SOMATO PUBLICATIONS ISSN: 2688-9587

Annals of Leukemia Research

Review Article

Early Response Assessment by Minimal Residual Disease in Adolescents with T-Cell Acute Lymphoblastic Leukemia (T-ALL)

Zoltan Szabo[1*], Aoife Brennan[2] and Giulia Rizzo[3]

[1]Department of Paediatric Haematology, Semmelweis University, Budapest, Hungary

[2]Department of Molecular Diagnostics, University College Dublin, Dublin, Ireland

[3]Department of Cell Therapy, University of Bologna, Bologna, Italy

***Address for Correspondence:** Zoltan Szabo, Department of Paediatric Haematology, Semmelweis University, Budapest, Hungary

Received: 28 February 2023; **Accepted:** 12 June 2023; **Published:** 27 August 2023

Citation of this article: Szabo, Z., Brennan, A., Rizzo, G. (2023) Early Response Assessment by Minimal Residual Disease in Adolescents with T-Cell Acute Lymphoblastic Leukemia (T-ALL). Ann Leuk Res, 4(1): 04-06. doi: 10.5281/zenodo.22213672

Copyright: © 2023 Zoltan Szabo, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Summary

Minimal residual disease has displaced almost every other prognostic variable in acute lymphoblastic leukaemia, but the timing that works for B-cell disease does not transfer to T-lineage disease. T-cell blasts clear more slowly, and an early measurement that would condemn a B-cell patient turns out to carry no information at all in T-ALL provided the later measurement is clear.

Objectives: To review the published evidence on minimal residual disease as an early response measure in T-cell acute lymphoblastic leukaemia, with attention to adolescents: which timepoints carry prognostic weight, how the kinetics differ from B-cell disease, how the available assays compare, and what the measurement has been used to change.

Material and Methods: Narrative review of cooperative group trials, methodological comparisons and response-adapted randomised studies indexed in PubMed and the major haematology journals. Studies were eligible if they reported the prognostic value of minimal residual disease in a defined acute lymphoblastic leukaemia population, compared assay platforms, or tested treatment modification on the basis of residual disease. No new patient data were generated and no patients were recruited; every estimate quoted is one published by the original investigators.

Results: Among 464 patients with T-ALL stratified within a large international trial, 16 per cent were residual disease negative at both timepoints, 63 per cent intermediate and 21 per cent had 10^{-3} or more at day 78. Their seven-year event-free survival was 91.1, 80.6 and 49.8 per cent respectively ($p < 0.001$). Only 16 per cent of T-ALL patients cleared at the first timepoint against 42 per cent of 3,184 patients with B-cell precursor disease. Critically, the 32 per cent of T-ALL patients who became negative only at the second timepoint did equally well, indicating that early residual disease level is irrelevant provided the later measurement is clear. Residual disease at or above 10^{-3} at day 78 was the single most important predictor of relapse. At day 29, hazard ratios for relapse were 3.55 by flow cytometry and 5.6 by polymerase chain reaction.

Conclusion: In T-ALL the informative timepoint is late rather than early, which inverts the logic applied in B-cell disease. Applying B-cell timing to T-lineage patients would misclassify roughly a third of them as high risk when their outcome is excellent.

Abbreviations: ALL – Acute Lymphoblastic Leukaemia, T-ALL – T-Cell Acute Lymphoblastic Leukaemia, BCP-ALL – B-Cell Precursor ALL, MRD – Minimal Residual Disease, TP1 – Time Point 1, TP2 – Time Point 2, FCM – Flow Cytometry, RQ-PCR – Real-Time Quantitative Polymerase Chain Reaction, Ig/TCR – Immunoglobulin and T-Cell Receptor, ETP – Early T-Cell Precursor, EFS – Event-Free Survival, HSCT – Haematopoietic Stem Cell Transplantation, AYA – Adolescent and Young Adult.

Keywords: *T-Cell Acute Lymphoblastic Leukaemia; Minimal Residual Disease; Adolescents; Risk Stratification; Treatment Response*

Introduction

T-cell acute lymphoblastic leukaemia accounts for roughly 15 per cent of new diagnoses and is biologically distinct from the B-cell precursor disease that dominates the literature [1,2]. Outcomes have converged with refined treatment, but the clinical variables used to stratify B-cell disease do not carry the same prognostic weight in T-lineage patients [1,3].

© 2023 Somato Publications. All rights reserved.

Adolescents occupy a particular position within this. T-lineage disease is proportionally commoner in older children and young adults than in infants [4,5], and the adolescent age band is where paediatric and adult protocols meet, with well-documented differences in outcome depending on which is applied [6,7]. Treatment-related mortality rather than relapse drives much of the adolescent disadvantage [8].

Minimal residual disease measurement was introduced into risk stratification through a large international trial that quantified residual leukaemia by polymerase chain reaction against immunoglobulin and T-cell receptor gene rearrangements at two defined timepoints [9,10]. In B-cell precursor disease the result reordered the entire prognostic hierarchy, displacing age, white cell count and cytogenetics [10].

Whether the same framework applies to T-lineage disease is the question this review addresses. The answer turns out to depend less on whether residual disease matters, which it plainly does, than on when it is measured.

Material and Methods

Search strategy: PubMed and the archives of the major haematology and paediatric oncology journals were searched for studies of minimal residual disease in T-lineage acute lymphoblastic leukaemia. Search terms combined T-cell acute lymphoblastic leukaemia with minimal residual disease, measurable residual disease, flow cytometry, Ig/TCR, risk stratification, AIEOP-BFM, adolescent and young adult. Reference lists of retrieved trials and methodological reviews were screened by hand.

Eligibility: Studies were included if they reported the prognostic value of minimal residual disease in a defined acute lymphoblastic leukaemia population, compared measurement platforms, or tested treatment modification based on residual disease. Studies in B-cell precursor disease are cited where they provide the comparator or established the method, and are identified as such throughout.

Data extraction and handling: Design, cohort size, lineage, assay, timepoint and threshold, and reported survival estimates were extracted as published. Timepoint and threshold are stated alongside every figure, because in this field a residual disease result has no meaning without both. No pooling or re-analysis was performed and no patient-level data were obtained. Figures 1 to 4 and Tables 1 to 3 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

Residual disease stratifies T-ALL powerfully: Within a large international trial, 464 patients with T-ALL were assigned to risk groups using two polymerase chain reaction measurements: standard risk if negative at both day 33 and day 78 with at least two sensitive markers, high risk if 10^{-3} or more at day 78, and intermediate risk otherwise. Sixteen per cent were standard risk, 63 per cent intermediate and 21 per cent high risk (Figure 2) [11].

Seven-year event-free survival was 91.1 per cent (SE 3.5) in the standard risk group, 80.6 per cent (SE 2.3) in the intermediate group and 49.8 per cent (SE 5.1) in the high risk group, with $p < 0.001$ across groups (Figure 1) [11]. A spread of more than forty percentage points between the extremes places residual disease well ahead of any clinical variable available at diagnosis in this disease [1,11].

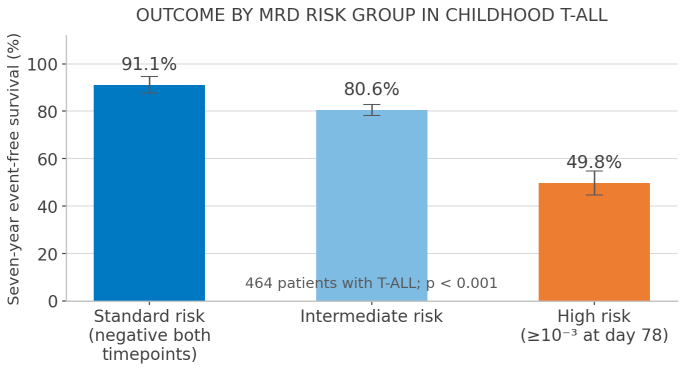

Figure 1: Seven-year event-free survival by minimal residual disease risk group in 464 patients with T-ALL [11]

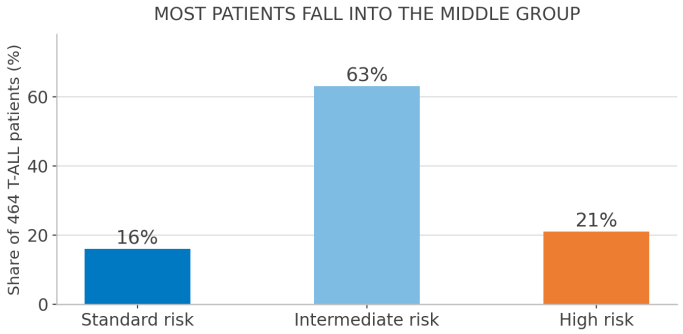

Figure 2: Distribution of the same 464 patients across the three residual disease risk groups [11]

The kinetics differ from B-cell disease: The comparison that matters is with the B-cell precursor population stratified by the same criteria in the same trial. Among 3,184 such patients, 42 per cent were residual disease negative at day 33 and classified standard risk, with five-year event-free survival of 92.3 per cent, while 52 per cent were intermediate risk with event-free survival of 77.6 per cent [10]. In T-ALL only 16 per cent cleared at the equivalent point (Figure 3) [11].

T-lineage blasts therefore regress more slowly, and the observed difference in early clearance reflects that rather than a difference in chemosensitivity [1,11]. Applying the B-cell interpretation to a

© 2023 Somato Publications. All rights reserved.

T-lineage patient would classify a large share of them as poor responders on the strength of a measurement that has not yet become informative.

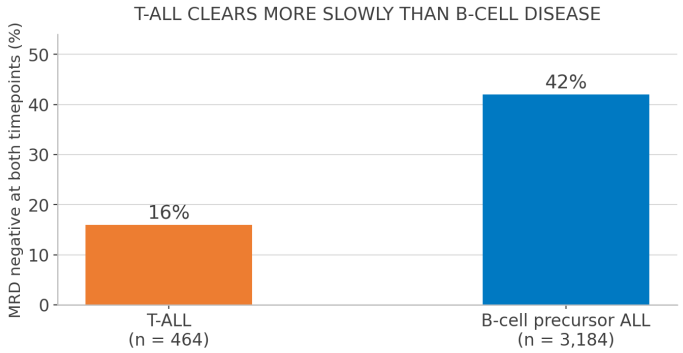

Figure 3: Proportion clearing residual disease at the first timepoint, T-ALL against B-cell precursor disease [10,11]

Study	n	Lineage	Principal reported finding
Flohr et al. 2008 [9]	—	Both	Standardised PCR-based stratification established
Conter et al. 2010 [10]	3,184	B-cell	Residual disease displaces all other prognostic factors
Schrappe et al. 2011 [11]	464	T-cell	Day 78 result decisive; day 33 uninformative if day 78 clear
Vora et al. 2013 [14]	Randomised	Both	Treatment reduction safe in residual disease-defined low risk
Pieters et al. 2016 [16]	—	Both	Reduction and intensification both guided successfully
Cario et al. 2025 [12]	—	T-cell	Prognostic factors under modern risk-adapted therapy

Table 1: Principal studies reviewed, with lineage and the finding as reported by the original investigators

The finding that inverts the logic: The most consequential result concerns the patients who cleared late. Thirty-two per cent of the T-ALL cohort became residual disease negative only at the second timepoint, and their outcome was excellent. The investigators concluded that early residual disease levels were irrelevant provided the day 78 measurement was negative, a condition met by 48 per cent of all patients [11].

This is the opposite of the B-cell finding, where negativity at the first timepoint identifies the best-prognosis group and later clearance carries a penalty [10]. In T-ALL the day 78 result subsumes the day 33 result entirely. Residual disease at or above 10^{-3} at day 78 was described as the single most important predictive factor for relapse in childhood T-ALL [11].

An uncomfortable corollary accompanies it. Using residual disease to assign risk group and treatment did not abolish its prognostic value: patients with high levels at day 78 still did poorly at around 50 per cent event-free survival despite receiving intensified high-risk therapy and transplantation [11]. The measurement identifies the patients who need more, and what is currently available as more does not fully rescue them.

How the assays compare: Two platforms are in routine use. Polymerase chain reaction against immunoglobulin and T-cell receptor rearrangements is the method on which the stratification above was built [9], while flow cytometry offers a faster and more widely available alternative. Direct comparison at day 29 gave a hazard ratio for relapse of 3.55 (95% CI 1.4-9.0, p = 0.008) for flow cytometric residual disease at or above 10^{-3}, against 5.6 (95% CI 2.0-16, p = 0.001) for the polymerase chain reaction measure at the same threshold (Figure 4) [13].

Both identify risk and the confidence intervals overlap substantially, so the practical difference is smaller than the point estimates suggest [13]. Flow cytometric and morphological assessment of remission have also been compared directly, with flow cytometry detecting disease that morphology misses [17]. Single-centre experience applying both day 15 and day 33 flow measurements found the day 33 result independently predictive of event-free and overall survival [18].

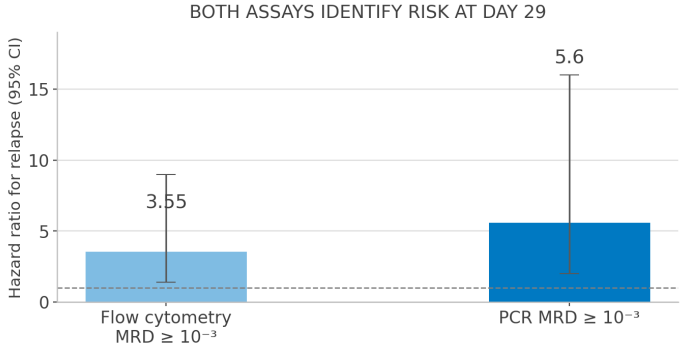

Figure 4: Hazard ratio for relapse at day 29 by assay platform at the same threshold [13]

Feature	T-cell ALL	B-cell precursor ALL
Clear at first timepoint	16%	42% [10,11]
Decisive timepoint	Day 78	Day 33 [10,11]
Early result if late result clear	Irrelevant	Retains prognostic weight [10,11]
EFS in highest risk group	49.8%	Comparable but smaller group [10,11]

Table 2: How residual disease behaves differently in the two lineages

© 2023 Somato Publications. All rights reserved.

What the measurement has been used to change: Residual disease is not only prognostic but actionable, and randomised evidence exists in both directions. Treatment reduction was tested in children and young adults with residual disease-defined low-risk disease and proved safe [14], while augmented post-remission therapy was tested in a residual disease-defined high-risk subgroup drawn from clinically standard and intermediate risk patients [15]. A national protocol subsequently combined both directions, reducing therapy for good responders and intensifying it for poor ones [16].

Earlier work had established that augmenting therapy improves outcome in paediatric high-risk disease [19], and residual disease-guided therapy is now standard across contemporary protocols [20]. The principle has been extended to other populations, including infants, where residual disease carries prognostic weight within the KMT2A-rearranged group [21,22].

What residual disease does not capture: A single quantitative result compresses a good deal of biology. Early T-cell precursor disease, defined by an immunophenotype closer to haematopoietic stem cells than to committed thymocytes, was initially reported as very high risk and has since been shown to do considerably better under contemporary protocols where residual disease guides therapy [1,12]. The phenotype and the response measure therefore carry overlapping rather than independent information.

Nor does the measurement identify why a patient is clearing slowly. Two children with identical day 33 levels may differ in whether the residual population is chemoresistant or simply large at baseline, and only the later timepoint distinguishes them [11]. This is the practical reason the T-lineage schedule works: it substitutes a second observation for a mechanistic explanation that is not available at the bedside.

Sequencing-based measurement offers greater sensitivity than either established platform and can track multiple clonal rearrangements simultaneously, which matters in T-lineage disease where clonal evolution of T-cell receptor rearrangements can cause false negatives with a single-marker assay [9,20]. It was not used in the trials that defined the current thresholds, so whether a more sensitive assay would move the informative timepoint earlier remains open.

Sample quality is the practical limit on all of them. Residual disease is measured on a marrow aspirate, and a haemodiluted sample underestimates the burden regardless of platform. Where the first pull is not used, or where the marrow is hypocellular after induction, a negative result may reflect the sample rather than the patient [9,17].

Assay	Typical sensitivity	Practical considerations
Flow cytometry	10^{-4}	Fast and widely available; requires fresh sample and expertise [13,17]
Ig/TCR polymerase chain reaction	10^{-4} to 10^{-5}	Basis of current stratification; needs patient-specific markers [9,11]
Next-generation sequencing	10^{-6}	Tracks multiple clones; not used in defining trials [20]
Morphology	10^{-2}	Misses disease detected by flow cytometry [17]

Table 3: Platforms available for residual disease measurement and their practical characteristics

The group the measurement cannot yet help: Roughly a fifth of T-lineage patients carry 10^{-3} or more at day 78, and their event-free survival of 49.8 per cent was achieved despite assignment to intensified high-risk therapy including transplantation [11]. Identifying them earlier would not obviously help, because the problem is not detection but the absence of an effective alternative.

This is where novel agents enter. Nelarabine and related purine analogues were developed specifically for T-lineage disease and have been positioned for patients identified as poor responders by residual disease [1,11]. Whether adding them converts the high-risk group's outcome is the question the current generation of trials was designed to answer, and it is the clearest example of a response measure driving drug development rather than merely describing prognosis [12,25].

Discussion

The central finding is a timing effect rather than a magnitude effect. Residual disease predicts outcome in T-ALL at least as powerfully as in B-cell disease, with seven-year event-free survival spanning 91.1 to 49.8 per cent across risk groups [11]. What differs is which measurement carries the information: in B-cell disease the day 33 result is decisive [10], in T-lineage disease it is superseded entirely by the day 78 result [11].

The practical consequence is specific. A T-lineage adolescent with detectable disease at day 33 who clears by day 78 has an excellent prognosis, and that describes 32 per cent of the cohort [11]. Treating such a patient as a poor responder on the strength of the early measurement would intensify therapy in roughly a third of T-ALL patients without benefit, in an age group where treatment-related mortality already contributes disproportionately to poor outcome [8].

Why the late timepoint carries the signal

The mechanistic reading is that T-lineage blasts regress more slowly under the same induction, so a day 33 measurement samples a

© 2023 Somato Publications. All rights reserved.

population still in the process of clearing rather than one that has failed to clear [1,11]. The measurement is not wrong; it is taken before the biology has resolved.

That framing suggests the lineage-specific timepoint matters more than the lineage-specific threshold, and the published stratification supports it, since the same 10^{-3} cutoff was applied to both lineages with different timing [10,11]. It also implies that any new agent accelerating early clearance would need its effect measured at the later timepoint to be visible.

Adolescents specifically

The cohorts underlying these findings are paediatric, extending into adolescence rather than focusing on it [10,11]. That matters because adolescents treated on adult rather than paediatric-inspired protocols do worse [6,7,23], and because their excess mortality is driven by toxicity rather than relapse [8,24].

Residual disease-guided de-escalation is therefore of particular value in this age band, since avoiding unnecessary intensification addresses the dominant cause of death directly [14,16]. The randomised reduction trials included young adults and found the approach safe [14], which is the evidence most directly applicable to adolescents with T-lineage disease.

Study limitations

The limitations belong to the underlying literature. The principal T-ALL analysis is a subgroup of a trial designed around B-cell disease, and 464 patients is a modest number for a three-way stratification with further subsets [11]. Assay comparisons are drawn from cohorts using differing timepoints, so the flow cytometry and polymerase chain reaction hazard ratios quoted are not from an identical design [13,17,18]. Adolescents are included within paediatric cohorts rather than analysed separately, so age-specific estimates are inferred [10,11]. Treatment was assigned on the basis of the measurement being evaluated, which complicates interpretation of the high-risk group's outcome [11]. And newer sequencing-based methods achieve greater sensitivity than either established platform but were not used in the trials that defined the current thresholds [20].

Two gaps deserve naming. No trial has compared residual disease timepoints prospectively within T-lineage disease, so the primacy of day 78 rests on retrospective analysis of a fixed schedule [11]. And no study reviewed here reports whether the high-risk group's persistent 50 per cent event-free survival can be improved by any currently available intensification, which is the question their outcome raises most directly [11].

Conclusion

Minimal residual disease stratifies T-cell acute lymphoblastic leukaemia into groups with seven-year event-free survival of 91.1, 80.6 and 49.8 per cent, a spread wider than any clinical variable available at diagnosis provides. But the timing that works in B-cell disease does not transfer. Only 16 per cent of T-lineage patients clear at the first timepoint against 42 per cent of B-cell patients, and the 32 per cent who clear only at the second timepoint do as well as those who cleared early. The day 78 measurement subsumes the day 33 measurement entirely, which means applying B-cell timing would misclassify roughly a third of T-lineage adolescents as poor responders and intensify their treatment without benefit. In an age group where toxicity rather than relapse drives excess mortality, that distinction is not academic.

Two questions follow. The first is whether a more sensitive sequencing-based assay would move the informative timepoint earlier, which would matter because a decision available at day 33 is worth more than the same decision at day 78 [20]. The second concerns the fifth of patients who remain positive at day 78 and reach only 49.8 per cent event-free survival despite intensified therapy and transplantation [11]. For them the measurement works and the treatment does not, and no amount of refinement in the assay addresses that.

Acknowledgements

The stratification described here exists because many laboratories agreed to measure the same thing in the same way, and the credit for that belongs to them.

Funding

This was written on the authors' own time. No award, contract or industry payment supported any part of it.

Conflict of Interest

Nothing bearing on the impartiality of this review is reported.

Ethics Statement

All material examined here had been published before this review began. No participant was enrolled, no sample taken and no record opened, so there was no protocol for a committee to review.

References

1. Marks, DI., Rowntree, C. (2017) Management of adults with T-cell lymphoblastic leukemia. Blood, 129(9): 1134-1142.
2. Roberts, KG. (2018) Genetics and prognosis of ALL in children vs adults. Hematology Am Soc Hematol Educ Program, 2018: 137-145.
3. Paul, S., Kantarjian, H., Jabbour, EJ. (2016) Adult acute lymphoblastic leukemia. Mayo Clin Proc, 91(11): 1645-1666.

© 2023 Somato Publications. All rights reserved.

4. Curran, E., Stock, W. (2015) How I treat acute lymphoblastic leukemia in older adolescents and young adults. Blood, 125(24): 3702-3710.

5. Stock, W., Luger, SM., Advani, AS., Yin, J., Harvey, RC., Mullighan, CG., et al. (2019) A pediatric regimen for older adolescents and young adults with acute lymphoblastic leukemia: results of CALGB 10403. Blood, 133(14): 1548-1559.

6. Boissel, N., Baruchel, A. (2018) Acute lymphoblastic leukemia in adolescent and young adults: treat as adults or as children? Blood, 132(4): 351-361.

7. Huguet, F., Leguay, T., Raffoux, E., Thomas, X., Beldjord, K., Delabesse, E., et al. (2009) Pediatric-inspired therapy in adults with Philadelphia chromosome-negative acute lymphoblastic leukemia: the GRAALL-2003 study. J Clin Oncol, 27(6): 911-918.

8. Pichler, H., Reismuller, B., Steiner, M., Dworzak, MN., Palfi, M., et al. (2013) The inferior prognosis of adolescents with acute lymphoblastic leukaemia (ALL) is caused by a higher rate of treatment-related mortality and not an increased relapse rate. Br J Haematol, 161(4): 556-565.

9. Flohr, T., Schrauder, A., Cazzaniga, G., Panzer-Grümayer, R., van der Velden, V., et al. (2008) Minimal residual disease-directed risk stratification using real-time quantitative PCR analysis of immunoglobulin and T-cell receptor gene rearrangements in the international multicenter trial AIEOP-BFM ALL 2000 for childhood acute lymphoblastic leukemia. Leukemia, 22(4): 771-782.

10. Conter, V., Bartram, CR., Valsecchi, MG., Schrauder, A., Panzer-Grümayer, R., Möricke, A., et al. (2010) Molecular response to treatment redefines all prognostic factors in children and adolescents with B-cell precursor acute lymphoblastic leukemia: results in 3184 patients of the AIEOP-BFM ALL 2000 study. Blood, 115(16): 3206-3214.

11. Schrappe, M., Valsecchi, MG., Bartram, CR., Schrauder, A., Panzer-Grümayer, R., Möricke, A., et al. (2011) Late MRD response determines relapse risk overall and in subsets of childhood T-cell ALL: results of the AIEOP-BFM-ALL 2000 study. Blood, 118(8): 2077-2084.

12. Cario, G., Valsecchi, MG., Conter, V., et al. (2025) Results in pediatric T-ALL patients treated in trial AIEOP-BFM ALL 2009: prognostic factors in the context of modern risk-adapted therapy. Hemasphere, 9: e70206.

13. Modvig, S., Madsen, HO., Siitonen, SM., Rosthoj, S., Tierens, A., et al. (2019) Minimal residual disease quantification by flow cytometry provides reliable risk stratification in T-cell acute lymphoblastic leukemia. Leukemia, 33(6): 1324-1336.

14. Vora, A., Goulden, N., Wade, R., Mitchell, C., Hancock, J., et al. (2013) Treatment reduction for children and young adults with low-risk acute lymphoblastic leukaemia defined by minimal residual disease (UKALL 2003): a randomised controlled trial. Lancet Oncol, 14(3): 199-209.

15. Vora, A., Goulden, N., Mitchell, C., Hancock, J., Hough, R., Rowntree, C., et al. (2014) Augmented post-remission therapy for a minimal residual disease-defined high-risk subgroup of children and young people with clinical standard-risk and intermediate-risk acute lymphoblastic leukaemia (UKALL 2003): a randomised controlled trial. Lancet Oncol, 15(8): 809-818.

16. Pieters, R., de Groot-Kruseman, H., Van der Velden, V., Fiocco, M., van den Berg, H., et al. (2016) Successful therapy reduction and intensification for childhood acute lymphoblastic leukemia based on minimal residual disease monitoring: study ALL10 from the Dutch Childhood Oncology Group. J Clin Oncol, 34(22): 2591-2601.

17. Gupta, S., Devidas, M., Loh, ML., Raetz, EA., Chen, S., et al. (2018) Flow-cytometric vs. morphologic assessment of remission in childhood acute lymphoblastic leukemia: a report from the Children's Oncology Group. Leukemia, 32(6): 1370-1379.

18. Radu, LE., Colita, A., Pasca, S., Tomuleasa, C., Popa, C., Serban, C., et al. (2020) Day 15 and day 33 minimal residual disease assessment for acute lymphoblastic leukemia patients treated according to the BFM ALL IC 2009 protocol: single-center experience of 133 cases. Front Oncol, 10: 923.

19. Bowman, WP., Larsen, EL., Devidas, M., Linda, SB., Blach, L., Carroll, AJ., et al. (2011) Augmented therapy improves outcome for pediatric high risk acute lymphocytic leukemia: results of Children's Oncology Group trial P9906. Pediatr Blood Cancer, 57(4): 569-577.

20. Campana, D., Pui, CH. (2017) Minimal residual disease-guided therapy in childhood acute lymphoblastic leukemia. Blood, 129(14): 1913-1918.

21. van der Velden, VH., Corral, L., Valsecchi, MG., Jansen, MW., De Lorenzo, P., Cazzaniga, G., et al. (2009) Prognostic significance of minimal residual disease in infants with acute lymphoblastic leukemia treated within the Interfant-99 protocol. Leukemia, 23(6): 1073-1079.

22. Stutterheim, J., van der Sluis, IM., de Lorenzo, P., Alten, J., Ancliffe, P., Attarbaschi, A., et al. (2021) Clinical implications of minimal residual disease detection in infants with KMT2A-rearranged acute lymphoblastic leukemia treated on the Interfant-06 protocol. J Clin Oncol, 39(6): 652-662.

23. Goldstone, AH., Richards, SM., Lazarus, HM., Tallman, MS., Buck, G., Fielding, AK., et al. (2008) In adults with standard-risk acute lymphoblastic leukemia, the greatest benefit is achieved from a matched sibling allogeneic transplantation in first complete remission: final results of the international ALL trial (MRC UKALL XII/ECOG E2993). Blood, 111(4): 1827-1833.

24. Patel, B., Kirkwood, AA., Dey, A., Marks, DI., McMillan, AK., Menne, TF., et al. (2017) Pegylated-asparaginase during induction therapy for adult acute lymphoblastic leukaemia: toxicity data from the UKALL14 trial. Leukemia, 31(1): 58-64.

25. Larsen, EC., Devidas, M., Chen, S., Salzer, WL., Raetz, EA., Loh, ML., et al. (2016) Dexamethasone and high-dose methotrexate improve outcome for children and young adults with high-risk B-acute lymphoblastic leukemia: a report from Children's Oncology Group study AALL0232. J Clin Oncol, 34(20): 2380-2388.

© 2023 Somato Publications. All rights reserved.