Supplemental Materials

Increased Incidence of IKZF1 Deletions and IGH-CRLF2 Translocations in B-ALL of Hispanic/Latino children – a Novel Health Disparity

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**Supplemental Materials**

**Supplemental Materials, Subjects and Methods:**

**Subjects.**
Deidentified clinical and molecular data from 239 pediatric B-ALL patients treated at the Children’s Hospital Los Angeles (CHLA) between 3/2016 and 7/2019 were analyzed in compliance with Institutional Review Board regulations. Of the 239 pediatric patients diagnosed with B-ALL at CHLA, 164 self-reported as H/L and 75 non-H/L. One additional patient with unknown ethnicity was excluded from this study. Three patients with B-lymphoblastic lymphoma were included (molecular studies were performed on tissue). Genetic ancestry was not assessed.

**Methods.** All testing was conducted as a part of the clinical care of children with newly diagnosed (N=201) or relapsed (N=38) leukemias. Testing for 98 of the cases included karyotype analysis, fluorescence in situ hybridization (FISH) testing for BCR/ABL1, ETV6/RUNX1, KMT2A rearrangements and trisomy 4 and 10, and Chromosomal microarray analysis (CMA); in 141 cases testing also included the OncoKids® NGS panel [1]. The presence of the IKZF1 deletion was detected by CMA analysis. CRLF2 expression was initially detected by flow-cytometry; in positive cases, CRLF2 rearrangements were confirmed and characterized by FISH, using CRLF2 and IGH break-apart probes.

**Statistical analysis:** Wilcoxon rank-sum test and the Fisher exact test were used to determine association between categorical variables.

**Reference**

1. Hiemenz MC, Ostrow DG, Busse TM, Buckley J, Maglinte DT, Bootwalla M, Done J, Ji J, Raca G, Ryutov A, Xu X, Zhen CJ, Conroy JM, Hazard FK, Deignan JL, Rogers BB, Treece AL, Parham DM, Gai X, Judkins AR, Triche TJ, Biegel JA. OncoKids: A Comprehensive Next-Generation Sequencing Panel for Pediatric Malignancies. J Mol Diagn. 2018;20(6):765-76. Epub 2018/08/24. doi: 10.1016/j.jmoldx.2018.06.009. PubMed PMID: 30138724.
## Supplemental Tables

| Characteristic           | Overall † | H/L † | Non-H/L † | p-value ‡ |
|--------------------------|-----------|-------|-----------|-----------|
|                          | N = 156   | N = 105 | N = 51    |           |
| **Age**                  | 3.00 (2.00, 6.00) | 4.00 (2.00, 6.00) | 3.00 (2.00, 5.00) | 0.4       |
| **Gender**               |           |       |           | 0.2       |
| Female                   | 72 (46%)  | 52 (50%) | 20 (39%)  |           |
| Male                     | 84 (54%)  | 53 (50%) | 31 (61%)  |           |
| **IKZF1 deletion**       | 19 (12%)  | 13 (12%) | 6 (12%)   | >0.9      |
| **CRLF2 translocation**  | 15 (9.6%) | 9 (8.6%) | 6 (12%)   | 0.6       |
| **IGH-CRLF2**            | 3 (1.9%)  | 1 (1.0%) | 2 (3.9%)  | 0.2       |
| **P2RY8-CRLF2**          | 12 (7.7%) | 8 (7.6%) | 4 (7.8%)  | >0.9      |
| **IKZF1 & CRLF2**        | 1 (0.6%)  | 1 (1.0%) | 0 (0%)    | >0.9      |
| **IKZF1 & IGH-CRLF2**    | 0 (0%)    | 0 (0%)  | 0 (0%)    | N/A       |
| **IKZF1 & P2RY8-CRLF2**  | 1 (0.6%)  | 1 (1.0%) | 0 (0%)    | >0.9      |
| **IKZF1 & no IGH-CRLF2** | 19 (12%)  | 13 (12%) | 6 (12%)   | >0.9      |
| **IGH-CRLF2 & no IKZF1** | 3 (1.9%)  | 1 (1.0%) | 2 (3.9%)  | 0.2       |
| **P2RY8-CRLF2 & no IKZF1** | 11 (7.1%) | 7 (6.7%) | 4 (7.8%)  | 0.8       |
| **Ph+ leukemia**         | 8 (5.1%)  | 3 (2.9%) | 5 (9.8%)  | 0.11      |

**Supplementary Table S1: Children Age <10 Only**

† Statistics presented: median (IQR); n (%)
‡ Statistical tests performed: Wilcoxon rank-sum test; Fisher’s exact test
| Characteristic          | Overall\(^1\) N = 227 | Hispanic/Latino\(^1\) N = 159 | Non-H/L\(^1\) N = 68 | p-value\(^2\) |
|------------------------|-------------------------|--------------------------------|------------------------|--------------|
| Age                    | 6.00 (3.00, 12.00)      | 7.00 (3.00, 12.00)             | 5.00 (2.8, 11.0)       | 0.3          |
| Gender                 |                         |                                |                        | 0.7          |
| Female                 | 103 (45%)               | 74 (47%)                       | 29 (43%)               |              |
| Male                   | 124 (55%)               | 85 (53%)                       | 39 (57%)               |              |
| **IKZF1 deletion**     | 50 (22%)                | 44 (28%)                       | 6 (8.8%)               | **0.001**    |
| **CRLF2 translocation**| 36 (16%)                | 28 (18%)                       | 8 (12%)                | 0.3          |
| **IGH-CRLF2**          | 21 (9.3%)               | 19 (12%)                       | 2 (2.9%)               | **0.043**    |
| **P2RY8-CRLF2\(^3\)** | 15 (6.6%)               | 9 (5.7%)                       | 6 (8.8%)               | 0.4          |
| **IKZF1 & CRLF2**      | 20 (8.8%)               | 20 (13%)                       | 0 (0%)                 | **<0.001**   |
| **IKZF1 & IGH-CRLF2**  | 18 (7.9%)               | 18 (11%)                       | 0 (0%)                 | **0.002**    |
| **IKZF1 & P2RY8-CRLF2**| 2 (0.9%)                | 2 (1.3%)                       | 0 (0%)                 | >0.9         |
| **IKZF1 & no IGH-CRLF2**| 32 (14%)               | 26 (16%)                       | 6 (8.8%)               | 0.2          |
| **IGH-CRLF2 & no IKZF1**| 3 (1.3%)               | 1 (0.6%)                       | 2 (2.9%)               | 0.2          |
| **P2RY8-CRLF2 & no IKZF1**| 13 (5.7%)             | 7 (4.4%)                       | 6 (8.8%)               | 0.2          |

**Supplementary Table S2: Children (all patients), Ph Negative B-ALL**

\(^1\) Statistics presented: median (IQR); n (%)

\(^2\) Statistical tests performed: Wilcoxon rank-sum test; Fisher’s exact test

\(^3\) The **P2RY8-CRLF2** translocation is more common in Down Syndrome B-ALL, the H/L cohort included 3 Down Syndrome cases (one **P2RY8-CRLF2** and two unknown genetics); the Other cohort included 4 Down Syndrome cases (3 cases **P2RY8-CRLF2**, and one hyperploidy).
| Characteristic               | Overall‡ | Hispanic/Latino‡ | Non-H/L‡ | p-value‡ |
|-----------------------------|----------|------------------|----------|----------|
|                             | N = 79   | N = 57           | N = 22   |          |
| Age                         | 15.00    | 14.00            | 15.00    | 0.7      |
|                             | (11.00, 17.00) | (12.00, 17.00)  | (11.00, 16.75) |          |
| Gender                      | 0.8      |                  |          |          |
| Female                      | 33 (42%) | 23 (40%)         | 10 (45%) |          |
| Male                        | 46 (58%) | 34 (60%)         | 12 (55%) |          |
| IKZF1 deletion              | 36 (46%) | 33 (58%)         | 3 (14%)  | <0.001   |
| CRLF2 translocation         | 21 (27%) | 19 (33%)         | 2 (9.1%) | 0.045    |
| IGH-CRLF2                   | 18 (23%) | 18 (32%)         | 0 (0%)   | 0.002    |
| P2RY8-CRLF2                 | 3 (3.8%) | 1 (1.8%)         | 2 (9.1%) | 0.2      |
| IKZF1 & CRLF2               | 19 (24%) | 19 (33%)         | 0 (0%)   | <0.001   |
| IKZF1 & IGH-CRLF2           | 18 (23%) | 18 (32%)         | 0 (0%)   | 0.002    |
| IKZF1 & P2RY8-CRLF2         | 1 (1.3%) | 1 (1.8%)         | 0 (0%)   | >0.9     |
| IKZF1 & no IGH-CRLF2        | 18 (23%) | 15 (26%)         | 3 (14%)  | 0.4      |
| IGH-CRLF2 & no IKZF1        | 0 (0%)   | 0 (0%)           | 0 (0%)   | N/A      |
| P2RY8-CRLF2 & no IKZF1      | 2 (2.5%) | 0 (0%)           | 2 (9.1%) | 0.075    |

Supplementary Table S3: Children Age ≥10 Only, Ph Negative B-ALL

‡ Statistics presented: median (IQR); n (%)  
‡ Statistical tests performed: Wilcoxon rank-sum test; Fisher’s exact test
| Characteristic          | Overall \(^1\) | Hispanic/Latino \(^1\) | Non-H/L \(^1\) | p-value \(^2\) |
|------------------------|----------------|------------------------|---------------|----------------|
|                        | N = 148        | N = 102                 | N = 46        |                |
| Age                    | 3.00 (2.00, 6.00) | 4.00 (2.00, 6.00) | 3.00 (2.00, 5.00) | 0.3            |
| Gender                 |                |                        |               | 0.4            |
| Female                 | 70 (47%)       | 51 (50%)               | 19 (41%)      |                |
| Male                   | 78 (53%)       | 51 (50%)               | 27 (59%)      |                |
| IKZF1 deletion         | 14 (9.5%)      | 11 (11%)               | 3 (6.5%)      | 0.6            |
| CRLF2 translocation    | 15 (10%)       | 9 (8.8%)               | 6 (13%)       | 0.6            |
| IGH-CRLF2              | 3 (2.0%)       | 1 (1.0%)               | 2 (4.3%)      | 0.2            |
| P2RY8-CRLF2            | 12 (8.1%)      | 8 (7.8%)               | 4 (8.7%)      | >0.9           |
| IKZF1 & CRLF2          | 1 (0.7%)       | 1 (1.0%)               | 0 (0%)        | >0.9           |
| IKZF1 & IGH-CRLF2      | 0 (0%)         | 0 (0%)                 | 0 (0%)        | N/A            |
| IKZF1 & P2RY8-CRLF2    | 1 (0.7%)       | 1 (1.0%)               | 0 (0%)        | >0.9           |
| IKZF1 & no IGH-CRLF2   | 14 (9.5%)      | 11 (11%)               | 3 (6.5%)      | 0.6            |
| IGH-CRLF2 & no IKZF1   | 3 (2.0%)       | 1 (1.0%)               | 2 (4.3%)      | 0.2            |
| P2RY8-CRLF2 & no IKZF1 | 11 (7.4%)      | 7 (6.9%)               | 4 (8.7%)      | 0.7            |

Supplementary Table S4: Children Age <10 Only, Ph Negative B-ALL

\(^1\) Statistics presented: median (IQR); n (%)  
\(^2\) Statistical tests performed: Wilcoxon rank-sum test; Fisher’s exact test