Acute Lymphoblastic and Myeloid Leukemia
Pre- and Post-Disease Form

Mary Eapen MD, MS
Acute Lymphoblastic Leukemia
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 of ALL

- This has prognostic implications
- Immunophenotype
  - Determine cell lineage
- Cytogenetics
- Genetic alteration/molecular marker
- This information is used to determine intensity of treatment so as to offer the best chance of survival
Classification - Cell lineage -

- Immunophenotyping is determined 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
- Prognostic significance
- Common abnormalities
  - Translocations: (9;22), (4;11)(1;19), (8;14), (10;14)
  - Structural abnormalities: 9p, 6q, 12p
  - Number of chromosomes in cell
    - Hypo, hyper, tri/tetra diploid
## Cytogenetics

<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>
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<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>
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<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

- 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
- Cytogenetics is predictive of outcome
- Time to 1st CR: > 4 weeks of induction therapy to achieve 1st remission signals “high risk”
- Minimal residual disease (MRD)
  - At end of induction also signals “high risk”
Indications for HCT

- **1st CR**
  - t(9;22), hypodiploidy, induction failure, >4 wks to 1st CR
- **2nd CR**
  - Bone marrow recurrence <36 months from diagnosis
- **3rd CR**
  - Outcome influenced by duration of 1st CR and interval between 1st & 2nd CR
  - Induction failure
Donor and Graft selection for HCT

- When available: matched family donor is ideal
- If none, suitably matched unrelated donor
- Indications for HCT are the same for either donor type
- Graft choices
  - Bone marrow
  - Peripheral blood progenitor cells
  - Umbilical cord blood
Donor and Graft selection for HCT

- Related donor HCT
  - Bone marrow is the most common graft used
- Unrelated donor HCT
  - Bone marrow and cord blood are the most common grafts used
- With either donor use of peripheral blood graft is discouraged
  - Higher chronic GVHD translates into higher mortality
The pre- and post ALL Report Forms
Pre-HCT data

- Disease-related variables
  - Date of diagnosis
  - Predisposing condition
    - AA, Bloom, Fanconi, Down, other
  - Presence of extramedullary disease
    - CNS, mediastinum, testes
- Cytogenetics
  - If tested → list the abnormality/normal cytogenetics/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 your patient’s cytogenetic abnormality is not listed please use ‘other’ option

- Abnormalities can be at diagnosis or anytime prior to conditioning for HCT
  - Both are relevant
Example

- TEL AML genetic alteration
  - t(12;21) (p13;q22)
  - TEL/AML positive (+/- same report)
    - (fusion of TEL gene at 12p13 with AML gene at 21q22)
- If 3 or more cytogenetic abnormalities occur this is referred to as ‘complex’
  - Please indicate all abnormalities; if you are unsure of the number of abnormalities please list them and the CIBMTR will determine whether complex or other
Treatment pre-HCT

- Purpose of therapy
  - Induction of remission after diagnosis
    - Attain remission (1st CR)
  - Consolidation of remission
  - Maintenance of remission
    - Both steps to ensure continued CR
  - 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 1\textsuperscript{st} line of therapy re-evaluate after 2\textsuperscript{nd} line and could achieve ‘complete response’
Response to pre-HCT treatment

- Date response achieved
  - 1st CR is critical

- Date of relapse (if relapse occurs)
  - Critical to determine interval between 1st CR and relapse

- Site of relapse
  - Bone marrow
  - CNS
  - Testes
  - Other sites
Other Laboratory Tests

- At diagnosis (Q 121 – 123)
  - White blood cell count
  - % blasts in blood
  - % blasts in bone marrow
  - Date of bone marrow examination
Other Laboratory Tests

- Q 125 – 130
- Molecular markers
  - BCR / ABL
  - TEL / AML
- Other molecular testing performed
  - Report test and results; example: MLL gene rearrangement
**Disease status prior to HCT**

- Based on hematological tests (Bone marrow)
  - 1\textsuperscript{st} CR; if in 1\textsuperscript{st} CR is the patient is 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 (not asked now)
- When available please provide date of assessment
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
- This does not refer to therapy if the patient relapses post-HCT
Post HCT disease assessment

- Was CR achieved in response to HCT?
  - Already in CR pre-HCT and continued in CR
  - If transplanted in relapse/PIF
    - Was CR achieved after HCT?
    - Yes – date; clinical /heamatologic CR
  - Cytogenetic test results if performed including date
Post HCT disease assessment

If CR was not achieved after HCT

- Indicate any treatment given
  - CNS irradiation
  - Systemic / intrathecal therapy
  - Donor leukocyte infusion
  - Second HCT
  - Other treatment - specify
Post HCT disease assessment

- If the patient has a relapse post-HCT
  - Specify: molecular, cytogenetic or clinical/hematologic
  - Indicate presence or absence of disease by method of assessment
- Important to indicate dates of assessment
Post HCT disease assessment

- Current disease status
  - Q 58 – 63
  - If assessment is “yes” to Q 25 then you have already reported the necessary information by answering Q 26 – 41
  - If answer to Q 25 is “no” then proceed to Q 58 and provide appropriate responses
Acute Myeloid Leukemia
Acute Myeloid Leukemia

- **SEER**
  - Age-adjusted incidence rate 3.5 per 100,000 men and women per year
  - Unlike ALL, only 6% of patients with AML are diagnosed under the age of 20 years

- **Treatment**
  - Chemotherapy ± irradiation
  - Hematopoietic cell transplantation
Classification of AML
- World Health Organization -

- AML with recurrent genetic abnormalities
  - Translocation of genes b/w chr 8 & 21
  - Translocation of genes b/w chr 15 & 17
  - Inversion or translocation of genes on chr 16
  - Abnormalities of chr 11
  - Acute promyelocytic leukemia
Classification of AML
- World Health Organization -

- AML with multilineage dysplasia (leukemia in which more than 1 myeloid cell type is involved)
  - With prior MDS
  - Without prior MDS

- AML with MDS, therapy related
Classification of AML
- World Health Organization -

- AML not otherwise categorized
  - AML minimally differentiated (M0)
  - AML without maturation (M1)
  - AML with maturation (M2)
  - Acute myelomonocytic leukemia (M4)
  - Acute monocytic leukemia (M5)
  - Acute erythroid leukemia (M6)
  - Acute megakaryocytic leukemia (M7)
  - Acute basophilic leukemia
  - Acute panmyelosis with myelofibrosis
Prognostic Features

- In addition to length of 1st CR
- Chromosomal abnormalities are very important
- By analyzing cytogenetic abnormalities at diagnosis we know:
  - $t(8;21), t(15;17)$ and inversion 16 are favorable cytogenetics (low risk)
  - Complex karyotype ($\geq 5$ abnr), monosomy 7, monosomy 5, del (5q) or abnormalities of 3q are unfavorable (high risk)
  - All others are assigned intermediate risk
Indications for HCT

- 80-90% of children treated on current chemotherapy trials achieve CR
- In N. America
  - Those in 1\textsuperscript{st} CR with matched sibling proceed to HCT
- Absence of a matched sibling – continue chemotherapy
  - 30-40% of these patients will relapse
- Alternative donor HCT is reserved for those in 2\textsuperscript{nd} CR, not in remission after relapse or induction failure
Graft choices for HCT

- Related donor HCT
  - Bone marrow is the most common graft used
- Unrelated donor HCT
  - Bone marrow and cord blood are the most common grafts used
- With either donor use of peripheral blood graft is discouraged
  - Higher chronic GVHD translates into higher mortality
The pre- and post AML Report Forms

There are several questions that are common to both the ALL and AML Forms
Pre-HCT data

- Disease-related variables
  - Date of diagnosis
  - Is this therapy-linked?
    - lymphoma, breast cancer, other
  - Prior hematologic disorder
    - Date of onset and indicate from list the prior hematologic disorder
- Predisposing condition
  - AA, Bloom, Fanconi, Down, other
Laboratory Tests

- At diagnosis (Q 16 – 18)
  - White blood cell count
  - % blasts in blood
  - % blasts in bone marrow
  - Date of bone marrow examination

- Though not a lab test:
  - Q19 asks for sites of extramedullary disease at diagnosis
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 your patient’s cytogenetic abnormality is not listed please use ‘other’ option

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

- Purpose of therapy
  - Induction
  - Consolidation
  - Maintenance
- Important to indicate:
  - Number of cycles & drugs administered
  - Dates / site of radiation
  - Response to treatment
- Indicate if remission was achieved; if not provide date of relapse
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 1\textsuperscript{st} line of therapy re-evaluate after 2\textsuperscript{nd} line and could achieve ‘complete response’
Prior to HCT

- Q 152 – 155
  - Assessment of leukemia: blood tests and bone marrow test
- Important to document
  - Disease status at transplantation. This is an important determinant of how well the patient will do after HCT
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
- This does not refer to therapy if the patient relapses post-HCT
Post HCT disease assessment

- Assess best response to HCT + any planned treatment
- Provide date of response if patient was not in CR at HCT and achieved CR after HCT
- Indicate all methods that were employed and dates tested:
  - Hematologic / molecular / cytogenetic
Post HCT disease assessment

- If the patient has a relapse post-HCT
  - Specify: molecular, cytogenetic or clinical/hematologic
  - Indicate presence or absence of disease by method of assessment
  - Important to indicate dates of assessment
Post HCT disease assessment

- Please remember to provide the current disease status and date of testing
- This particularly important for those patients who relapse after HCT
  - Document what happened to patients if they were treated for their relapse
Summary

- ALL and AML are acute leukemias
- Though biologically different, data collection forms have several common features
- Some dates are critical: date of 1st CR, date of relapse (pre- & post-HCT) and response to HCT
- Documenting response to HCT particularly for patients who relapse after HCT can be challenging
I would like to thank Diane Knutson for graciously agreeing to give this presentation on my behalf.

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