Acute lymphoblastic leukemia
Pre- and Post-Disease Form

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Acute lymphoblastic leukemia

- SEER
  - Age-adjusted incidence rate 1.6 per 100,000 men and women per year
  - ~60% were diagnosed under age 20
  - Overall survival ~ 65%
- Treatment
  - Chemotherapy ± irradiation
  - Hematopoietic cell transplantation
Classification

- Immunophenotyping by flow cytometry
  - Important in diagnostic evaluation
  - Allows classification of ALL
    - B-lineage (B lymphocytes)
    - T-lineage (T lymphocytes)
  - B-lineage = pre-B and mature B ALL
  - T-lineage = T cell
Classification

- Cytogenetics
  - Important for classification/prognosis
- Common abnormalities
  - Translocations: t(9;22), t(4;11), t(1;19), t(8;14), t(10;14)
  - Structural abnormalities: 9p, 6q, 12p
  - Number of chromosomes in cell
    - Hypo, hyper, tri/tetra diploid
<table>
<thead>
<tr>
<th>Cytogenetic abnormality</th>
<th>Genetic alteration</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(9;22)</td>
<td>BCR/ABL</td>
<td>Unfavorable</td>
</tr>
<tr>
<td>t(4;11)</td>
<td>AF4/MLL</td>
<td>Unfavorable</td>
</tr>
<tr>
<td>t(1;19)</td>
<td>PBX/E2A</td>
<td>Unfavorable</td>
</tr>
<tr>
<td>t(12;21)</td>
<td>TEL/AML1</td>
<td>Favorable</td>
</tr>
<tr>
<td>Hyperdiploid &gt;50</td>
<td>__</td>
<td>Favorable</td>
</tr>
<tr>
<td>Hypodiploid ≤45</td>
<td>__</td>
<td>Unfavorable</td>
</tr>
</tbody>
</table>
**Prognostic Features (adults)**

- White blood cell count (>30,000 µL)
- Age > 50 years
- Lack of mediastinal mass
- Poor performance status at diagnosis
- Cytogenetic abnormalities
  - t(9;22) or bcr-abl rearrangement
  - t(4;11), t(1;19), t(8;14)
- > 4 weeks of induction therapy to achieve 1\textsuperscript{st} remission
- MRD
Indications for HCT (adults)

- 1st CR and HLA-matched sibling donor
  - t(9;22), undifferentiated ALL, >4 weeks to achieve CR1, age>35 years, WBC >30,000/mL

- Other indications
  - Induction failure
  - Leukemia relapse (independent of CR1 duration)
Prognostic Features (children)

- National Cancer Institute risk group
  - Age at diagnosis and WBC count
  - Good risk:
    - Age 1-10 years and WBC < 50,000
  - Poor risk:
    - All others
- As with adults cytogenetics is predictive of outcome
- > 4 weeks of induction therapy to achieve 1st remission
- MRD
Indications for HCT (children)

- 1\textsuperscript{st} CR
  - t(9;22), hypodiploidy, induction failure
- 2\textsuperscript{nd} CR
  - Bone marrow recurrence <36 months from diagnosis
- 3\textsuperscript{rd} CR
  - Outcome influenced by duration of CR1 and CR2
  - Induction failure
Donor and Graft selection for HCT

- When available: matched family donor
- If none, suitably matched unrelated donor
- Graft choices
  - Bone marrow
  - Peripheral blood progenitor cells
  - Umbilical cord blood
Pre-HCT data

- Type of HCT and graft type
- Disease-related variables
  - Date of diagnosis
  - Presence of extramedullary disease
  - Predisposing condition
    - AA, Bloom, Fanconi, Down, other
- Cytogenetics
  - If tested → abnormality/none/not evaluable
Cytogenetics

- If ‘yes’ abnormalities identified
  - List of probable cytogenetic abnormalities provided
  - If more than 1, tick all that apply
  - If report available please attach copy
  - If patient’s cytogenetic abnormality (not breakpoints) is not listed please use ‘other’ option

- Abnormalities can be at diagnosis or anytime prior to conditioning for HCT
Treatment pre-HCT

- Purpose of therapy
  - Induction of remission
  - Consolidation of remission
  - Maintenance of remission
  - Treatment for relapse
  - Central nervous system (CNS)
    - CNS prophylaxis given during induction, consolidation and maintenance periods
Response to pre-HCT treatment

- Complete response
  - Continuous complete response (if the patient achieves CR and continues in CR)
- If not a ‘complete response’ then mark the ‘no complete response’ option
  - e.g. if ‘no complete response’ after 1st line of therapy re-evaluate after 2nd line and could achieve ‘complete response’
Response to pre-HCT treatment

- Date response achieved
  - 1\textsuperscript{st} complete remission is critical
- Date of relapse (if relapse occurs)
- Interval between 1\textsuperscript{st} CR and relapse is an important prognostic variable
- Site of relapse
  - Bone marrow
  - CNS
  - Testes
  - Other sites
Laboratory studies

- At diagnosis (Q 121 – 124)
  - White blood cell count
  - % blasts in blood
  - % blasts in bone marrow
  - Date of bone marrow examination

- Tests for molecular markers
  - BCR / ABL
  - TEL / AML
  - Other (if applicable)
Disease status prior to HCT

- Based on hematological tests (Bone marrow)
  - 1\textsuperscript{st} CR; if in 1\textsuperscript{st} CR is the patient in cytogenetic and/or molecular remission
  - 2\textsuperscript{nd} CR, ≥ 3\textsuperscript{rd} CR
  - Primary induction failure (not in CR after multiple cycles of induction chemotherapy)
  - 1\textsuperscript{st}, 2\textsuperscript{nd}, ≥ 3\textsuperscript{rd} relapse
    - If not in remission indicate the sites of disease, cytogenetic and/or molecular test results
- Minimal residual disease
Post-HCT planned treatment

- Planned post-HCT therapy: this is treatment that has been planned prior to HCT and executed after HCT
  - CNS irradiation
  - Systemic therapy
    - List of drugs provided or use ‘other’ option
  - Donor leukocyte infusion
  - Other treatment
Post HCT - Best Response

- Was CR achieved in response to HCT?
  - Already in CR pre-HCT and continued in CR ("Not applicable")
  - If transplanted in relapse/PIF
    - Was CR achieved post-HCT?
      - Yes give date
      - No, CR was not achieved
        - Give date assessed in reporting period.
Post HCT disease assessment

- Leukemia recurrence (Q 25 – 41)
  - If yes, dates of molecular and/or cytogenetic and/or hematological assessments
  - Evidence of disease by each of the above-mentioned methods

- Status
  - Hematological: relapse
  - Other methods: relapse or progression
Post HCT disease assessment

- If patient had recurrent or persistent leukemia
  - Did he/she receive treatment?
  - If yes, type of treatment
    - Systemic therapy
    - Donor leukocyte infusion
    - Subsequent HCT
Post HCT disease assessment

- Current disease status
  - If same as in Q 25-41 and no treatment given no further information required
  - Else: molecular and/or cytogenetic and/or hematological assessments as in Q 25-41