ADULT ACUTE LEUKEMIA

Frederick R. Appelbaum, MD
Northern California Blood Cancer Conference
February 4, 2017
## Acute Leukemia – 2016\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>New Cases</th>
<th>Deaths</th>
<th>5yr Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML</td>
<td>20,830</td>
<td>10,460</td>
<td>25.9%</td>
</tr>
<tr>
<td>ALL</td>
<td>6,250</td>
<td>1,450</td>
<td>67.5%</td>
</tr>
</tbody>
</table>

\(^1\)SEER Results
Acute Leukemia Incidence by Age
<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>Undifferentiated</td>
<td>5%</td>
</tr>
<tr>
<td>M1</td>
<td>Minimal maturation</td>
<td>15%</td>
</tr>
<tr>
<td>M2</td>
<td>With maturation</td>
<td>25%</td>
</tr>
<tr>
<td>M3</td>
<td>Promyelocytic</td>
<td>10%</td>
</tr>
<tr>
<td>M4</td>
<td>Myelomonocytic</td>
<td>25%</td>
</tr>
<tr>
<td>M4eo-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M5</td>
<td>Monocytic</td>
<td>10%</td>
</tr>
<tr>
<td>M5A and M5B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M6</td>
<td>Erythroid</td>
<td>5%</td>
</tr>
<tr>
<td>M7</td>
<td>Megakaryoblastic</td>
<td>10%</td>
</tr>
</tbody>
</table>
AML Morphology
Adult ALL Classification
Morphology

L1  25-30%
L2  65-70%
L3  2-7%
ALL Morphology
Factors Essential for Determining Prognosis in Acute Leukemia

Cytogenetics
Mutational analysis
Primary vs secondary
Patient co-morbidities
Clonal Cytogenetic Abnormalities in Adult AML

- Normal: 41%
- t(15;17): 10%
- t(8;21): 6%
- t(6;9): 2%
- 11q23: 5%
- Inv(16): 5%
- -7/7q-: 7%
- -5/5q-: 4%
- Other: 20%
Survival by Cytogenetic Risk Group in AML

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>At Risk</th>
<th>Deaths</th>
<th>Estimate (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favored</td>
<td>121</td>
<td>53</td>
<td>55% (45-64%)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>278</td>
<td>168</td>
<td>38% (32-44%)</td>
</tr>
<tr>
<td>Unfavorable</td>
<td>184</td>
<td>162</td>
<td>11% (7-16%)</td>
</tr>
</tbody>
</table>

Heterogeneity of 3 groups: $p < .0001$

Slovak, Blood 96: 4075, 2000
Genomic Landscape of AML\textsuperscript{1}

Average # of mutations per case – 13
Average # of “driver” mutations per case – 5
Total # of significantly mutated genes – 23
Total # mutated in two or more samples – 237
Recurrent Mutations in AML

Significantly Mutated Genes

No. of Samples with Mutations

1NEJM 368:2059, 2013
Clonal Evolution and Heterogeneity in AML

## Non-cytogenetic Gene Mutations Relevant to Clinical Practice

<table>
<thead>
<tr>
<th>Gene</th>
<th>Incidence</th>
<th>Relevance</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPM1</td>
<td>33%</td>
<td>Improved outcome</td>
</tr>
<tr>
<td>CEBPA</td>
<td>8%</td>
<td>Improved outcome</td>
</tr>
<tr>
<td>FLT3</td>
<td>25%</td>
<td>Inferior outcome</td>
</tr>
<tr>
<td>KIT</td>
<td>8%</td>
<td>Inferior outcome</td>
</tr>
</tbody>
</table>
# AML — 2016

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Genetic Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable</td>
<td>t(8;21)</td>
</tr>
<tr>
<td></td>
<td>inv(16)</td>
</tr>
<tr>
<td></td>
<td>NPM1+ FLT3-</td>
</tr>
<tr>
<td></td>
<td>CEBPA+ (biallelic)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>NPM1+ FLT3+</td>
</tr>
<tr>
<td></td>
<td>NPM1- FLT3-</td>
</tr>
<tr>
<td></td>
<td>t(9;11)</td>
</tr>
<tr>
<td></td>
<td>Cyto+, not fav or unfav</td>
</tr>
<tr>
<td>Adverse</td>
<td>t(6;9), t(v;11q23)</td>
</tr>
<tr>
<td></td>
<td>t(9;22), inv(3)</td>
</tr>
<tr>
<td></td>
<td>-5,-7,-17</td>
</tr>
<tr>
<td></td>
<td>Complex, NPM1- FLT3+</td>
</tr>
<tr>
<td></td>
<td>RUNX1+, ASXL1+, p53+</td>
</tr>
</tbody>
</table>
AML Survival by Risk Group\textsuperscript{1}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{aml_survival.png}
\caption{Survival analysis of AML patients divided by risk group.}
\end{figure}

\textsuperscript{1}JCO 29:2758, 2011
Clonal Hematopoiesis in Normal Adults

![Bar graph showing the number of mutations for various genes.](image1)

- **DNMT3A**: 190
- **ASXL1**: 35
- **TET2**: 31
- **JAK2**: 24
- **PPM1D**: 15
- **SF3B1**: 13
- **SRSF2**: 7
- **TP53**: 4
- **CBL**: 3
- **MYD88**: 1
- **U2AF1**: 1
- **STAT3**: 1
- **IDH2**: 1
- **ATM**: 1

![Line graph showing the percentage of participants with clonal hematopoiesis over age.](image2)

- **Clonal hematopoiesis with candidate drivers**
- **Clonal hematopoiesis with unknown drivers**
- **Clonal hematopoiesis**

1 Genovese et al NEJM, 371:2477, 2014
Cumulative Incidence of Therapy-Related AML in Patients with and without CHIP

\[ ^1 \text{Takahashi et al. Lancet Oncology 18:100, 2017} \]
Secondary AML

Frequency – 19.8%

Latency
MDS – 17 mo.
CMML – 18 mo.
MPN – 43 mo.

1Ostgard et al. JCO 33:3641, 2015
Survival Following Intensive Therapy for AML

Primary vs. Secondary vs. Treatment related

Ostgard et al., JCO 33:3641, 2014
# Major Cytogenetic Categories in Adult ALL

<table>
<thead>
<tr>
<th>Category</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Favorable</strong></td>
<td></td>
</tr>
<tr>
<td>High hyperdiploidy</td>
<td>10%</td>
</tr>
<tr>
<td>del 9p</td>
<td>9%</td>
</tr>
<tr>
<td><strong>Unfavorable</strong></td>
<td></td>
</tr>
<tr>
<td>t(4;11)</td>
<td>7%</td>
</tr>
<tr>
<td>Low hypodiploidy/near triploidy</td>
<td>4%</td>
</tr>
<tr>
<td>Complex</td>
<td>5%</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td>t(9;22)</td>
<td>19%</td>
</tr>
<tr>
<td>t(8;14)</td>
<td>2%</td>
</tr>
</tbody>
</table>
Overall Survival by Cytogenetic Subgroup: MRC UKALL XII / ECOG 2993

Genome-wide Analysis of Genetic Alterations in ALL\textsuperscript{1}

B-cell mutations:  \textit{ETV6, TCF3, MLL, CRLF2, RUNX1, PBX1, PAX5, IK2F1}

T-cell mutations:  \textit{NOTCH1}

\textsuperscript{1}Robert et al. Nat Rev 12:344, 2014
Ph-like ALL¹

1. Approximately 15% of B-cell ALL
2. Increase with age, males and high WBC
3. Molecular Abnormalities:
   - Abl-class fusions
   - JAK2 rearrangements
   - CRLF2 rearrangements
   - Other JAK-STAT abnormalities
   - RAS mutations
4. Poorer prognosis
5. May respond to TKIs

¹ Roberts, NEJM 371:1005, 2014
Adult ALL

Risk Factors

1. Age > 30

2. WBC
   > 30,000/μL (B lineage)
   > 100,000/μL (T lineage)

3. Cytogenetics
   t(9;22)
   t(4;11)
   t(8;14)
   Complex
   LoHypo/Near Trip
AML Induction Dosing (Age <65)

**Anthracycline/Anthracenedione**

- Daunorubicin 60 to 90 x 3
- Idarubicin 10 to 12 x 3
- Mitoxantrone 12 to 15 x 3

**Cytarabine 100 to 200 x 7**

**Third drugs?**
60 vs 90 mg/m² of Daunorubicin for AML¹

N – 1206
Design – 10 + 3  DNR 60 vs 90

Outcome

<table>
<thead>
<tr>
<th></th>
<th>DNR 60</th>
<th>DNR 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>84%</td>
<td>81%</td>
</tr>
<tr>
<td>ED</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>RFS (2 yr)</td>
<td>50%</td>
<td>52%</td>
</tr>
<tr>
<td>Relapse</td>
<td>41%</td>
<td>37%</td>
</tr>
</tbody>
</table>

¹ Burnett et al ASH, 2014
CPX 351 for Secondary AML¹

N – 309
Age – 60-75

<table>
<thead>
<tr>
<th></th>
<th>CPX 100m/m² d1,3,5</th>
<th>DNR 60x3, AraC 100x7</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR+CRi</td>
<td>47%</td>
<td>33%</td>
</tr>
<tr>
<td>CR</td>
<td>37%</td>
<td>26%</td>
</tr>
<tr>
<td>OS 12 mo.</td>
<td>41%</td>
<td>27%</td>
</tr>
<tr>
<td>OS 24 mo.</td>
<td>31%</td>
<td>12%</td>
</tr>
</tbody>
</table>

¹Lancet ASCO, 2016
Standard Induction +/- Midostaurin in \( FLT3 +AML \)\(^1\)

\[\text{Overall Survival}
\]

\[\text{With Number of Subjects at Risk}
\]

\[\text{Survival Probability}
\]

\[\text{survival time (months)}
\]

\[\text{Arm} \quad 1: \text{Midostaurin} \quad 2: \text{Placebo}
\]

\[\text{Midostaurin 1}
\]

\[\text{Placebo 2}
\]

\[\text{360} \quad 221 \quad 178 \quad 77 \quad 0
\]

\[\text{357} \quad 172 \quad 143 \quad 71 \quad 0
\]

\(^1\)Stone et al., ASH, 2015
# Alternative FLT3 Inhibitors

<table>
<thead>
<tr>
<th>1st generation</th>
<th>2nd generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorafenib</td>
<td>Quizartinib</td>
</tr>
<tr>
<td>Sunitinib</td>
<td>Crenolanib</td>
</tr>
<tr>
<td>Lesaurtinib</td>
<td>Gilteritinib</td>
</tr>
<tr>
<td>Midostaurin</td>
<td></td>
</tr>
</tbody>
</table>
Meta-Analysis of Chemo Therapy +/- GO

CD33 Expression and Impact of Gemtuzumab Ozogamicin

Pollard, JCO, 2016
Novel Anti-CD33 Targeted Therapies

SGN-CD33A
-pyrrolobenzodiazepine

AMG 330
-CD33/CD3 BITE

CD33 CARTs
Survival in S0106 Induction Failures

- S0106, n = 181 (d = 128), 5-year = 26%

Years since registration

\(^1\)Othus, et al. BBMT 21:559, 2015
S0106 PIF – OS After Day 90

\[ \text{Time (years) from registration} \]

- No transplant, \( n = 47 \)
- Transplant, \( n = 74 \)

\[ ^1 \text{Othus, et al. BBMT 21:559, 2015} \]
Meta-Analysis of RCTs of HCT for AML CR1

Trials = 23
Patients = 5,839

Overall OS benefit in AML-CR1
OS benefit for Good Risk AML-CR1
OS benefit for Intermediate Risk AML-CR1
OS benefit for Poor Risk AML-CR1

Hazard Ratio of Death

Overall OS benefit in AML-CR1: 0.90 (0.82-0.98)
OS benefit for Good Risk AML-CR1: 1.37 (0.97-1.95)
OS benefit for Intermediate Risk AML-CR1: 0.82 (0.73-0.93)
OS benefit for Poor Risk AML-CR1: 0.74 (0.60-0.92)

Koreth, et al  JAMA 301:2349, 2009
Measurement of MRD after Induction

Polymerase-chain reaction

Multiparameter flow cytometry

Next generation sequencing
MRD in NPM-1 Mutated AML by PCR

Overall Survival

<table>
<thead>
<tr>
<th></th>
<th>No. of Patients</th>
<th>No. of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRD-negative</td>
<td>164</td>
<td>40</td>
</tr>
<tr>
<td>MRD-positive</td>
<td>30</td>
<td>21</td>
</tr>
</tbody>
</table>

P<0.001

Survival (%)

- MRD-negative: 73%
- MRD-positive: 24%

Years since Entry

Ivey, NEJM, 374:422, 2016
Targets for PCR Detection of AML in Adults

15-60
- None: 38%
- NPM1: 32%
- Other: 30%

>60
- None: 68%
- NPM1: 23%
- Other: 9%

FHCRC Study of Quality of CR¹

Non-Transplant Cohort

Cumulative Incidence of Relapse

Kaplan-Meier Curve of Relapse-Free Survival

¹Chen et al. JCO 33:1258, 2015
Favorable Risk AML

Post-remission therapy

Multiple cycles of HDAC containing chemotherapy

Reserve HCT until 1\textsuperscript{st} relapse

Consider HCT in CR1 if <3 log reduction in MRD or reappearance
Intermediate Risk AML

Post-remission therapy

Allogeneic HCT in CR1 if appropriate donor available

Consider withholding HCT if MRD negative and HCT CI >2
Advance Risk AML

Post-remission therapy

Allogeneic HCT if possible
Survival and Relapse Following CB vs MUD vs MMUD

Survival

P=0.57 for comparison of HLA-matched vs. cord blood
P=0.004 for comparison of HLA-mismatched vs. cord blood

Relapse

P=0.01 for comparison of HLA-matched vs. cord blood
P=0.04 for comparison of HLA-mismatched vs. cord blood

Milano, NEJM 375:944, 2016
AML in Older Patients

1. Increased incidence of MDR\(^1\) expression
2. Higher probability of unfavorable cytogenetics
3. More frequently associated with MDS
4. Comorbidities more common

\(^1\)Appelbaum et al. Blood 107:3481, 2006
HOVON Study\textsuperscript{1}

\textbf{Overall Survival}

<table>
<thead>
<tr>
<th>Total No.</th>
<th>No. Who Have Died</th>
<th>Conventional</th>
<th>Escalated</th>
</tr>
</thead>
<tbody>
<tr>
<td>411</td>
<td>340</td>
<td>402</td>
<td>325</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P=0.16</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total No.</th>
<th>No. Who Died</th>
<th>Conventional</th>
<th>Escalated</th>
</tr>
</thead>
<tbody>
<tr>
<td>149</td>
<td>128</td>
<td>150</td>
<td>109</td>
</tr>
<tr>
<td></td>
<td>P&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textbf{Overall Survival, Age 60–65 Yr}

<table>
<thead>
<tr>
<th>Total No.</th>
<th>No. Who Died</th>
<th>Conventional</th>
<th>Escalated</th>
</tr>
</thead>
<tbody>
<tr>
<td>262</td>
<td>212</td>
<td>252</td>
<td>216</td>
</tr>
<tr>
<td></td>
<td>P=0.43</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{1}Lowenberg at al. NEJM 361:1235, 2009
Allogeneic HCT versus Chemotherapy for AML CR1 age 50-70

National Cancer Center Hospital, Tokyo
Alternatives to LD ARA-C in Older AML Patients Unfit for Intensive Chemotherapy

5-azacytadine

decitabine

clofarabine

lenolidomide (5q-)

International Azacitidine Trial


The graph shows the survival probability over time from randomization (months) for patients on azacitidine treatment. The survival probability drops significantly after approximately 12 months, with 46.5% of patients surviving to that point. This is compared to the control group, where the survival probability drops to 34.2% after approximately 6.5 months. The CCR (complete cytogenetic response) is indicated as well, with azacitidine patients showing a higher CCR compared to the control group.
Generation of WT1-specific CTL

Stimulate with HLA-A*02:01 EBV/CMV peptide

Leukapheresis

Total production time: ~ 6 weeks
### Preliminary Clinical Outcomes: Treatment Arm

Patients on ARM 2 had many risk factors entering transplant

<table>
<thead>
<tr>
<th>Arm</th>
<th>Pt#</th>
<th>&gt;CR1</th>
<th>cyto</th>
<th>refractory (≥1cycle to achieve CR)</th>
<th>Dz at HCT</th>
<th>MDS-&gt;AML or secondary AML</th>
<th>2ND TX</th>
<th>chloroma</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>0.02% blasts</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>0.02% blasts</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>3.8% by cyto</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>0.01% blasts</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>no counts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>0.02% blasts</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>17</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Mielcarek M. et al., Biol Blood and Marrow Trans, 2007**

**Overall survival**

- Relapsed ≤100 days from HCT

**OS since 1st CTL infusion**

- Median days between HCT and 1st CTL infusion: 104
Preliminary Clinical Outcomes: Prophylactic Arm

Cumulation of risk factors on the prophylactic Arm

<table>
<thead>
<tr>
<th>Pt#</th>
<th>&gt;CR1</th>
<th>Cyto</th>
<th>refractory (&gt;1 cycle to achieve CR)</th>
<th>Dz at HCT</th>
<th>MDS-&gt;AML or secondary AML</th>
<th>Chloroma</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>X</td>
<td>(FLT3+)</td>
<td></td>
<td></td>
<td>MRD (cyto)</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>X</td>
<td>X</td>
<td>5.5% blasts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>X</td>
<td>(MLL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Historical PFS

Progression-Free Survival Arm 1 since 1st CTL infusion

*Chen GL et al., Biol Blood Marrow Trans. 2014.

Median days between HCT and 1st CTL infusion: 104
## Adult ALL – Remission Induction

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Remission Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>V + P</td>
<td>46%</td>
</tr>
<tr>
<td>V + P + LASP</td>
<td>47%</td>
</tr>
<tr>
<td>V + P + DNR</td>
<td>68%</td>
</tr>
<tr>
<td>V + P + DNR + LASP</td>
<td>83%</td>
</tr>
</tbody>
</table>
Adult ALL- CNS Prophylaxis

Without prophylaxis – risk is 35%
  risk factors include ↑ WBC, ↑ LDH, T-cell or mature B-cell phenotype

With prophylaxis – risk is 10%
  ? need for CXRT if IT-MTX is used
Post-Remission Therapy of Adult ALL

- Intensive multi-drug consolidation
- Autologous transplantation
- Allogeneic transplantation
## Contemporary Treatment

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Median age (range)</th>
<th>Ph+ (%)</th>
<th>T-cell (%)</th>
<th>CR</th>
<th>DFS at 3-9 yrs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRC/ECOG E2993</td>
<td>1826</td>
<td>31 (15-65)</td>
<td>19</td>
<td>20</td>
<td>91</td>
<td>38</td>
</tr>
<tr>
<td>CALGB 19802</td>
<td>163</td>
<td>41 (16-82)</td>
<td>18</td>
<td>-</td>
<td>78</td>
<td>35</td>
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<tr>
<td>GIMEMA ALL 0288</td>
<td>778</td>
<td>27.5 (12-60)</td>
<td>22</td>
<td>22</td>
<td>82</td>
<td>29</td>
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<tr>
<td>GMALL 05/03</td>
<td>1163</td>
<td>35 (15-65)</td>
<td>24</td>
<td>24</td>
<td>83</td>
<td>35</td>
</tr>
<tr>
<td>GOELAMS 02</td>
<td>198</td>
<td>33 (15-59)</td>
<td>22</td>
<td>21</td>
<td>86</td>
<td>41</td>
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<tr>
<td>Hyper-CVAD</td>
<td>288</td>
<td>40 (15-92)</td>
<td>17</td>
<td>13</td>
<td>92</td>
<td>38</td>
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<tr>
<td>JALSG-ALL93</td>
<td>263</td>
<td>31 (15-59)</td>
<td>22</td>
<td>21</td>
<td>78</td>
<td>30</td>
</tr>
<tr>
<td>LALA-94</td>
<td>922</td>
<td>33 (15-55)</td>
<td>23</td>
<td>26</td>
<td>84</td>
<td>36</td>
</tr>
</tbody>
</table>
High Risk ALL in CR1

Meta-analysis: 7 studies

- Sebban et al. 1994
- Takeuchi et al. 2002
- Dombert et al. 2002
- Hunault et al. 2004
- Thomas et al. 2004
- Labar et al. 2004
- Ribera et al. 2005

n=978 patients
p=.019

Hazard Ratio

No Donor
Donor
EFS of Young Adults 16-21 years old on CCG and CALGB Trials for ALL (1988-1995)

Proportion

0.0 0.2 0.4 0.6 0.8 1.0

CCG

CALGB (median = 2.5 yrs)

Years

0 2 4 6 8 10
Rituximab in B-Lineage Adult ALL

Maury, NEJM 375:1044, 2016

1
The Philadelphia Chromosome: t(9;22) Translocation
Survival in Ph-ALL by Treatment

- Hyper-CVAD + imatinib: 51 patients, 21 failed
- Hyper-CVAD: 50 patients, 46 failed

$p = .002$

Median follow-up: 3 years (range, 2-60 months)
Impact of Dasatinib plus Allogeneic HCT in Ph+ ALL\(^1\)

\(^1\)Ravandi et al. Blood Advances, 2016
Chemotherapy for Recurrent ALL\textsuperscript{1}

Salvage CR rate - 34%

CR duration - 6 months

1 yr survival - 24%

5 yr survival - 3%

\textsuperscript{1}Thomas, ASH, 1998
Inotuzumab Ozogamicin for Recurrent Adult ALL

1Kantarjian et al. NEJM 375:740, 2016
Blinatumomab for Recurrent Adult ALL\textsuperscript{1}

\textsuperscript{1}Topp et al., Lancet Oncology 16:57, 2015
CD19 CAR T Cells for Recurrent Adult ALL

N = 29
CR = 27 (93%)

1Turtle et al., JCI 126:2123, 2016
Acknowledgements

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