

Role of Ikaros Zinc Finger Protein 1 (IKZF1) Gene Deletion in Patients with Acute Lymphoblastic Leukemia

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ABSTRACT

Objective: To determine the frequency of Ikaros zinc finger protein 1 (IKZF1) gene deletions in patients with acute lymphoblastic leukemia (ALL), and to assess their association with early hematological remission following induction therapy.

Study Design: Cross-sectional study.

Place and Duration of Study: Armed Forces Bone Marrow Transplant Centre (AFBMTTC) and Department of Haematology, Army Medical College Rawalpindi, Pakistan, from Dec 2019 to Dec 2020.

Methodology: Bone marrow and peripheral blood samples from 44 newly diagnosed ALL patients were analyzed for IKZF1 deletions (exons $\Delta 2-7$, $\Delta 2-8$, $\Delta 4-7$, $\Delta 4-8$) using allele-specific PCR followed by Sanger sequencing. Day-29 hematological remission was assessed morphologically and correlated with IKZF1 status. Statistical analysis was performed using Chi-square and Mann Whitney U tests, with a p -value <0.05 being considered significant.

Results: IKZF1 deletions were detected in 8(18.2%) patients, predominantly among the B-cell subtype (18.4%). Deletion variants included $\Delta 2-7$ (11.1%), $\Delta 2-8$ (22.2%), $\Delta 4-7$ (38.9%), and $\Delta 4-8$ (27.8%). Day-29 remission was achieved in 87.5% of IKZF1-deleted and 94.4% of wild-type patients ($p=0.46$). The mean day-1 blast count was significantly lower in the deleted group ($p=0.042$).

Conclusion: IKZF1 deletions were present in nearly one-fifth of patients with ALL, with $\Delta 4-7$ being the most frequent variant. Although not significantly associated with early remission, their identification provides insight into the molecular profile of Pakistani ALL patients.

Keywords: Acute Lymphoblastic Leukemia, IKZF1 Protein, Gene Deletion, Prognosis, Polymerase Chain Reaction.

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INTRODUCTION

Acute Lymphoblastic Leukemia (ALL) is a hematologic malignancy that results from proliferation of lymphoid precursor cells (lymphoblasts) in the bone marrow.¹ It represents 75-80% of childhood leukemia cases, but because of better treatment protocols, survival rates are 80%.² National Cancer Institute estimated 6550 new cases of ALL in 2024 with, 1330 deaths. In adults, where ALL comprises about 20% of leukemia cases, it presents heterogeneously due to differences in biology, immunology, and genetics compared to children.³ This makes predicting survival rates in adults challenging.⁴

Numerous clinical, laboratory, and genetic risk factors contribute to the pathogenesis of ALL, and their identification is essential for predicting treatment

outcomes. At the end of induction treatment minimal residual disease (MRD) is assessed by using immunoglobulin and T-cell receptor gene analysis. The risk of recurrence is closely linked to the level of MRD.⁵ It is challenging to predict disease with higher recurrence and mortality rates before treatment is started. This necessitates need for reliable prognostic markers that can aid the clinicians and pathologists to plan appropriate treatment strategies.⁶

Genomic analysis has identified the Ikaros zinc finger protein 1 gene (IKZF1) deletions are significant across all categories of ALL.⁷ These genetic alterations can be present at diagnosis or emerge during significant disease events. When combined with MRD status, IKZF1 deletions can predict relapse in many ALL patients.⁸

This study aimed to determine the frequency of IKZF1 gene deletions at diagnosis in our population and correlate it with hematological remission on day 29.

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METHODOLOGY

This cross-sectional study was conducted from Dec 2019 to Dec 2020, at the Armed Forces Bone Marrow Transplant Centre and the Department of Hematology, Army Medical College Rawalpindi, Pakistan, after approval was obtained from the Institutional Ethics Review Committee (ERC/ID/81).

Inclusion Criteria: Patients of all ages and either gender, identified based on bone marrow morphology and immunophenotyping were included.

Exclusion Criteria: Patients already undergoing treatment, with refractory disease at the time of the hospital visit, and those lost to follow-up were excluded.

WHO calculator was used to calculate the sample size keeping an anticipated population of 2.6% for ALL, which came to 44.9. Informed consent was acquired from all participants, and non-probability consecutive sampling was used to collect data.

Peripheral blood and bone marrow samples from newly diagnosed patients reporting to oncology units were collected under sterile conditions. All patients were assigned codes to maintain confidentiality. Demographic, clinical, and laboratory data were recorded. Diagnosis of ALL was based on lymphoblast count/ morphology (>20%) on aspirate biopsy and immunophenotyping by flow cytometry (B- cell type was defined with CD10, CD19, CD79a expression and T-cell with CD3, CD5 and CD7). Cytogenetic analysis was part of routine workup and included the Giemsa trypsin banding method. The molecular analysis involved BCR-ABL1 transcripts, E2A-PBX1, TEL-AML1, and MLL rearrangements. Peripheral blood counts and bone marrow morphology assessments were conducted on days 8, 15, and 29 respectively. Other baseline investigations were done to assess the central nervous system (CNS), myocardial, and testicular involvement.

Patients were assigned risk groups for the selection of treatment protocols and treated uniformly with United Kingdom Acute Lymphoblastic Leukemia (UKALL) -14 for adults and UKALL-11 protocols for pediatric age groups, once diagnosed. Induction therapy with standard doses of vincristine, daunorubicin, dexamethasone, and L-asparaginase was given to patients according to protocols they fit in. Those with BCR-ABL1 transcript received Imatinib therapy. Intrathecal methotrexate for CNS prophylaxis was part of the regimen.

Complete remission was defined as leukemic blast count less than 5% of nucleated blood cells with the revival of cell lines (neutrophils $0.75 \times 10^9 /l$ and platelets to $75 \times 10^9/l$). No remission at end of induction therapy warrants refractory disease and relapse was marked as the re-emergence of lymphoblasts in primary sites.

For IKZF1 gene deletions detection, 03 ml of ethylene diamine tetra acetic acid (EDTA) mixed peripheral/bone marrow blood sample were used. DNA was extracted using Gentra Puregene kit as per provider's protocol. Conventional PCR was done for detection of deletions in IKZF1 exons (2-7, 2-8, 4-7 and 4-8) with Applied Biosystems using allele-specific primers¹⁸ followed by 2% gel electrophoresis. Sequence and annealing temperatures of primers used in PCR are given in Table-I. PCR Samples that showed amplified bands were subjected to Sanger sequencing to reconfirm deletion patterns. Thermo-scientific GeneJET PCR purification Kit (K0701) was used for the initial purification cycle, followed by cycle sequencing on BigDye™ Terminator v3.1 Cycle Sequencing Kit using standard protocols. DNA was sequenced using Genetic Analyzer ABI 3500 GA.

Table-I: Sequencing and Annealing Temperatures of Primers used in Polymerase Chain Reaction

Exon	Base Pair Sequence	Annealing Temperatures
Δ2-7	F2A- 5'- ACTACAGAGACTTCAGCTCTATTCCATTTC -3' F2B- 5'- TGATTGGATGTGTGTGTTTCATGCGTGG- 3' R7- 5'- AGGGACTCTCTAGACAAAATGGCAGGA-3	61°C
Δ2-8	F2A- 5'- ACTACAGAGACTTCAGCTCTATTCCATTTC -3' F2B- 5'- TGATTGGATGTGTGTGTTTCATGCGTGG- 3' R8- 5'-CCTCCTGCTATTGCACGTCTCGGT-3'	58°C
Δ4-7	F4- 5'- CTTAGAAGTCTGGAGTCTGTGAAGGTC-3' R7- 5'- AGGGACTCTCTAGACAAAATGGCAGGA-3'	59°C
Δ4-8	F4-5'- CTTAGAAGTCTGGAGTCTGTGAAGGTC-3' R8- 5'-CCTCCTGCTATTGCACGTCTCGGT-3'	59.5°C
B-actin (540bp)	F- 5'GTGGGGCGCCCCAGGCACCA-3' R-5'GTCCTTAATGTCACGCACGATTTC-3'	
Thermocycling Conditions	5 min at 95°C, 1 min at 95° C, 1 min at 61°C, 1.5 min at 72° C, 3 min at 72° C, 4 °C - infinite hold. 35 cycles	

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 24. Variables were assessed for normality using the Shapiro-Wilk test. Quantitative variables included age, hemoglobin, total leukocyte count, platelet count, and day-1 blast percentage/count. Hemoglobin showed a normal distribution and is summarized as Mean±SD. Age, total leukocyte count, platelet count, and day-1 blast percentage/count were non-normally distributed and are presented as median with interquartile range. Comparisons between groups (wild-type vs deleted) were performed using Mann-Whitney U test for non-normally distributed variables. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. All tests were two-tailed, and a *p*-value <0.05 was considered statistically significant.

RESULTS

A total of 44 patients with Acute Lymphoblastic Leukemia (ALL) were included in this cross-sectional study. The median age at diagnosis was 5.3 years (range: 1.6–65 years), with a male predominance across all age groups; 16 patients (36.4%) were female, resulting in a male-to-female ratio of 1.75:1. The median total leukocyte count (TLC) at presentation was $14.4 \times 10^9/L$ (IQR: 41.25), reflecting marked variability consistent with the wide clinical range observed (1.2 – $996 \times 10^9/L$). Immunophenotyping revealed that 38 patients (86.4%) had B-cell ALL (B-ALL), while 6 patients (13.6%) had T-cell phenotype (T-ALL/T-LBL). Cytogenetic analysis identified the Philadelphia chromosome translocation in two patients. Baseline clinical and laboratory parameters of the study participants are summarized in Table-II.

IKZF1 deletions were detected in 8(18.2%) of the 44 patients with Acute Lymphoblastic Leukemia. Among paediatric patients, deletions were observed in 7 of 39 cases (17.9%), while 1 of 5 adult patients (20.0%) demonstrated IKZF1 deletion. Wild-type IKZF1 status was identified in 36 patients (81.8%). The distribution of IKZF1 deletions across immunophenotypic subtypes is presented in Table-III. Deletions were identified in 7 of 38 B-ALL cases (18.4%) and 1 of 6 T-ALL cases (16.7%). No statistically significant association was observed between IKZF1 deletion status and age group (*p*=0.46) or immunophenotype (*p*=0.66).

IKZF1 deletions were identified in 8(18.2%) of the 44 patients. Among these deletion-positive cases, a total of 18 distinct IKZF1 deletion patterns were

detected, indicating the presence of multiple deletion events within individual patients. The distribution of deletion patterns included $\Delta 4$ –7 in 7 events (38.9%), $\Delta 2$ –8 in 4 events (22.2%), $\Delta 2$ –7 in 2 events (11.1%), and $\Delta 4$ –8 in 5 events (27.8%). The distribution of IKZF1 deletion patterns across age groups and immunophenotypic subtypes is summarized in Table-IV. All deletion patterns detected by PCR were subsequently confirmed by Sanger sequencing, corroborating the initial gel electrophoresis findings.

Table-II: Characteristics of Patients with Acute Lymphoblastic Leukemia (n=44)

Variable	Distribution (n=44) n (%)
Gender	
Male	28(63.6)
Female	16(36.4)
Age (years), Median (IQR)	5.3(8.8)
Total Leucocyte Count ($\times 10^9/L$), Median (IQR)	14.4(41.2)
Haemoglobin (g/dl), Mean $\pm$ SD	8.96 $\pm$ 2.5
Platelet count ($10^9/ul$), Median (IQR)	55(98.8)
Cytogenetics (n=31)	
Normal	26(84)
Abnormal	5(16.1)
Genetics (n=7)	
BCR-ABL 1	2(28.6)
TEL	3(42.9)
E2A	1(14.3)
MLL	1(14.3)
Risk group	
High	26(59.1)
Low	18(40.9)
IKZF1	
Deletion	8(18.2)
Wild -type	36(81.8)
Remission Status achieved (with blast count)	
Day8	1(2.3)
Day 15	9(20.5)
Day 29	41(93.2)
Outcome (30 days)	
Under Treatment	41(93.2)
Refractory	2(4.5)
Relapsed	0
Expired	1(2.3)

*IKZF1: Ikaros Zinc Finger Protein 1, BCR-ABL: Breakpoint Cluster Region – Abelson 1, TEL: Translocation ETS Leukemia, E2A: E2A transcription factor, MLL: Mixed Lineage Leukemia

Table-III: Association of Ikaros Zinc Finger Protein 1 (IKZF1) Deletion Status with Age Group and Immunophenotyping in patients with Acute Lymphoblastic Leukemia (n= 44)

Variable	Category	Total (n)	IKZF1 Deletion Present n (%)	IKZF1 Wild-type n (%)	p-value
Age Group	Paediatric	39	7(17.9)	32(82.0)	0.46
	Adult	5	1(20.0)	4(80.0)	
Immunophenotype	B-ALL	38	7(18.4)	31(81.6)	0.66
	T-ALL	6	1(16.7)	5(83.3)	
Total		44	8(18.2)	36(81.8)	

*IKZF1: Ikaros Zinc Finger Protein 1, B-ALL: B-cell Acute Lymphoblastic Leukemia, T-ALL: T-cell Acute Lymphoblastic Leukemia

Comparison between the IKZF1 deleted and wild-type groups revealed no statistically significant differences in baseline demographic or clinical variables, except for day-1 blast count, which differed significantly between groups ($p=0.042$; Table-V). Day-1 blast count was significantly different between the IKZF1 deleted and wild-type groups (median [IQR]: 57 [65] vs. 83.5 [27], $p=0.042$). Hematological remission on day 29 was achieved in 7 of 8 patients (87.5%) in the IKZF1 deleted group compared to 34 of 36 patients (94.4%) in the wild-type group, with no statistically significant difference ($p=0.46$). At 30 days, a higher proportion of patients in the wild-type group (94.4%) remained under treatment compared to the deleted group (87.5%). One patient in the IKZF1 deleted group expired during follow-up, while no deaths were observed in the wild-type group.

Table-V: Comparison of Clinical and Laboratory Characteristics between IKZF1 Wild-Type and Deleted Groups (n = 44)

Features	Wild-type (n=36) n (%)	IKZF1 Deleted (n=8) n (%)	p-value
Gender			
Male	21(58.3%)	7(87.5%)	0.120
Female	15(41.7%)	1(12.5%)	
Total Leucocyte Count			
×109/l			0.40
≥50	9(25%)	1(12.5%)	
<50	27(75%)	7(87.5%)	
Immunophenotyping			
B-ALL	31 (86.1 %)	7(87.5 %)	0.700
T-ALL	5 (13.9 %)	1(12.5 %)	
Median Blast count Day 1	83.5 (27)	57(65)	0.042
Risk group			
High	20(55.6 %)	6(62.5 %)	0.200
Low	16(44.4 %)	2(37.5 %)	
Response rate			
Slow	9(25%)	2(25%)	0.687
Rapid	27(75%)	6(75%)	
Remission Day 29			
Yes	34 (94.4%)	7(87.5%)	0.460
No	2(5.6%)	1(12.5%)	
Outcome (30days)			
Under Treatment	34 (94.4%)	7(87.5%)	0.080
Refractory	2 (5.6%)	-	
Relapsed	-	-	
Expired	-	1(12.5%)	

* IKZF1: Ikaros Zinc Finger Protein 1, BLL: B-cell Acute Lymphoblastic Leukemia, T-ALL: T-cell Acute Lymphoblastic Leukemia

DISCUSSION

Genetic alterations are the hallmark of pathogenesis in ALL. One study highlighted the role of the IKZF1 gene in lymphoid development.¹⁰ The deletion of exons in the gene is commonly responsible for initiating relapses and reducing the survival index of all ages.¹¹ Given its role in risk stratification among ALL patients, this study aimed to determine the prevalence of IKZF1 gene deletions in our ALL population and assess their impact on remission status.

In this study, we analyzed 44 bone marrow samples of newly diagnosed B and T-ALL patients and detected deletions in 18.2%. Male predominance was noted in all ages and also documented by earlier studies.^{8,12} Higher incidence of disease and deletion status in age groups less than five years was due to more participants from this age category. It was unlike the findings of a previous study, which reported them more in ages 10-18years.¹² Patients with deletions exhibited higher median leucocyte counts and was also seen in previous literature.^{12,13}

The prevalence of deletions was 18.42% in B-ALL cases comprising of all ages and risk categories. The incidence of deletion in our pediatric (18.2%) population was close to data from Mexico.¹⁴ Studies conducted in Japan, Taiwan, and Germany observed a lower number of cases with IKZF1 deletions (9.4%, 10.7%, and 12% respectively) unlike data generated from Northern India, which showed 24 % of the pediatric population with different deletion patterns.^{8,11,13,15}

Our cohort had a small number of elderly participants. Among them, we identified IKZF1 deletion in less than a quarter of cases, which contrasts with other studies (27- 47%).⁸

The published prevalence of IKZF1 deletions in BCR-ABL1 positive B-ALL is much higher and ranges from 63-83.7% irrespective of age category category.^{8,16} Few elderly participants, a small number of Philadelphia chromosome-positive B-ALL cases (n=2), and wild-type pattern in our observation suggests no adequate comparison of this subtype in. Whether these deletions (if found later) will affect the response to TKI based therapy in our population or not can only be understood if larger cohorts are included in future studies.

T-ALL patients in our cohort showed one patient with deletion pattern. This finding has attracted attention from quite a few researchers in the past and linked with poor prognosis in all age groups.^{8,16}

Deletions in the IKZF1 gene can be divided into functional categories depending on the number of exons deleted. Based on our analysis, we identified an overall eight patients with different deletions patterns, of which dominant-negative ($\Delta 4-7$) were the highest found (38.9%). Multiple studies that comprised of similar cohorts reported the predominance of this variant.^{17,18} We observed an almost equal share of deletion variants in our younger population. Investigation of this can happen in larger cohorts,

where a true prevalence of these variants, can be established in our ALL population.

Validated researches show the clinical utility of assessing remission status at day 15 and 29, in patients with ALL and delayed response, subjects them to more intense chemotherapy protocols.¹⁹ Therefore, we assessed the early response to treatment in our group. In our IKZF1 deleted group, all achieved complete remission assessed on Day 29 on bone marrow morphology. More wild-type variants (94.4%) successfully moved on to the consolidation phase, as compared to the deleted group (87.5%). MRD status detected higher levels of residual disease (>1%) at day 29 in patients with IKZF1 deletion through immunophenotyping.²⁰ This may explain our findings of complete remission in our IKZF1 deleted patients who underwent morphological assessment only. No deaths were observed in the wild-type group, unlike deleted groups where one death occurred within two weeks of the start of therapy. The rest (of the members) in the IKZF1 deleted group were still under treatment till the end of the study period. No relapse was documented.

LIMITATIONS OF STUDY

Our limitations include a short duration, limited financial resources, and a small sample size. Our study does not provide insight into the exact impact of IKZF1 deletions on long-term response and survival.

CONCLUSION

We conclude that IKZF1 deletion is prevalent in our ALL population and deleted group exhibited insignificant lower remission rates than the wild-type group. The prognostic significance of the IKZF1 gene cannot be conclusively established from this analysis alone.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

NA & SAK: Data acquisition, data analysis, critical review, approval of the final version to be published.

FA & NS & ZA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

TAK & TG & QN: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Bain BJ, Hoffbrand AV, Steensma DP. Hoffbrand's Essential Haematology, 8th ed. Oxford: Wiley Blackwell; 2020.
2. Jaime-Pérez JC, García-Arellano G, Herrera-Garza JL, Marfil-Rivera LJ, Gómez-Almaguer D. Revisiting the complete blood count and clinical findings at diagnosis of childhood acute lymphoblastic leukemia: 10-year experience at a single center. *Hematol Transfus Cell Ther* 2019; 41(1): 57-61. <https://doi.org/10.1016/j.htct.2018.05.010>
3. Ahmed F, Mundada MC, Khera R, Nambaru L, Mallavarapu K, Boyella PK, et al. Retrospective Study of B Lymphoblastic Leukemia to Assess the Prevalence of TEL/AML1 in South India: A Study of 214 Cases and Review of Literature. *Indian J Med Paediatr Oncol* 2025; 46(03): 259-268. <http://doi.org/10.1055/s-0042-1742611>
4. Abdelmabood S, Fouda AE, Boujettif F, Mansour A. Treatment outcomes of children with acute lymphoblastic leukemia in a middle-income developing country: high mortalities, early relapses, and poor survival. *J Pediatr* 2020; 96(1): 108-116. <https://doi.org/10.1016/j.jpdp.2018.11.005>
5. Maloney KW, Devidas M, Wang C, Mattano LA, Friedmann AM, Buckley P, et al. Outcome in Children With Standard-Risk B-Cell Acute Lymphoblastic Leukemia: Results of Children's Oncology Group Trial AALL0331. *J Clin Oncol* 2020; 38(6): 602-612. <https://doi.org/10.1200/JCO.19.01086>
6. Zhang D, Cheng Y, Fan J, Yao J, Zhao Z, Jiang Y, et al. A Nomogram for the Prediction of Progression and Overall Survival in Childhood Acute Lymphoblastic Leukemia. *Front Oncol* 2020; 10: 1550. <https://doi.org/10.3389/fonc.2020.01550>
7. Inaba H, Mullighan CG. Pediatric acute lymphoblastic leukemia. *Haematologica* 2020; 105(11): 2524-2539. <https://doi.org/10.3324/haematol.2020.247031>
8. Vairy S, Tran TH. IKZF1 alterations in acute lymphoblastic leukemia: the good, the bad and the ugly. *Blood Rev* 2020; 44: 100677. <https://doi.org/10.1016/j.blre.2020.100677>
9. Pui C-H. Acute Lymphoblastic Leukemia. In: Schwab M, editor. *Encyclopedia of Cancer*. Springer 2011. p. 23-26. https://doi.org/10.1007/978-3-642-16483-5_57
10. Powell M, Read K, Sreekumar B, Oestreich K. Ikaros Zinc Finger Transcription Factors: Regulators of Cytokine Signaling Pathways and CD4+ T Helper Cell Differentiation. *Front Immunol* 2019; 10:1299. <https://doi.org/10.3389/fimmu.2019.01299>
11. Stanulla M, Cavé H, Moorman AV. IKZF1 deletions in pediatric acute lymphoblastic leukemia: still a poor prognostic marker? *Blood* 2020; 135(4): 252-260. <https://doi.org/10.1182/blood.2019000813>
12. Sasaki Y, Kantarjian HM, Short NJ, Wang F, Furudate K, Uryu H, et al. Genetic correlates in patients with Philadelphia chromosome-positive acute lymphoblastic leukemia treated with Hyper-CVAD plus dasatinib or ponatinib. *Leukemia* 2022; 36(5): 1253-1260. <https://doi.org/10.1038/s41375-021-01496-8>
13. Asai D, Imamura T, Suenobu Si, Saito A, Hasegawa D, Deguchi T, et al. IKZF 1 deletion is associated with a poor outcome in pediatric B-cell precursor acute lymphoblastic leukemia in Japan. *Cancer Med* 2013; 2(3): 412-419. <https://doi.org/10.1002/cam4.87>
14. Ayón-Pérez F, Pimentel H, Durán-Avelar M, Vibanco N, Pérez-Peraza V, Pérez-González Ó, et al. IKZF1 Gene Deletion in Pediatric Patients Diagnosed with Acute Lymphoblastic Leukemia in Mexico. *Cytogenet Genome Res* 2019; 158. <https://doi.org/10.1159/000499641>

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15. Gupta SK, Bakhshi S, Kamal VK, Gupta R, Sharma P, Pushpam D, et al. Proposal and clinical application of molecular genetic risk scoring system, "MRplus", for BCR-ABL1 negative pediatric B-cell acute lymphoblastic leukemia-report from a single centre. *Leuk Res* 2021; 111: 106683. <https://doi.org/10.1016/j.leukres.2021.106683>
 16. Srinivasan S, Ramanathan S, Kumar S, Peyam S, Radhakrishnan V. Prevalence and prognostic significance of IKZF1 deletion in paediatric acute lymphoblastic leukemia: A systematic review and meta-analysis. *Ann Hematol* 2023; 102(8): 2165-2179. <https://doi.org/10.1007/s00277-023-05250-1>
 17. Simonin M, Lhermitte L, Dourthe ME, Lengliné E, Graux C, Gardel N, et al. IKZF1 alterations predict poor prognosis in adult and pediatric T-ALL. *Blood J Am Soc Hematol* 2021; 137(12): 1690-1694. <https://doi.org/10.1182/blood.2020007959>
 18. Kobitzsch B, Gökbuget N, Schwartz S, Reinhardt R, Brüggemann M, Viardot A, et al. Loss-of-function but not dominant-negative intragenic IKZF1 deletions are associated with an adverse prognosis in adult BCR-ABL-negative acute lymphoblastic leukemia. *Haematologica* 2017; 102(10): 1739. <https://doi.org/10.3324/haematol.2016.161273>
 19. Campana D. Minimal residual disease in acute lymphoblastic leukemia. *Hematology* 2010; 2010(1): 7-12. <https://doi.org/10.1182/asheducation-2010.1.7>
 20. Mullighan CG, Su X, Zhang J, Radtke I, Phillips LA, Miller CB, et al. Deletion of IKZF1 and prognosis in acute lymphoblastic leukemia. *New Engl J Med* 2009; 360(5): 470-480. <https://doi.org/10.1056/nejmoa0808253>
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