Adult lymphoblastic lymphoma
Lymphoma Tumor Board
February 3, 2017
Diagnosis

- Lymphoblastic Lymphoma (LBL) is rare
- Sub-type of lymphoma that is generally of T-cell origin
- Comprises about 2% of all NHLs in adults
- Characteristics are almost identical to acute lymphoblastic leukemia (ALL)
- Patients with predominately nodal disease at presentation are classified as LBL whereas those with primarily disease in the marrow or peripheral blood are classified as ALL.
- Historically, no standard of care treatment specifically designed for LBL
- Pathology:
  - IHC panel: CD45 (LCA), CD19, CD20, CD79a, CD3, CD2, CD5, CD7, TdT, CD1a, CD10, or Cell surface marker analysis by flow cytometry: kappa/lambda, CD45, CD3, CD5, CD19, CD10, TdT, CD13, CD33, CD1a, cytoplasmic CD3, CD22, myeloperoxidase
Classification

ALL - CLASSIFICATION WHO

- Uses immunophenotypic classification:
  - Acute lymphoblastic leukemia/lymphoma (Former Fab L1/L2)
    - Precursor B acute lymphoblastic leukemia/lymphoma.
      - Cytogenetic subtypes:
        - t(12;21)(p12;q22) TEL/AML-1
        - t(1;19)(q23;p13) PBX/E2A
        - t(9;22)(q34;q11) ABL/BCR
        - T(V,11)(V;q23) V/MLL
    - Precursor T acute lymphoblastic leukemia/lymphoma
  - Burkitt's leukemia/lymphoma (Former FAB L3) (mature B cell ALL)
  - Biphenotypic acute leukemia (2 to 5%)
**Image A.** T-cell lymphoblastic lymphoma/leukemia in bone marrow biopsy. Neoplastic lymphocytes surround residual megakaryocytes and erythroid precursors. H&E section of formalin fixed tissue.

**Image B.** T-cell lymphoblastic lymphoma/leukemia. Cytology of lymphoblasts reveals medium sized cells with delicate unclumped chromatin, convoluted nuclear membrane and small but distinct nucleoli.
Treatment

• Adaptation of pediatric protocols of intensive chemotherapy and CNS prophylaxis has led to marked improvements in outcomes in adults

• Numerous chemotherapy/radiotherapy regimens are similar in dose and schedule to ALL regimens

• Common features of these regimens include:
  • Induction therapy
  • CNS prophylaxis
  • Consolidation therapy
  • Subsequent maintenance therapy for 12 to 18 months

• Long-term disease-free survival rates between 40-70%
The landscape of genetic alterations in T-ALL

Mark R. Litzow, and Adolfo A. Ferrando Blood
2015;126:833-841
ALL: TYPICAL TREATMENT

- Primary objective: to achieve and maintain a complete remission (CR)
- Induction, consolidation, maintenance phases
  - CNS prophylaxis with IT-MTX during induction and consolidation phases

```
CNS Prophylaxis (IT-MTX)

Induction → Consolidation → Maintenance
```

Over a period of months 2-3 years
# Treatment

## Table 1

<table>
<thead>
<tr>
<th>Author</th>
<th>Regimen</th>
<th>N</th>
<th>Response Rate</th>
<th>Failure-Free Survival/Relapse-Free Survival</th>
<th>Overall Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coleman et al</td>
<td>Two ALL-type protocols with intensified CNS</td>
<td>44</td>
<td>100%</td>
<td>3-yr FFS = 56%</td>
<td>NA</td>
</tr>
<tr>
<td>Slater et al</td>
<td>Various ALL protocols</td>
<td>51</td>
<td>80% CR for “nonleukemic”; 77% CR for leukemia</td>
<td>NA</td>
<td>5-yr actuarial OS = 45%</td>
</tr>
<tr>
<td>Bernasconi et al</td>
<td>Various ALL protocols</td>
<td>31</td>
<td>77% OR</td>
<td>3-yr RFS = 45%</td>
<td>3-yr OS = 59%</td>
</tr>
<tr>
<td>Levine et al</td>
<td>Modified LSA₃L₂</td>
<td>15</td>
<td>73% CR; 27% PR</td>
<td>5-yr actuarial FFS = 35%</td>
<td>5-yr actuarial OS = 40%</td>
</tr>
<tr>
<td>Weinstein et al</td>
<td>APO</td>
<td>21</td>
<td>95% CR</td>
<td>3-yr actuarial FFS = 58%</td>
<td>5-yr actuarial OS = 69%</td>
</tr>
<tr>
<td>Hoelzer et al</td>
<td>Two ALL-type protocols, both including CNS and</td>
<td>45</td>
<td>93% CR</td>
<td>7-yr actuarial DFS = 62%</td>
<td>7-yr actuarial OS = 51%</td>
</tr>
<tr>
<td>Thomas et al</td>
<td>HyperCVAD</td>
<td>33</td>
<td>91%</td>
<td>3-yr PFS = 66%</td>
<td>3-yr OS = 70%</td>
</tr>
<tr>
<td>Jabbour et al</td>
<td>LMT-89 (ALL-type induction regimen derived)</td>
<td>27</td>
<td>85% OR</td>
<td>5-yr FFP = 44%</td>
<td>5-yr OS = 63%</td>
</tr>
<tr>
<td>Song</td>
<td>“Hybrid” NHL/ALL regimen</td>
<td>34</td>
<td>100% OR</td>
<td>4-yr EFS = 68%</td>
<td>4-yr OS = 72%</td>
</tr>
</tbody>
</table>

ALL = acute lymphoblastic leukemia; APO = doxorubicin (Adriamycin), prednisone, vincristine (Oncovin); CHOP = cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone; CNS = central nervous system; CR = complete response; DFS = disease-free survival; EFS = event-free survival; FFP = freedom from progression; FFS = failure-free survival; HyperCVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone, cytarabine, methotrexate; IPI = International Prognostic Index; NA = not available; NHL = non-Hodgkin lymphoma; OR = overall response; PR = partial response; RFS = relapse-free survival; SCT = stem cell transplantation.
Treatment

Newly Diagnosed T-ALL

Suitable for pediatric-intensive chemotherapy

Pediatric-intensive multi-agent chemotherapy regimen

CR

MRD negative/no adverse genetics*

Consolidation / Maintenance Chemotherapy

No CR

MRD positive and/or adverse genetics*

Nelarabine/clinical trial/other salvage chemotherapy

Allogeneic SCT (MA or RIC)

Not suited for pediatric-intensive chemotherapy (older age, co-morbidities)

Conventional multi-agent chemotherapy

No CR

MRD positive and/or adverse genetics*#

MRD negative/no adverse genetics*#

CR

Consolidation / Maintenance Chemotherapy

Observe

Blood 2015 126:833-841; doi: https://doi.org/10.1182/blood-2014-10-551895
Supportive care

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

- Antimicrobial prophylaxis, antiviral and *Pneumocystis jiroveci* pneumonia prophylaxis throughout treatment.

- Fungal prophylaxis should include mold coverage throughout induction therapy.
  - Broader spectrum azole antifungals should be used with caution when using vincristine.

- Asparaginase-related toxicities
  - Asparaginase-related hypersensitivity reactions can occur in 20% of children and adults.
OS from the diagnosis of patients with B- vs T-ALL in the UKALLXII/E2993 trial

Mark R. Litzow, and Adolfo A. Ferrando Blood 2015;126:833-841
References

- https://www.verywell.com/lymphoblastic-lymphoma-2252372
- ASH Image Bank: http://imagebank.hematology.org/
- http://www.slideshare.net/usmlegalaxy/acute-lymphoblastic-lymphoma
- http://www.cancernetwork.com/articles/treatment-lymphoblastic-lymphoma-adults