Treatment of Acute Leukemia In Adolescents and Young Adults
Common Types of Cancer Affecting AYAs

Source: http://www.cancer.gov/types/aya
FIGURE 3
Age-specific incidence of ALL and AML, children and adults

![Bar chart showing age-specific incidence of ALL and AML in children and adults. The chart displays the number of cases per 1,000,000 children and adults across different age groups.]
Case 1

BP

• 22 Yo Female, Ugandan
  – High school student
• ʰh/o Alcohol, ʰtobacco use
• HIV Negative
• Nulliparous

2 June 2016

Referral Diagnosis

POORLY DIFFERENTIATED ACUTE LEUKEMIA
(BMA/Bx)
Case 2

MI
- 21 Yo Male Ugandan (African)
- DJ,
- Single, with no children
- +ve Hx of alcohol intake
- HIV-Ve

August 2016

Referral Diagnosis
- ACUTE LYMPHOBLASTIC LEUKEMIA
Distinguishing between AML and ALL by morphology*

**Myeloid**
- Larger blasts with more voluminous cytoplasm
- Auer rods (most specific)

**Lymphoid**
- Smaller blasts with very little cytoplasm
- “Hand mirror” sign with pinched cytoplasm

*Except for Auer rods, these features are helpful, but not entirely specific*
<table>
<thead>
<tr>
<th>Cytochemical Reaction</th>
<th>Cellular Element Stained</th>
<th>Positive Staining</th>
<th>Negative Staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myeloperoxidase (MPO)</td>
<td>Myeloid granules</td>
<td><strong>Myeloblasts</strong></td>
<td>Lymphoblasts Early myeloblasts</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Promyelocytes (strong)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Monoblasts (weak +/−)</strong></td>
<td></td>
</tr>
<tr>
<td>Sudan Black B (SBB)</td>
<td>Phospholipid</td>
<td><strong>Myeloblasts</strong></td>
<td>Erythroblasts Megakaryoblasts</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Lymphoblasts (+/-)</strong></td>
<td></td>
</tr>
<tr>
<td>Non-specific esterase (NSE)</td>
<td>Cellular enzyme</td>
<td><strong>Monoblasts and promonocytes</strong></td>
<td>Most myeloblasts and lymphoblasts</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Megakaryoblasts (+/-)</strong></td>
<td></td>
</tr>
<tr>
<td>Periodic-Acid Schiff (PAS)</td>
<td>Glycogen</td>
<td><strong>Erythroblasts</strong></td>
<td>Most myeloblasts/monoblasts</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Lymphoblasts</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>(granular)</strong></td>
<td></td>
</tr>
</tbody>
</table>
Distinguishing between AML and ALL using cytochemical stains (2)

<table>
<thead>
<tr>
<th></th>
<th>MPO</th>
<th>SBB</th>
<th>SPE</th>
<th>NSE</th>
<th>PAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myeloblasts</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>Diffuse-Weak</td>
</tr>
<tr>
<td>Lymphoblasts</td>
<td>-</td>
<td>- / weak +</td>
<td>-</td>
<td>+/-</td>
<td>Block-Granular</td>
</tr>
<tr>
<td>Monoblasts</td>
<td>+/-</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>Diffuse-Weak</td>
</tr>
</tbody>
</table>

- Myeloblast: M0: neg for all; M1 through M6: +MPO; M7: neg for MPO
- Lymphoblast: +PAS and acid phosphatase, +/- sudan black, neg for others
- Monoblast: strong +NSE, Lysozyme; neg to weak for MPO

![SBB, MPO, Wright-Giemsa, Brown: α-naphthyl acetate esterase (NSE), Blue: chloroacetate esterase (SPE)]
Adolescents and Young Adults with ALL

• Acute Lymphoblastic Leukemia (ALL) survival rate is close to 90% in young children.

• In older adolescents and young adults (AYA), event-free survival is only 30-45%.

• Improved outcome, with disease-free survival rates of 60-70%, are achieved when AYA patients are treated with “pediatric-inspired” approaches.

• National Cancer Institute has defined the AYA population as those between 15 and 39 years of age.
Treatment Regimens - ALL

• Adult Regimens:
  – Intensive use of myelosuppressive agents:
    • Daunorubicin
    • Cytarabine
    • Cyclophosphamidnede
    • Allogeneic stem cell transplantation (SCT)

• Pediatric Regimens:
  – Berlin-Frankfurt-Munster (BFM) backbone:
    • Glucocorticoids
    • Vincristine
    • Asparaginase
    • Early and frequent CNS prophylaxis and prolonged maintenance therapy
Standard supportive care and monitoring

• Allopurinol is recommended for the first 10 days of induction therapy to prevent hyperuricemia.

• Antimicrobial prophylaxis: antiviral and *Pneumocystis jiroveci* prophylaxis should be used throughout treatment.

• Fungal prophylaxis should include mold coverage throughout induction therapy.
  – Broader spectrumazole antifungals cannot be used with vincristine.

• Asparaginase-related toxicities
  – Asparaginase-related hypersensitivity reactions can occur in 20% of children and adults.
Adolescent and Young Adults with AML

• Acute Myeloid Leukemia (AML) represents 33% of adolescent and 50% of young adult leukemia.

• Diagnosis should be based on cytogenetic and molecular factors to avoid overtreatment.

• Poorer prognosis of AYAs with ALL can be overcome with intensive pediatric protocols; whether a similar approach would benefit AYAs with AML has not yet been established.

• Intensifying therapy, or “one-size-fits-all” therapy, does not improve survival rates.
Treatment Regimens - AML

• “3+7” continues to be the backbone of induction therapy.
  – (daunorubicin 60–90 mg/m²/day idarubicin 10–12 mg/m²/day or mitoxantrone 10–12 mg/m²/day) and seven days of cytarabine (100–200 mg/m²/day)

• AYA patients usually receive one or two cycles of induction therapy.

• Additional CNS therapy is routine in most pediatric protocols.

• Bone marrow assessment on the 7th or 10th day after completion of induction treatment.
AML in AYA is often curable with chemotherapy alone

Retrospective analysis of 432 AYA (16-29) with AML at MDACC, 1965-2009:

• Median age 23
• 17% had core binding factor (CBF; t(8;21) or inv(16) AML)
• 12% had acute promyelocytic leukemia (APL; t(15;17))
• CR rates:
  – 93% for CBF AML
  – 78% for APL
  – 77% with diploid karyotype
  – 68% for other AML
• AML outcome in AYA superior to that in older adults
Factors contributing to improved AML outcome in AYA

• Disease biology is different in AYA
  – Lower incidence of abnormal/complex cytogenetics
  – Reduced incidence of secondary/therapy-related AML than is seen in older patients

• Better tolerance of AML chemotherapy
  – Better suited for more dose-intense regimens

• Less comorbid conditions at baseline

• Taking less concomitant medications
  – Fewer drug-drug interactions and toxicities

• Lower incidence of abnormal/complex cytogenetics
References

- http://www.cancer.gov/types/aya

- http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4470138

- Pemmaraju et al., Clinical characteristics and outcomes of AYA with AML. Clin Lymph Myel Leuk, in press (2016).