Leukemia and Lymphoma Overview

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CALGB CRA Orientation, April 2008

For CALGB Participants Only

Topics

• Acute leukemias
  – Acute lymphocytic leukemia (ALL)
  – Acute myelogenous (granulocytic) leukemia (AML or AGL, rarely “ANLL”)

• Chronic leukemias
  – Chronic myelogenous (granulocytic) leukemia (CML, or CGL)
  – Chronic lymphocytic leukemia (CLL)

• Multiple myeloma (MM)
## 2008 Estimated US Cancer Cases*

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td>Prostate</td>
<td>25%</td>
<td>Breast</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>15%</td>
<td>14%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>10%</td>
<td>10%</td>
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<tr>
<td>Urinary bladder</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>5%</td>
<td>4%</td>
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<tr>
<td>Melanoma of skin</td>
<td>5%</td>
<td>4%</td>
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<tr>
<td>Kidney &amp; renal pelvis</td>
<td>4%</td>
<td>4%</td>
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<tr>
<td>Oral cavity</td>
<td>3%</td>
<td>3%</td>
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<tr>
<td>Leukemia</td>
<td>3%</td>
<td>3%</td>
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<tr>
<td>Pancreas</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>All Other Sites</td>
<td>20%</td>
<td>23%</td>
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## 2008 Estimated US Cancer Deaths*

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
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</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>31%</td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>10%</td>
<td>Breast</td>
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<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>All other sites</td>
<td>24%</td>
<td>25%</td>
</tr>
</tbody>
</table>

*ONS=Other nervous system. Source: American Cancer Society, 2008.
**Diagnostic Studies**

- Peripheral blood
- Bone marrow
- Cytogenetics
- Flow cytometry
- Cytochemistry (special stains)
- Molecular markers
- For myeloma - SPEP, UPEP, Quantitative immunoglobulins, immuno-electropheresis

**Staging**

- Most leukemias are not staged
- Chronic lymphocytic leukemia (CLL)
  - 5 Stages (Rai-Sawitsky) classification), 0 - IV
  - Based upon lymphocyte numbers, adenopathy, anemia, thrombocytopenia
- Multiple myeloma
  - 3 stages, based upon multiple factors: hemoglobin, M protein, calcium, bone lesions
Prognostic Factors

• Vary with leukemia type
  - AML
    • 7 subtypes, M1 through M7 (M3 especially important)
    • Cytogenetics
  - ALL
    • Cytogenetics
  - CGL
    • Stage: Chronic, accelerated, Blast crisis

Treatment – Acute Leukemias

• Chemotherapy
  - Induction
  - Consolidation/re-induction
  - Maintenance
• Central nervous system prophylaxis-
  intrathecal chemotherapy
• Supportive therapy
  - Growth factors
Other Treatments – Acute Leukemias

- High dose chemotherapy with stem cell rescue-autologous or allogeneic
- Monoclonal antibodies – Mylotarg, etc.
- For acute progranulocytic leukemia (M3)-All-trans retinoic acid (ATRA)

Treatment – Chronic Leukemias

- CLL - chlorambucil, cyclophosphamide, prednisone, fludarabine, rituximab, Campath 1-H, now combinations
- CML - Hydroxyurea, α-interferon, Gleevec
- MM - alkeran/prednisone, thalidomide, dexamethasone, VAD (vincristine, adriamycin, dexamethasone), bortezomib, stem cell transplant
Response Assessment

- Complete (hematologic) response
- Partial response
- New categories of response: CR-platelet
- Relapse

Follow-up

- Blood counts
- Bone marrows
- Cytogenetics
- Other genetic markers
- Myeloma - SPEP, UPEP, bone x-rays,
  - β2 microglobulin
Two Major Types

- Hodgkin’s Disease (HD)
- Non-Hodgkin Lymphomas (NHL)
Lymphoma Pathology

- Accurate diagnosis is key to good clinical trials and slide may be reviewed centrally to assure the correct diagnosis.
- Cytogenetics and molecular diagnostics may be needed to adequately diagnose a lymphoma.
- There are also benign conditions that mimic lymphomas.

Diagnostic Studies

- Lymph node biopsy
- Bone marrow aspiration and biopsy
- Flow cytometry
- Genetic studies
- Cytogenetics
Staging Studies

- Bone marrow aspiration and biopsy
- CTs
- Radionuclide scans: bone, Gallium, PET
- GI x-rays
- Spinal fluid analysis
- Others

Staging

- Same system for HD and NHL
- Four Stages
  - I: One lymph node group
  - II: Two lymph node groups
  - III: Nodes above and below diaphragm
  - IV: Organ involvement
Prognostic Factors

• Stage - which factors in systemic symptoms, extranodal disease, and tumor bulk

• Histologic subtype
  - Hodgkin’s Disease
    • Lymphocyte dominant
    • Nodular sclerosing
    • Mixed cellularity
    • Lymphocyte depletion

• Non-Hodgkin Disease (up to 17 subtypes)
  • Follicular/diffuse
  • Cell type
  • Patterns
Prognostic Factors

• Histologic subtype
  – Non-Hodgkin Disease - many subtypes and variations
    • Low grade (indolent)
    • Intermediate grade
    • High grade (aggressive)

Treatment

• Chemotherapy
• Radiation therapy
• Monoclonal antibodies - with or without radiolabel or toxin
• High dose chemotherapy with stem cell rescue
Response Assessment

- Complete response
- Partial response
- Stable disease
- Progression/relapse

Special Considerations

- Leukemia <-> lymphoma?
- Transformation from one cell type to another
- Composite lymphomas
- HD - nodal distribution until disseminated
- NHL - frequently extranodal, and may be only extranodal
Follow-up

- Relapse (Progression free survival)
- Overall survival
- Toxicity (including second malignancies, fertility)
- Quality of life