk infants, provided the decision-making process carefully weighs the curative potential against the high burden of transplant-related morbidity and long-term sequelae.

CONFLICTS OF INTEREST

Nothing to declare.

DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS

Exclusive use for grammar and orthography.

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DATA AVAILABILITY STATEMENT

Data will be provided upon request.

AUTHOR CONTRIBUTIONS

Conceptualization: Faria BL; **Methodology:** Faria BL, Simão AMS; **Original – draft writing:** Faria BL; **Investigation:** Simão AMS; **Data curation:** Vijendra B, Bertol AB; **Writing – review and editing:** Freitas PHAG, Duarte BA,Gomes AS; **Supervision:** Cristofani LM.

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REFERENCES

1. Pieters R, Mullighan CG, Hunger SP. Advancing diagnostics and therapy to reach universal cure in childhood ALL. J Clin Oncol. 2023;41(36):5579-91. https://doi.org/10.1200/JCO.23.01286
2. Pui C, Kane J, Crist W. Biology and treatment of infant leukemias. Leukemia. 1995;9(5):762-9.
3. Kotecha RS, Pieters R, Stutterheim J. KMT2A-rearranged acute lymphoblastic leukaemia. EJC Paediatr Oncol. 2024;100204. https://doi.org/10.1016/j.ejcped.2024.100204
4. Górecki M, Kozioł I, Kopystecka A, Budzyńska J, Zawitkowska J, Lejman M. Updates in KMT2A gene rearrangement in pediatric acute lymphoblastic leukemia. Biomedicines. 2023;11(3):821. https://doi.org/10.3390/biomedicines11030821
5. Bartram J, Ancliff P, Vora A. How I treat infant acute lymphoblastic leukemia. Blood. 2025;145(1):35-42. https://doi.org/10.1182/blood.2023023154
6. Tomizawa D. Evolution and optimization of therapies for acute lymphoblastic leukemia in infants. Int J Hematol. 2023;117(2):162-72. https://doi.org/10.1007/s12185-022-03502-w
7. Pieters R, De Lorenzo P, Ancliffe P, Aversa LA, Brethon B, Biondi A, et al. Outcome of infants younger than 1 year with acute lymphoblastic leukemia treated with the interfant-06 protocol: results from an international phase III randomized study. J Clin Oncol. 2019;37(25):2246-56. https://doi.org/10.1200/JCO.19.00261
8. Sanders JE, Im HJ, Hoffmeister PA, Gooley TA, Woolfrey AE, Carpenter PA, et al. Allogeneic hematopoietic cell transplantation for infants with acute lymphoblastic leukemia. Blood. 2005;105(9):3749-56. https://doi.org/10.1182/blood-2004-08-3312
9. Pieters R. Infant acute lymphoblastic leukemia: Lessons learned and future directions. Curr Hematol Malig Rep. 2009;4(3):167-74. https://doi.org/10.1007/s11899-009-0023-4
10. Armstrong SA, Staunton JE, Silverman LB, Pieters R, den Boer ML, Minden MD, et al. MLL translocations specify a distinct gene expression profile that distinguishes a unique leukemia. Nat Genet. 2002;30(1):41-7. https://doi.org/10.1038/ng765
11. Tomizawa D, Goussetis E. New insights into hematopoietic cell transplantation in ALL: who should be transplanted, when, and how. EJC Paediatr Oncol. 2024;100200. https://doi.org/10.1016/j.ejcped.2024.100200
12. Jacobsohn DA, Hewlett B, Morgan E, Tse W, Duerst RE, Kletzel M. Favorable outcome for infant acute lymphoblastic leukemia after hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2005;11(12):999-1005. https://doi.org/10.1016/j.bbmt.2005.08.031
13. Mann G, Attarbaschi A, Schrappe M, De Lorenzo P, Peters C, Hann I, et al. Improved outcome with hematopoietic stem cell transplantation in a poor prognostic subgroup of infants with mixed-lineage-leukemia (MLL)-rearranged acute lymphoblastic leukemia: results from the Interfant-99 Study. Blood J Am Soc Hematol. 2010;116(15):2644-50. https://doi.org/10.1182/blood-2010-03-273532

14. Marco F, Bureo E, Ortega JJ, Badell I, Verdaguer A, Martínez A, et al. High survival rate in infant acute leukemia treated with early high-dose chemotherapy and stem-cell support. J Clin Oncol. 2000;18(18):3256-61. https://doi.org/10.1200/JCO.2000.18.18.3256

15. Kotecha R, Gottardo N, Kees U, Cole C. The evolution of clinical trials for infant acute lymphoblastic leukemia. Blood Cancer J. 2014;4(4):e200. https://doi.org/10.1038/bcj.2014.17

16. Guest EM, Stam RW. Updates in the biology and therapy for infant acute lymphoblastic leukemia. Curr Opin Pediatr. 2017;29(1):20-6. https://doi.org/10.1097/MOP.0000000000000437

17. Sison EAR, Brown P. Does hematopoietic stem cell transplantation benefit infants with acute leukemia? Hematol 2013 Am Soc Hematol Educ Program Book. 2013;2013(1):601-4. https://doi.org/10.1182/asheducation-2013.1.601

18. Kotecha RS. Updates in infant acute lymphoblastic leukemia and the potential for targeted therapy. Hematology. 2022;2022(1):611-7. https://doi.org/10.1182/hematology.2022000359

19. Balduzzi A, Buechner J, Ifversen M, Dalle JH, Colita AM, Bierings M. Acute lymphoblastic leukaemia in the youngest: haematopoietic stem cell transplantation and beyond. Front Pediatr. 2022;10:807992. https://doi.org/10.3389/fped.2022.807992

20. Brown P, Inaba H, Annesley C, Beck J, Colace S, Dallas M, et al. Pediatric acute lymphoblastic leukemia, version 2.2020, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2020;18(1):81-112. https://doi.org/10.6004/jnccn.2020.0001

21. Combescure C, Foucher Y, Jackson D. Meta-analysis of single-arm survival studies: a distribution-free approach for estimating summary survival curves with random effects. Stat Med. 2014;33(15):2521-37. https://doi.org/10.1002/sim.6111

22. Munn Z, Barker TH, Moola S, Tufanaru C, Stern C, McArthur A, et al. Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. JBI Evid Synth. 2020;18(10):2127-33. https://doi.org/10.11124/JBISRIR-D-19-00099

23. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355. https://doi.org/10.1136/bmj.i4919

24. Pieters R, Schrappe M, De Lorenzo P, Hann I, De Rossi G, Felice M, et al. A treatment protocol for infants younger than 1 year with acute lymphoblastic leukaemia (Interfant-99): an observational study and a multicentre randomised trial. The Lancet. 2007;370(9583):240-50. https://doi.org/10.1016/S0140-6736(07)61126-X

25. Tomizawa D, Koh K, Sato T, Kinukawa N, Morimoto A, Isoyama K, et al. Outcome of risk-based therapy for infant acute lymphoblastic leukemia with or without an MLL gene rearrangement, with emphasis on late effects: a final report of two consecutive studies, MLL96 and MLL98, of the Japan Infant Leukemia Study Group. Leukemia. 2007;21(11):2258-63. https://doi.org/10.1038/sj.leu.2404903

26. Tomizawa D, Miyamura T, Imamura T, Watanabe T, Moriya Saito A, Ogawa A, et al. A risk-stratified therapy for infants with acute lymphoblastic leukemia: a report from the JPLSG MLL-10 trial. Blood J Am Soc Hematol. 2020;136(16):1813-23. https://doi.org/10.1182/blood.2019004741

27. Kato M, Hasegawa D, Koh K, Kato K, Takita J, Inagaki J, et al. Allogeneic haematopoietic stem cell transplantation for infant acute lymphoblastic leukaemia with KMT 2A (MLL) rearrangements: a retrospective study from the paediatric acute lymphoblastic leukaemia working group of the Japan Society for Haematopoietic Cell Transplantation. Br J Haematol. 2015;168(4):564-70. https://doi.org/10.1111/bjh.13174

28. Kosaka Y, Koh K, Kinukawa N, Wakazono Y, Isoyama K, Oda T, et al. Infant acute lymphoblastic leukemia with MLL gene rearrangements: outcome following intensive chemotherapy and hematopoietic stem cell transplantation. Blood. 2004;104(12):3527-34. https://doi.org/10.1182/blood-2004-04-1390

29. Dreyer ZE, Dinndorf PA, Camitta B, Sather H, La MK, Devidas M, et al. Analysis of the role of hematopoietic stem-cell transplantation in infants with acute lymphoblastic leukemia in first remission and MLL gene rearrangements: a report from the Children's Oncology Group. J Clin Oncol. 2011;29(2):214-22. https://doi.org/10.1200/JCO.2009.26.8938

30. Pui CH, Gaynon PS, Boyett JM, Chessells JM, Baruchel A, Kamps W, et al. Outcome of treatment in childhood acute lymphoblastic leukaemia with rearrangements of the 11q23 chromosomal region. The Lancet. 2002;359(9321):1909-15. https://doi.org/10.1016/S0140-6736(02)08782-2

31. Pui C, Chessells J, Camitta B, Baruchel A, Biondi A, Boyett J, et al. Clinical heterogeneity in childhood acute lymphoblastic leukemia with 11q23 rearrangements. Leukemia. 2003;17(4):700-6. https://doi.org/10.1038/sj.leu.2402883

32. Takachi T, Watanabe T, Miyamura T, Moriya Saito A, Deguchi T, Hori T, et al. Hematopoietic stem cell transplantation for infants with high-risk KMT2A gene-rearranged acute lymphoblastic leukemia. Blood Adv. 2021;5(19):3891-9. https://doi.org/10.1182/bloodadvances.2020004157