AML: Understanding your diagnosis and current and emerging treatments

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Disclosures
• Nothing to disclose.

Objectives
• Understand what is AML
• Understand the symptoms, signs and diagnosis of AML
• Standard treatment options for AML
• Emerging treatments for AML

Normal blood cells production
• Hematopoietic “blood-forming” stem cells
• They produce all the
  – White blood cells: neutrophils (if low → neutropenia), lymphocytes, etc
  – Red blood cells (if low anemia)
  – Platelets (if low thrombocytopenia)

Story of DNA

Bone marrow failure syndromes
What is acute myeloid leukemia (AML)

- A type of blood cancer.
- Usually fast-growing and needs to be treated quickly.
- Cancer of early cells that are distend to develop into neutrophils (type of WBC).
- Bone marrow usually shows more than 20% blasts.
- 1% of all adult cancer deaths.
- Average age at diagnosis is approximately 65 years.

MDS

- MDS is a malignant blood disease.
- MDS is a form of bone marrow failure.
- Stem cells do not mature as they should → ineffective blood production.
- Bone marrow has less than 20% blasts.

Myeloproliferative neoplasms (MPN)

- Polycythemia vera.
- Essential thrombocytopenia.
- Chronic myeloid leukemia (CML).
- Primary myelofibrosis.

Chronic myelomonocytic leukemia (CMML)

- Malignant stem cell disorder with clinical and pathological features of both a myeloproliferative neoplasm (MPN) and myelodysplastic syndrome (MDS).
- Characterized by a peripheral blood monocytosis, bone marrow dysplasia; cytopenias and hepatosplenomegaly.
- High rate of transformation to AML.

Risk factors for AML

- Age.
- Male gender (5:3 male:female).
- Previous cancer treatment.
- Exposure to radiation.
- Dangerous chemical exposure.
- Smoking.
- Other blood disorders (MDS, MPN, CMML).
- Genetic disorders (e.g., trisomy 21; Fanconi anemia; Bloom's syndrome).

Symptoms of AML

- Feeling very tired and weak.
- Bleeding more easily than normal.
- Getting sick from infections more easily than normal.
How to get tested for AML

- Complete blood counts (CBC): very high or very low WBC, low RBC, low platelets
- Peripheral blood smear: blasts (immature WBC)
- Bone marrow biopsy: more than 20% blasts

Bone marrow biopsy

Cytogenetics and FISH

Medinger and Passweg, BJC, 2017

WHO Classification

- AML with recurrent genetic abnormalities (which includes specific AML subtypes with defined structural or molecular abnormalities).
- AML with myelodysplasia-related features, without a history of prior cytotoxic therapy
- Therapy-related AML
- AML, not otherwise specified (NOS), which does not meet the criteria for the categories described above.
- Myeloid sarcoma.
- Acute promyelocytic leukemia (APL)
Management of Leukemia

- Goals of treatment:
  - Needs careful discussion with the treating physician
  - Achieving a complete remission is necessary for cure and is a reasonable goal for most patients.
  - For some patients, treatment with the intent of achieving CR may be inadvisable because of advanced age, debility, coexisting medical problems, and/or prior treatment.
  - In such circumstances, it may be appropriate to provide supportive care alone (e.g., blood transfusions, antibiotics)

Induction Therapy

- Induction therapy: intensive combination chemotherapy to achieve a remission
  - Usually a combination of anthracycline/cytarabine 7+3
  - Given as IV infusion
  - About 4 week hospitalization
  - Requires close monitoring to treat infections and other complications (e.g., Tumor lysis syndrome) awaiting blood counts recovery

Adding a third drug

- Midostaurin in AML with FLT3 mutation:
  - Oral medication
  - Improves survival (average 75 months versus 26 months)
- Gemtuzumab ozogamicin (Mylotarg)
  - anti-CD33 antibody linked to the cytotoxic agent, IV infusion
  - Decreases chances of relapse, improves survival
  - Risk of liver toxicity

Therapy related AML

- Newly approved drug is Vyxeos (Liposomal daunorubicin and cytarabine)
- Induction (first cycle): Daunorubicin 44 mg/m² and cytarabine 100 mg/m² (liposomal) on days 1, 3, and 5
- Induction (second cycle in patients who do not achieve remission with first cycle): Daunorubicin 44 mg/m² and cytarabine 100 mg/m² (liposomal) on days 1 and 3
- Consolidation: Daunorubicin 29 mg/m² and cytarabine 65 mg/m² (liposomal) on days 1 and 3

Acute promyelocytic leukemia (APL or APML)

- Special type of AML
- Translocation (15;17)
  - Low- or intermediate-risk APL – Initial WBC count ≤10,000
    - ATRA: Oral
    - ATO: arsenic trioxide, IV
  - High-risk APL – Initial WBC count >10,000
    - ATRA plus anthracyclin based chemo
Post remission therapy

- Consolidation with chemotherapy:
  - Usually high dose cytarabine IV infusion for 4 or 5 days
  - For up to 4 rounds (cycles) of therapy

- Hematopoietic stem cell transplantation

Hematopoietic stem cell transplantation or BMT

- Finding a donor
- Majority of time it is the only potential cure
- Has high early toxicity
- Finding a donor
- Conditioning regimen
- Graft versus host disease (GVHD)

What if I don’t achieve a remission

- Clinical trial
  - Clinicaltrials.gov
  - Beat AML Master Trial
- Targeted therapy
  - Enasidenib (IDHIFA) (IDH2 mutated AML)

Questions