Less is More in Childhood B-ALL:
Targeted Immunotherapies, MRD by HTS, and
De-escalation of Therapy in COG Trials
AALL1731/AALL1732

Sue Zupanec, MN NP Pediatrics
Christine S. Yun, MSN NP Pediatrics

COG Educational Track at APHON 2020
Disclosure

- Sue Zupanec and Christine Yun have no industry relationships.
- Off label use will be discussed.
COG Disclosure

The information in this presentation is intended for educational purposes only and is solely for the use of the individual nurse learner. This information is not intended as the sole source of guidance in providing Children’s Oncology Group (COG) protocol-directed nursing care, and current COG protocols should always be consulted prior to making patient care decisions for any patient enrolled on a COG protocol. Learners should also be aware that COG protocols are research plans designed to investigate particular study questions, that recommendations for treatment and dosing are made within the context of specific research aims, and that these recommendations are intended only for use within a structured research setting. Although every attempt has been made to assure that the informational content contained herein is as accurate and complete as possible as of the date of presentation, no warranty or representation, express or implied, is made as to the accuracy, reliability, completeness, relevance, or timeliness of this content. This information may not be copied or redistributed in any form, or used for any purpose other than nursing education.
Pediatric B-ALL Survival
How did we improve pediatric B-ALL survival?

- How did we get here?
  - Clinical Trials!

- What led to the improved survival in pediatric ALL over the last few decades?
  - Improved risk stratification
  - Identifying groups who need intensified therapy and/or targeted therapies

- Can we do even better?
  - Yes - we can further define risk groups
    - Are there groups still at high risk for relapse that we can identify?
  - Can we further prevent relapse with immunotherapy?
Who’s Cutting to the Front of the Line, and Why?

- Blinatumomab
- Inotuzumab
Why Immunotherapy?

- Intensification of chemotherapy was not successful
- Immunotherapy!
  - Improved OS on AALL1331
  - AALL1621 – Primary aim successful
ALL1331 HR and IR Results

Brown, P. Abstract #LBA-1. Presented at the 2019 ASH Annual Meeting, December 10, 2019; Orlando, FL.

© 2019
AALL1621 ASH Abstract 2019 – Primary Aim Outcomes

- AALL1621: A Phase 2 Trial of Inotuzumab Ozogamicin (InO) in Children and Young Adults with Relapsed or Refractory CD22+ ALL
  - InO demonstrated a CR or CRi in 58% of patients
  - Minimal hepatic toxicity observed during InO cycles
  - SOS occurred in 26% of patients who underwent subsequent HCT

O'Brien, M. 61st American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2019; Orlando, FL. Abstract 741
AALL1621

- Trial expansion in development
What we did learn from the biology samples and MRD on previous ALL trials?
Looking back at MRD

- Banked samples
- 9900 series ALL
MRD and EFS 9900 Series Trials

- MRD negative (≤ 0.01%) (n = 1588)
- 0.01% < MRD ≤ 0.1% (n = 175)
- 0.1% < MRD ≤ 1.0% (n = 141)
- MRD > 1.0% (n = 67)

Event-free survival probability vs. Years

- P < .0001
- 97 ± 1%
- 88 ± 1%
- 59 ± 5%
- 49 ± 6%
- 30 ± 8%

© 2008 Borowitz, M. (2008), Blood
HTS – why might it help us with risk stratification?

- MRD currently measured by flow cytometry, which can detect down to 1/10,000 leukemia cells
- The new “High Throughput Sequencing” (HTS) is much more sensitive and can detect to a level of 1/1,000,000
- Retrospective data shows that patients who are flow MRD negative can still have detectable disease by HTS MRD (predicted up to 42%)
- Patients with HTS MRD negative EOI results have excellent survival!

Negative EOI FLOW MRD but Positive HTS MRD Evidence of Resistant Disease
Looking back - HTS MRD Survival on AALL0331/0232

Wood, D. et al. (Blood) 2017

© 2017
Improved Risk Stratification has led to better outcomes but, has become very complex…
Increasing Complexity = Improved Survival

9900 Series
- 9904 Low Risk
- 9905 Standard Risk
- 9906 High Risk

NOW
B-ALL Frontline Trials 2019

- **Very High Risk 1.7%**
  - ALL1721
  - CAR-T in CR1

- **High Risk 25%**
  - ALL1732
  - Randomized to inotuzumab

- **HR-Favorable 1.8%**
  - ALL1732
  - No randomization

- **Precision Medicine 5.5%**
  - Ph+
  - Ph-like

- **SR-Avg/High 33%**
  - ALL1731
  - Randomized to Blinatumomab

- **SR Favorable 33%**
  - ALL1731
  - No randomization

C210_Less is More in Childhood B-ALL
Remember to...

![Image: Keep Calm and Take a Deep Breath]

© 2013 KeepCalmStudio.com

The world's childhood cancer experts
Let’s take a look at ALL1731, Standard Risk B Lineage ALL...
Risk Groups AALL1731

- **APEC14B1**
  - **SR B-ALL**
    - **AALL1731 (on study)**
    - **Induction**
      - **SR-Fav B-ALL** 51%
      - **SR-Average B-ALL** 34%
      - **SR-High B-ALL** 15%
    - CNS3, Testicular leukemia, Steroid pre-treatment eligible for AALL1732
    - Ph+ pts may be eligible to transfer to AALL1631

*With Permission from Dr. S. Gupta*
ALL1731

- All NCI SR patients will enroll on and stay on AALL1731
- There will be an investigational agent – Blinatumomab
  - SR – Avg B ALL: Randomization Blinatumomab
  - SR – High B ALL: Randomization Blinatumomab
- SR – Fav B ALL Arm will NOT be randomized
SR-Favorable

- NCI SR (non-DS and DS)
- Favorable cytogenetics (ETV6/RUNX1 or DT)
- Day 8 PB MRD <1%
- EOI BM MRD <0.01%
- CNS 1&2

No Randomization – Predicted EFS 97%
Down Syndrome DS and ALL

- All patients with B-ALL and DS will remain on AALL1731
  - BOTH NCI SR and HR
  - 3 drug induction – NO day 15 BMA
    - Previously day 15 BMA was used to determine escalation of therapy
- Three risk groups:
  - Standard Risk-Favorable (SR-Fav) DS B-ALL
  - Standard Risk-Average (SR-Avg) DS B-ALL
  - DS-High B-ALL
**SR-Average**

- **NCI SR (non-DS and DS)**
  - CNS 1&2, fav cyto, D8 PB MRD >1%, EOI MRD <0.01%
  - CNS1, neutral cyto, EOI MRD <0.01%
  - CNS2, 1&2, DT any Day 8, EOI MRD 0.01-<0.1%

- **EOI HTS MRD Stratification**
  - EOI HTS undetectable
    - Non-random, standard treatment
  - EOI HTS detectable/indeterminate/unavailable
    - Randomized to chemo +/- Blin
**SR-High**

- **NCI SR (non DS ONLY)**
  - EOI MRD ≥0.01% (>0.1% for DT pts)
  - Unfavorable cytogenetics
  - CNS2 and neutral cytogenetics

- **EOI MRD+ SR-High pts: EOC MRD**
  - <0.1% - Randomized
  - 0.1-0.99% NON-RANDOM assignment to Experimental Arm D (Blinatumomab)
  - ≥1% = Consolidation failures, off protocol therapy

---

**Diagram: SR-High B-ALL Arm**

- **EOC MRD**
  - ≥1%
  - Off Protocol

- **EOC MRD**
  - <1%
  - 0.1-0.99%
  - Randomization

- **SR-High**
  - Control Arm C
  - Exp Arm D

- **Randomization**
  - IM # I - HDMTX
  - Blin Block 1
  - IM # II - CMTX
  - Blin Block 2
  - DI
  - IM # II - CMTX

- **Maintenance**
Down Syndrome and ALL

- DS patients will follow the same risk classification criteria as non-DS SR patients
- Standard Risk-Fav DS B-ALL
  - Standard chemotherapy with no randomization
- Standard Risk-Avg DS B-ALL
  - Eligible for randomization – Blinatumomab

**EXCEPTION:** DS patient with any HR features – Single Arm Trial

Illustration by Aimee Ermel, 2013
DS High B-ALL

- DS B-ALL patients with **ANY** HR features will be non-randomly assigned to:
  - Single arm of SR-high ALL therapy
  - 3 cycles of Blinatumomab
- This arm remains under the SR trial AALL1731
DS High B-ALL Treatment Schema

DS-High Arm

HR Consolidation

NCI SR: EOI MRD <0.1%
NCI HR: EOI MRD <0.01%

Blin Block 1

Intermediate Dose MTX IM

NCI SR: EOI MRD ≥0.1%
NCI HR: EOI MRD ≥0.01%

Blin Block 2

DI (Days 1-29)

Blin Block 3

NCI HR pts with EOC MRD ≥0.01%
may remain on protocol or choose to transfer to AALL1721 if eligible

NCI HR pts with EOC MRD >0.01%
may remain on protocol or choose to transfer to AALL1723 if eligible

EOC BM Flow MRD+

EOC MRD <1%

Consolidation Failure ≥1%

OFF Protocol
NCI HR pts may transfer to AALL1723 if eligible
Blinatumomab

FAQs

- Adaptive Standard Operating Procedure
- Blinatumomab Administration and Preparation Training
- Blinatumomab Home Health Care Manual
- Blinatumomab FAQ
- Blinatumomab Drug Information Sheet for Patients
Interruptions of Blinatumomab

- New Protocol Language – **interruptions are unavoidable**
- Dose Clarification – due to unavoidable interruptions for patient care
  - Consideration of PORT care

...when the interruption time over 28 days is greater than 24 hours, missed hours of Blin may be added to the overall infusion time...at the discretion of the treating physician...
AALL1731 – Localized B-LLy (B Lymphoblastic Lymphoma)

- Current standard of care for these pts remains unknown
- Included on ALL trials within COG since AALL0932
- Rare group – between March 2013-June 2016 only 30 patients with localized B-LLy enrolled on AALL0932
- Therapy will remain consistent from ALL0932 to AALL1731 to increase the number of evaluable patients

**GOAL:** Define SOC for this sub-group with combined analysis

- Localized BLLY
  - 3 drug induction
  - SR Consolidation
  - EscMTX
  - DI
  - Maintenance
There are a few other changes (hint – less is more) that overlap both protocols, AALL1731 and AALL1732…
What we have learned from previous frontline high risk B lineage studies...

Perhaps more is not always better.....
No Advantage of 2\textsuperscript{nd} DI in Rapid Responders

Therapies Still Failing a Subset of HR patients

Event-Free Survival by End Induction MRD (Day 29): COG AALL0232 HR B-ALL²

Borowitz M et al. *Blood* 2015
# Ceiling Effect of Intensifying via Conventional Chemotherapy

**Toxicity Associated with Intensive Post-Induction Therapy Incorporating Clofarabine in the Very High Risk Stratum of Patients with Newly Diagnosed High Risk B-Lymphoblastic Leukemia: a Report from the Children’s Oncology Group Study AALL1131**

<table>
<thead>
<tr>
<th>Consolidation Part 2</th>
<th>Experimental Arm 1</th>
<th>Experimental Arm 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control Arm</strong></td>
<td><strong>Experimental Arm 1</strong></td>
<td><strong>Experimental Arm 2</strong></td>
</tr>
<tr>
<td>CPM 1000 mg/m² Day 29</td>
<td>CPM 440 mg/m² Days 29-33</td>
<td>CPM 440 mg/m² Days 29-33</td>
</tr>
<tr>
<td>ARAC 75 mg/m² Days 29-32, 36-39</td>
<td>ETOP 100 mg/m² Days 29-33</td>
<td>ETOP 100 mg/m² Days 29-33</td>
</tr>
<tr>
<td>MP 60 mg/m² Days 29-42</td>
<td>VCR 1.5 mg/m² (2 mg max) Days 43, 50</td>
<td>CLOF 30 mg/m² Days 29-33 (20 mg/m² post amendment)</td>
</tr>
<tr>
<td>VCR 1.5 mg/m² (2 mg max) Days 43, 50</td>
<td>PEG-ASP 2,500 units/m² Day 43</td>
<td>VCR 1.5 mg/m² (2 mg max) Days 43, 50</td>
</tr>
<tr>
<td>PEG-ASP 2,500 units/m² Day 43</td>
<td></td>
<td>PEG-ASP 2,500 units/m² Day 43</td>
</tr>
</tbody>
</table>

**CLOF as administered with CPM/ETOP on AALL1131 was associated with unacceptable toxicity**

Salzer W and Burke M, *Cancer*, 2018
Let’s take a look at AALL1732, High Risk B lineage ALL...
Risk Groups AALL1732

All NCI HR Ph-like patients (ABL-class, CRLF2/JAK, or other lesions) may remain on protocol to receive post-Induction therapy or come off protocol therapy to pursue alternative therapy.

With permission from Dr. J. McNeer
AALL1732

- ALL NCI HR patients will enroll on and stay on AALL1732
- Subset of NCI SR B-ALL are included
  - With CNS3, testicular leukemia, or steroid pretreatment
- MPAL and HR B-LLy included
- Down syndrome excluded
  - Both NCI-SR and NCI-HR will enroll on AALL1731
- There is an investigational agent – inotuzumab
  - HR B-ALL: Randomization inotuzumab after Consolidation
- HR- Fav B ALL arm will not be randomized
HR-Favorable B-ALL

NCI HR patients with:
- Favorable clinical features:
  - <10 years old but WBC $\geq 50K/\mu L$ at diagnosis
  - CNS1
  - No testicular leukemia
- Favorable cytogenetics:
  - ETV6-RUNX1
  - Trisomy 4 & 10
- End of induction MRD < 0.01%

No Randomization – Predicted EFS 94%
**HR B-ALL**

- Must have CD22 expression on leukemic blasts **ON DIAGNOSTIC SAMPLE**
  - NCI HR with EOC MRD <0.01%
  - NCI HR EOC MRD <1%

---

**HR B-ALL**

- Consolidation
- EOC MRD
- NCI HR < 0.01%
- NCI SR <1%
- Randomization

**Consolidation**

- CD22 negative/unknown

**Off protocol therapy**

**EOC MRD**

- NCI HR ≥ 0.01%
- NCI SR ≥ 1%

**VHR B-ALL**

- Off protocol therapy
- NCI HR patients may be eligible to enroll on AALL1721

**NCI HR EOC MRD**

- <1%

---

**Children's Oncology Group**

The world's childhood cancer experts
**HR B-ALL**

**Maintenance**
- 2 years from start of phase after Consolidation regardless of sex
- VCR/PDN pulses q12 weeks

**Randomization +/− 2 cycles of Inotuzumab – Predicted EFS 65-90%**

**HR B-ALL**

- Randomization

**Arm A Control**
- Interim Maintenance I HD-MTX
- Delayed Intensification
- Interim Maintenance II CMTX
- Maintenance

**Arm B Experimental**
- InO Block 1
- Interim Maintenance I HD-MTX
- InO Block 2
- Delayed Intensification
- Interim Maintenance II CMTX
- Maintenance

**Inotuzumab**
- 2 cycles
Relationship between InO and hepatic toxicity…

Illustration by Aimee Ermel, 2013
Hepatic Toxicity Assessment

- Monitor for SOS
- Assess d-bili and ALT
  - Prior to each dose of InO in
    - Block 1 and Block 2
- Appendix XV11:
  - InO Dose Modifications for Toxicities Schema
Hepatic Toxicity Assessment cont’d

- **CTCAE guidelines for hepatic toxicity:**

<table>
<thead>
<tr>
<th>Grade</th>
<th>ALT</th>
<th>d-bili</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt; 1-3x ULN</td>
<td>&lt;2 mg/dL</td>
</tr>
<tr>
<td>2</td>
<td>&gt;3-5x ULN</td>
<td>2-5 mg/dL</td>
</tr>
<tr>
<td>3</td>
<td>&gt;5-20x ULN</td>
<td>&gt;5 mg/dL</td>
</tr>
<tr>
<td>4</td>
<td>&gt;20x ULN</td>
<td></td>
</tr>
</tbody>
</table>
Mixed Phenotype Acute Leukemia (MPAL) and HR B-Lymphoblastic Lymphoma (B-LLy)
**WHO2016 Definition of MPAL**

### WHO2016

**Table 19. Criteria for lineage assignment for a diagnosis of MPAL**

<table>
<thead>
<tr>
<th>Lineage assignment criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Myeloid lineage</strong></td>
</tr>
<tr>
<td>MPO* (flow cytometry, immunohistochemistry, or cytochemistry)</td>
</tr>
<tr>
<td>or</td>
</tr>
<tr>
<td>Monocytic differentiation (at least 2 of the following: nonspecific esterase, cytochemistry, CD11c, CD14, CD64, lysozyme)</td>
</tr>
<tr>
<td><strong>T-lineage</strong></td>
</tr>
<tr>
<td>Strong cytoplasmic CD3 (with antibodies to CD3 epsilon chain)</td>
</tr>
<tr>
<td>or</td>
</tr>
<tr>
<td>Surface CD3</td>
</tr>
<tr>
<td><strong>B-lineage</strong></td>
</tr>
<tr>
<td>Strong CD19 with at least 1 of the following strongly expressed: CD79a, cytoplasmic CD22, or CD10</td>
</tr>
<tr>
<td>or</td>
</tr>
<tr>
<td>Weak CD19 with at least 2 of the following strongly expressed: CD79a, cytoplasmic CD22, or CD10</td>
</tr>
</tbody>
</table>

*See “Acute leukemias of ambiguous lineage” for caveats related to weaker antigen expression, or to expression by immunohistochemistry only.*

---

**Arber DA et al. Blood 2016**

---

C210_Less is More in Childhood B-ALL
Inclusion criteria:
- Meets WHO2016 criteria
- Subtypes:
  - B/myeloid
  - T/myeloid
  - B/T myeloid
  - B/T

Central confirmation required
No randomizations

**Maintenance:**
- 2 years from start of IM1 regardless of sex for all arms
- VCR/PDN pulse q12 weeks

MPAL
**B-LLy**

- **Inclusion criteria:**
  - Murphy Stage III/IV
  - Murphy Stage I/II with steroid pretreatment
    - >48 hours of IV or oral steroids
  - Must have CR by EOC to continue protocol therapy
    - By imaging (CT scans, bone scan, +/- PET scan)
  - No randomization

**Maintenance:**
- 2 years from start of IM1 regardless of sex for all arms
- VCR/PDN pulse q12 weeks

---

**Diagram:**

- Induction
  - Imaging Evaluation
  - (CR, PR, SD)
    - HR Consolidation
      - Imaging Evaluation
      - CR
        - Interim Maintenance I HD-MTX
          - Delayed Intensification
            - Interim Maintenance II CMTX
              - Maintenance
MMD vs. MRD Definitions

- **MMD = minimal marrow disease**
  - Diagnostic marrow
- **MRD = minimal residual disease**
  - End of Induction
How does adherence impact risk of relapse...
Oral 6-MP Adherence

Age < 12 years (93.1%)

Age ≥ 12 years (86.8%)

AALL1732 Primary Aim (Adherence Study): Coming Soon

- To determine the impact of proposed interventions (IP vs. iIP vs. pIP) on adherence to oral 6 MP in children with HR B-ALL
  - Adherence to oral 6 MP will be measured with the Medication Event Monitoring System (MEMS)

<table>
<thead>
<tr>
<th>Intervention Components</th>
<th>IP</th>
<th>iIP</th>
<th>pIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education (MIPE) (once)</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Customized printed 6MP schedule</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Oncologist-initiated electronic reminder (one every night)</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncologist-initiated customized electronic reminder + real-time feedback reminders</td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Patient/Parent-established reminders</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Directly supervised therapy</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Slide courtesy of Smita Bhatia, MD
Take Home Message: Less is More...
Same length of therapy regardless of biologic sex!

2 years from start of Interim Maintenance, regardless of sex
## Consortium Outcomes for ALL by Sex

<table>
<thead>
<tr>
<th>Trial Group</th>
<th>Length of Therapy</th>
<th>Gender-based difference?</th>
<th>Outcomes (5 yr EFS)</th>
<th>Statistically Significant diff in gender?</th>
</tr>
</thead>
<tbody>
<tr>
<td>BFM-ALL 2000</td>
<td>24 mos from diagnosis</td>
<td>NO</td>
<td>85%</td>
<td>83%</td>
</tr>
<tr>
<td>DFCI 05-001</td>
<td>104 wks post CR</td>
<td>No</td>
<td>86% (95% CI: 81-90)</td>
<td>85% (95% CI: 81-89)</td>
</tr>
<tr>
<td>UK ALL 2003</td>
<td>2-3 yrs from beginning of IM</td>
<td>Yes</td>
<td>Haz ratio (female vs male): 0.78 (95% CI: 9.54-1.13)</td>
<td>N/S in multivar analysis</td>
</tr>
<tr>
<td>DCOG ALL-9</td>
<td>109 wks</td>
<td>No</td>
<td>84.8 ± 2%</td>
<td>78 ± 1.8%</td>
</tr>
<tr>
<td>NOPHO ALL-2000</td>
<td>2-2.5 yrs post dx</td>
<td>No</td>
<td>81 ± 2%</td>
<td>78 ± 2%</td>
</tr>
<tr>
<td>St. Jude Total XV</td>
<td>120-146 wks</td>
<td>Yes</td>
<td>88.8 ± 4.3%</td>
<td>83.5 ± 4.1%</td>
</tr>
<tr>
<td>St. Jude Total XVI</td>
<td>120 wks</td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Same length of therapy regardless of sex!

- Both AALL1731 and AALL1732:
  - Length of therapy will NOT be a randomized question
  - Outcomes will be compared to historical trials of similar populations
  - Stopping rules in place to ensure safety
Reduced VCR/Steroid pulses to every 12 weeks!

Results: AALL0932

Figure 1: DFS by VCR/DEX pulse randomization

Figure 2: OS by VCR/DEX pulse randomization

Angiolillo, A. (2019), Blood
Summary

- ALL treatment has evolved to identify subgroups with outstanding outcomes
- Ceiling effect of intensifying treatment via conventional chemotherapy
- Less acute toxicities with immunotherapy although time will tell with late effects
- Uniform length of Maintenance regardless of sex!
  - 2 years from start of IM#1, Blinatumomab cycle #1, or Inotuzumab cycle #1
- Reduced VCR/Steroid pulses in maintenance to every 12 weeks
  - For both risk groups!

Hence, Less is More!!
### Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
<th>ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine transaminase</td>
<td>ALT</td>
</tr>
<tr>
<td>$^{18}$fluoro-2-deoxy-D-glucose positron emission tomography</td>
<td>FDG-PET</td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>ALL</td>
</tr>
<tr>
<td>American Society of Hematology</td>
<td>ASH</td>
</tr>
<tr>
<td>Average</td>
<td>Avg</td>
</tr>
<tr>
<td>B-cell Acute Lymphoblastic Leukemia</td>
<td>B-ALL</td>
</tr>
<tr>
<td>Berlin Frankfurt Munster</td>
<td>BFM</td>
</tr>
<tr>
<td>Blinatumomab</td>
<td>Blin</td>
</tr>
<tr>
<td>B-Lymphoblastic Lymphoma</td>
<td>B-LLy</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>BM</td>
</tr>
<tr>
<td>Bone marrow aspirate</td>
<td>BMA</td>
</tr>
</tbody>
</table>
## Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
<th>ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct bilirubin</td>
<td>d-bili</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>DS</td>
</tr>
<tr>
<td>End of Induction</td>
<td>EOI</td>
</tr>
<tr>
<td>Escalating Methotrexate</td>
<td>EscMTX</td>
</tr>
<tr>
<td>Etoposide</td>
<td>ETOP or VP</td>
</tr>
<tr>
<td>Event free survival</td>
<td>EFS</td>
</tr>
<tr>
<td>Every</td>
<td>q</td>
</tr>
<tr>
<td>Favorable</td>
<td>Fav</td>
</tr>
<tr>
<td>Frequently asked questions</td>
<td>FAQ(s)</td>
</tr>
<tr>
<td>Hazard</td>
<td>Haz</td>
</tr>
<tr>
<td>Hematopoietic cell transplant</td>
<td>HCT</td>
</tr>
</tbody>
</table>
## Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
<th>ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose methotrexate</td>
<td>HD-MTX</td>
</tr>
<tr>
<td>High risk</td>
<td>HR</td>
</tr>
<tr>
<td>High-Throughout Sequencing</td>
<td>HTS</td>
</tr>
<tr>
<td>Inotuzomab Ozogamicin</td>
<td>InO</td>
</tr>
<tr>
<td>Interim maintenance</td>
<td>IM</td>
</tr>
<tr>
<td>Intravenous</td>
<td>IV</td>
</tr>
<tr>
<td>Janus kinase</td>
<td>JAK</td>
</tr>
<tr>
<td>Mercaptopurine</td>
<td>6MP</td>
</tr>
<tr>
<td>Minimal Marrow Disease</td>
<td>MMD</td>
</tr>
<tr>
<td>Minimal residual disease</td>
<td>MRD</td>
</tr>
<tr>
<td>Mixed Phenotype Acute Leukemia</td>
<td>MPAL</td>
</tr>
</tbody>
</table>
## Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
<th>ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoclonal antibody/antibodies</td>
<td>MoAb(s)</td>
</tr>
<tr>
<td>Multimedia interactive patient/parent education</td>
<td>MIPE</td>
</tr>
<tr>
<td>National Cancer Institute</td>
<td>NCI</td>
</tr>
<tr>
<td>Nordic Society for Pediatric Hematology and Oncology</td>
<td>NOPHO</td>
</tr>
<tr>
<td>Not Significant</td>
<td>N/S</td>
</tr>
<tr>
<td>Nurse practitioner(s)</td>
<td>NP(s)</td>
</tr>
<tr>
<td>One thousand</td>
<td>K</td>
</tr>
<tr>
<td>Overall survival</td>
<td>OS</td>
</tr>
<tr>
<td>Partial remission or response</td>
<td>PR</td>
</tr>
<tr>
<td>Patient(s)</td>
<td>pt(s)</td>
</tr>
<tr>
<td>Peripheral blood</td>
<td>PB</td>
</tr>
</tbody>
</table>
### Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
<th>ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philadelphia positive</td>
<td>Ph+</td>
</tr>
<tr>
<td>Philadelphia-like acute lymphoblastic leukemia</td>
<td>Ph-like ALL</td>
</tr>
<tr>
<td>Prednisone</td>
<td>PRED</td>
</tr>
<tr>
<td>Project: EveryChild, A Registry, Eligibility Screening, Biology and Outcome Study</td>
<td>APEC14B1</td>
</tr>
<tr>
<td>Sinusoidal Obstruction Syndrome</td>
<td>SOS</td>
</tr>
<tr>
<td>Stable disease</td>
<td>SD</td>
</tr>
<tr>
<td>Standard of care</td>
<td>SOC</td>
</tr>
<tr>
<td>Standard risk</td>
<td>SR</td>
</tr>
<tr>
<td>Upper Limit of Normal</td>
<td>ULN</td>
</tr>
</tbody>
</table>
# Abbreviations

<table>
<thead>
<tr>
<th>FULL TERM</th>
<th>ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high risk</td>
<td>VHR</td>
</tr>
<tr>
<td>Vincristine</td>
<td>VCR</td>
</tr>
<tr>
<td>Week(s)</td>
<td>wk(s)</td>
</tr>
<tr>
<td>World health organization</td>
<td>WHO</td>
</tr>
<tr>
<td>Year(s)</td>
<td>yr(s)</td>
</tr>
</tbody>
</table>
References


References


References
