Welcome and Introductions

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Disclosures

• Has no affiliations with commercial interests to disclose

Objectives of the Talk

• To learn about AML and subtypes
• To review current and emerging treatments
• To discuss managing side-effects from the AML and treatment
• To review the importance of communicating with your team
Etiology of AML

• A disease derived from a new, single, genetically aberrant cell
• Family factors – some families have increased susceptibility to accumulate genetic injury during life
• Environment – medications, harmful chemicals, radiation, chemotherapy can cause problems
• Time (age) – allows accumulation of events

As We Live, Mutations Accumulate
Mutations Accumulate and Get Fixed (Mostly When We’re Young)

Mutations Accumulate and Get Fixed (Less Well as We Age)
Fewer Mutations Accumulate in Healthy Individuals

More Mutations Accumulate in Unhealthy Individuals
Mutations May Occur in Critical Areas of Our Genes
AML Incidence By Age
In the United States

SEER database

Stem Cells Grow and Mature to
Make Blood Cells

Renewing stem cell
Growing AND maturing
“Grown-up”
Growth *WITHOUT* Maturing Leads to AML

Renewing stem cell

Growth of immature cells

"BLASTS"

Low blood counts

How to Classify Complex Systems?
Major Subtypes of AML  
World Health Organization

- Acute myeloid leukemia with specific genetic abnormalities
  - AML with t(8;21)
  - AML with inv(16)
  - AML with t(15;17)
- AML associated with myelodysplastic syndrome
- AML associated with previous chemo or radiotherapy
- AML (not otherwise specified)
  - Subtypes based on appearance under the microscope


Risk Stratification

<table>
<thead>
<tr>
<th>Risk Status</th>
<th>Cytogenetics</th>
<th>Molecular Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable Risk</td>
<td>Inv(16) or t(16;16) or t(8;21)</td>
<td>Normal cytogenetics: NPM1 mutation (without FLT3-ITD) or CEBPA mutation</td>
</tr>
<tr>
<td>Intermediate Risk</td>
<td>Normal Cytogenetics</td>
<td>C-kit mutation</td>
</tr>
<tr>
<td></td>
<td>Inv(16) or t(16;16) or t(8;21)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>+8 or t(9;11)</td>
<td></td>
</tr>
<tr>
<td>Poor Risk</td>
<td>3 or more abnormalities</td>
<td>Normal cytogenetics: FLT3-ITD mutation</td>
</tr>
<tr>
<td></td>
<td>Monosomal karyotype</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abnormal 5 or 7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11q23 or inv(3) or t(3;3) or t(6;9) or t(9;22)</td>
<td></td>
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</tbody>
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NCCN Guidelines Version 1.2015
“Practical” Subtypes of AML

- Acute Promyelocytic Leukemia t(15;17)
  - Very different than other types of AML
  - Excellent prognosis with unique treatment
- AML that is reliably cured with chemotherapy ("core binding factor AML")
  - t(8;21), inv(16), t(16;16), NPM1 mutation
- AML not reliably cured with chemotherapy
  - Most of the other forms of AML

Important Testing at Diagnosis

- Bone marrow sample
- Cytogenetics
- Testing for genes:
  - KIT, FLT3, NPM1, CEBPA
- Flow cytometry (defines what the cells look like to other cells)
- Lumbar puncture
- Test of the strength of the heart
- HLA typing of the patient and family
Everyone Starts With Chemotherapy

- Starts with “Induction” aka “3+7”
  - Goal: to achieve a complete remission
  - 3 days of idarubicin/daunorubicin
  - 7 days of cytarabine
- Check the bone marrow around 10 -14 days later
- Then wait for blood count recovery

Responsive AML

Vanderhoek Leuk Res. 2011 Mar;35(3):310-6
Refractory AML

Induction chemotherapy

Before Chemotherapy

After Chemotherapy

Vanderhoek Leuk Res. 2011 Mar;35(3):310-6

What to do after remission?

Goal: to make the remission “stick” = CURE

Favorable-risk AML

“Consolidation” chemotherapy

Intermediate-risk AML

Blood/Marrow stem cell transplantation

Poor-risk AML
“Consolidation” Chemotherapy

- Usually, high doses of cytarabine
- Can often be given in the clinic
- Patients must pay careful attention to their health during treatment
- Close monitoring
- Usually for 3 to 4 “cycles” of treatment

Blood or Marrow Stem Cell Transplantation

- Many donor options
  - Matched siblings, volunteers
  - Mismatched family members
  - Cord blood
- Upper age limit “fuzzy”
  - Depends on the patient’s overall health
- Transplant best option when patient is healthy with low chance of cure with chemotherapy
Why Not Do Transplant for Everybody?

- Chemotherapy has fewer side-effects
- Recovery is faster, and more predictable with chemotherapy
- Transplant has more likelihood of curing, but is far more dangerous

### The Decision

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Disease</th>
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<tbody>
<tr>
<td>Risk</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>% Survival</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Transplant</td>
<td>Transplant</td>
</tr>
</tbody>
</table>

27

28
What Kind of Treatments Are Coming?

- Special labs can “sequence” all the genes in the leukemia cell
- Some of the genes control how the leukemia cells grow
Mixtures of Mutated Genes Predict Behavior

- Proliferation Genes
  - FLT3
  - WT1
  - KIT

- Differentiation Genes
  - CEBPA
  - RUNX1
  - WT1

- Epigenetic Genes
  - TET1/2/3
  - IDH1/2
  - DNMT3A
  - ASXL1

How Does Knowing How Leukemia “Works” Help Take Care of Patients?

- Helps predict behavior
- Helps to plan treatment

In the future, treatment will be increasingly based on mutated genes in the AML cells
Symptoms of Acute Leukemia

- Bone marrow failure
  - Anemia (pale, fatigue, problems breathing)
  - Fever, infections
  - Bruises, bleeding
- Organ Impairment
  - Bone pain, swollen glands, headache, skin rash, pulmonary infiltrates

*These symptoms are usually emergencies!*

Supporting Patients Through Treatment

- Maintain blood counts
  - Red cell and platelet transfusions
    - We can't give white cells reliably
- Treat/Prevent infections
  - Antibacterial, antiviral, antifungal agents important
- Control bleeding problems
- Control nausea, diarrhea
What Can Patients Do To Stay Healthy?

- Stay in the loop!
  - Ask questions, know the plan, keep your family around for important conversations.

- Wash your hands!
  - Soap and water the best in the hospital, the gel is second best.
  - Always wash after the bathroom, before eating and after walking out of the room.

What Can Patients Do To stay Healthy?

- Keep moving!
  - Walking and moving can be hard but SO important to help maintain strength.
  - Ask to speak to a physical therapist.
  - Wear a mask in the hospital.

- Keep eating!
  - If eating is tough, ask to speak to a nutrition specialist.
  - Eat safe food: fresh, washed, or cooked. Plant-based diets are generally healthy diets.
What Can Patients Do To Stay Healthy?

- Keep your social contacts!
  - But avoid crowds in small spaces
  - Let friends/family help

- Discuss your mood!
  - It is normal to be depressed at times *BUT*
  - Depression can be an impediment to healing

- Protect your time and space!
  - Getting better is a full time job
  - Keep a perspective on work

What is a Clinical Trial?

- Doctors are always trying to find better treatments.
- A clinical trial is the method to find new medical knowledge about AML that may improve patient’s lives.
- Ask your doctor whether there is a clinical trial for you.
- Ask about the benefits and the risks.
Conclusions

- Many patients with AML will be cured
- The road to cure is difficult and requires support from your family, friends and medical team.
- Good communication with your medical team is essential every step of the way
- Use resources such as LLS.org.

Information for Patients With Acute Myeloid Leukemia (AML)

Question & Answer Session

The speaker's slides are available for download at www.LLS.org/programs
Information for Patients With Acute Myeloid Leukemia (AML)

The Leukemia & Lymphoma Society (LLS) offers:

• Live, weekly Online Chats are moderated by an oncology social worker and provide a friendly forum to share experiences. Living with Acute Leukemia chat held on Thursday from 8:00pm-10:00pm ET.
  ➢ WEBSITE: www.LLS.org/chat

• What to ask: For a list of suggested questions to ask about certain topics, download and print any of the following guides.
  ➢ WEBSITE: www.LLS.org/whatatoask

• Free publications are available ranging from disease specific information to health insurance options and resources to help patients and their families cope with the financial aspects of cancer.
  ➢ WEBSITE: www.LLS.org/publications

• For more information about blood cancers and other LLS programs, please contact an LLS Information Specialist.
  ➢ TOLL-FREE PHONE: (800) 955-4572
  ➢ EMAIL: infocenter@LLS.org