

Update on Acute Myeloid Leukemia: The Year in Review

These concise summaries highlight key
developments in AML research in 2021

By Leo Robert

Update on Acute Myeloid Leukemia: *The Year in Review*

Progress in understanding of acute myeloid leukemia (AML) pathophysiology has been fairly slow over the years, according to numerous studies and reports. More recently, however, AML research efforts have advanced AML understanding at a much quicker pace, showing great promise for improved patient care.

Scroll through the slides for concise summaries of key developments in AML research in 2021.

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AML by the numbers



- An estimated 20,240 new cases and 11,400 deaths were expected to occur in 2021, mostly in adults.
- A common type of leukemia in adults, but accounts for only about 1% of all cancers.
- Common in older patients and uncommon before age 45 years; average age at first diagnosis is about 68 years.
- Slightly more common among men than women.
- Average lifetime risk of AML in both sexes: about 0.5%.

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Recent trends



- After decades of few advances in AML patient care, increased understanding has led to improvements in diagnosis, monitoring, and treatment.
- Genomics is playing a bigger role in identifying new treatments.
- The range of therapeutic options is expanding.
- Gaining greater consideration: cost, quality of life, time spent in treatment, and patients' preferences.
- Ongoing research efforts are showing promise for more improvements in the near future.

After decades of few advances in AML patient care, increased understanding has led to improvements in diagnosis, monitoring, and treatment, according to the authors of a recent review. Genomics is playing a bigger role. The range of therapeutic options is expanding. Cost, quality of life, time spent in treatment, and patients' preferences are gaining greater consideration. Ongoing research efforts are showing promise for more improvements in the near future. **BMJ.**

Revised guidelines



- In response to new information about AML and improvements in treatment, a 2021 update of the National Comprehensive Cancer Network guidelines revised several of its recommendations.
- Updates addressed screening of patients and families for germline mutations in hereditary syndromes and postinduction or postremission treatment strategies.
- Other updates: optimal use of venetoclax-based therapies and considerations for patients who prefer not to receive blood transfusions during treatment.

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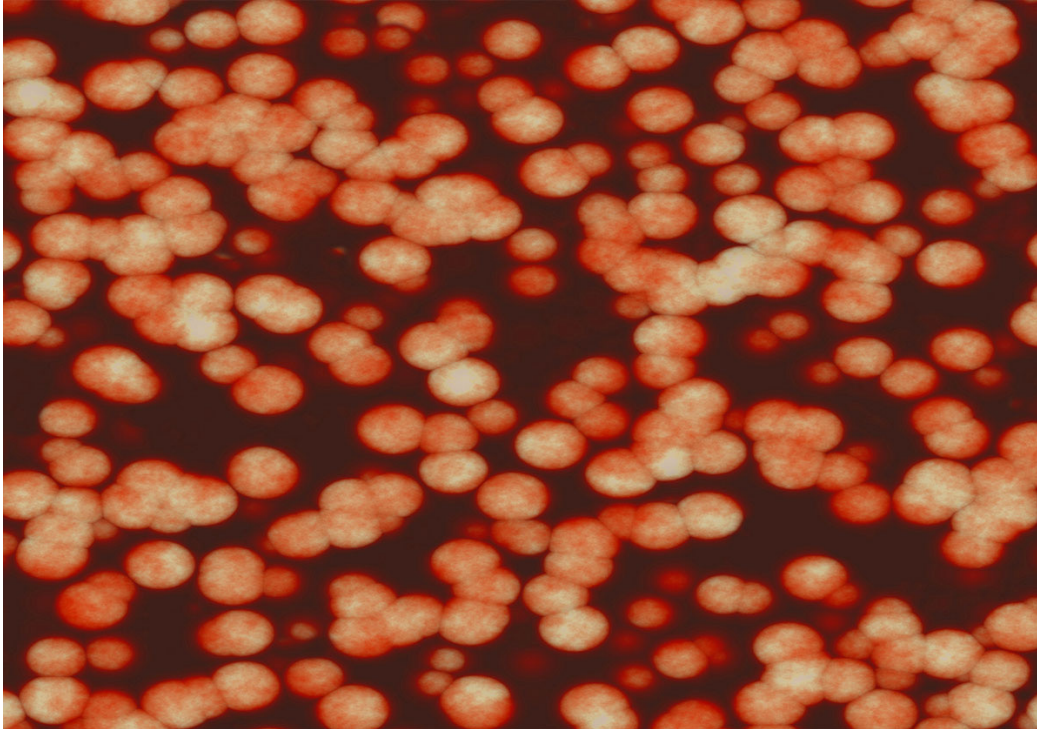
Genetic susceptibility linked to risk



- A genome-wide association study identified common susceptibility alleles at 4 genomic locations that modify AML risk.
- Evidence of subtype-specific risk loci reflects the existence of multiple etiological pathways to disease development.
- The findings support existing evidence of genetic and biological heterogeneity in AML.

Common susceptibility alleles at 4 genomic locations that modify AML risk were identified in a genome-wide association study. Evidence of subtype-specific risk loci reflects the existence of multiple etiological pathways to disease development, the authors noted. The findings support existing evidence of genetic and biological heterogeneity in AML. **Nature Communications.**

Mutant cell mechanism revealed



- Researchers discovered that AML cells can modify mutant isocitrate dehydrogenase 2 (IDH2), regulate its activity, and control the amount of oncometabolite 2-hydroxyglutarate (2-HG) it can produce.
- They determined the threshold of 2-HG concentration that allows it to switch from a cancer-causing to a cancer-killing agent.
- Better understanding of the IDH2 mechanism in AML could lead to improved treatments.

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Survival determinants ID'd



- A recent analysis showed poor long-term overall survival among patients with AML, especially older patients.
- Ten-year overall survival was higher for patients aged 18 to 59 years treated with chemotherapy who were younger or female or had core binding factor AML and those treated without upfront hematopoietic cell transplant.
- Likelihood of death decreased with fewer comorbidities, treatment at an academic center, and use of multiagent chemotherapy.

Long-term overall survival was poor among patients with AML, especially older patients, in a recent analysis. Ten-year overall survival was higher for patients aged 18 to 59 years treated with chemotherapy who were younger or female or had core binding factor AML and those treated without upfront hematopoietic cell transplant. Likelihood of death decreased with fewer comorbidities, treatment at an academic center, and use of multiagent chemotherapy. **Leukemia & Lymphoma.**

Less certainty about less-intensive therapies



- A study questioned the survival and quality of life benefits of less-intensive therapies vs intensive induction for patients with AML, including those aged 70 to 79 years or with high comorbidity burden.
- Less-intensive therapies were associated with a higher risk of mortality, but mortality risks and quality of life were similar in adjusted models and patients treated with less-intensive therapies spent fewer days in the hospital.
- Reevaluation of intensity of therapy for AML in older patients was recommended.

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Addressing CNS involvement



- Review authors: Even with improved diagnosis and treatment of acute leukemias, CNS involvement is limiting long-term treatment.
- CNS involvement in adults often goes undiagnosed, mainly because of a lack of routine diagnostic lumbar puncture.
- Recommended for early detection are cerebrospinal fluid analysis, MRI, and flow cytometry.

Even with improved diagnosis and treatment of acute leukemias, CNS involvement is limiting long-term treatment, according to the authors of a narrative review. CNS involvement in adults often goes undiagnosed, mainly because of a lack of routine diagnostic lumbar puncture. Recommended for early detection are cerebrospinal fluid analysis, MRI, and flow cytometry. **Annals of Translational Medicine.**

Limited availability for lifesaving ATRA



- Survey: All-trans retinoic acid (ATRA), often used to treat patients with the acute promyelocytic leukemia (APL) subtype of AML, is unavailable at many hospitals.
- Fewer than one-third (31%) of responding hospitals had ATRA (only 14% of referring hospitals).
- The authors suggested that instituting treatment with ATRA for patients with APL in the first 24 hours is crucial in reversing disseminated intravascular coagulation, a life-threatening coagulopathy.

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Deferred end of life decisions



- Interviewed caregivers: Clinicians' beliefs in transfusion at end of life may put up a greater barrier to hospice enrollment than patients' preferences.
- Caregivers said that transfusions were necessary but decisions about them often were deferred to clinicians.
- Cited as more relevant barriers: difficulties in recognizing that death was imminent, hope for miracles, and the necessity of accepting that life was ending.

Clinicians' beliefs in transfusion at end of life may put up a greater barrier to hospice enrollment than patients' preferences, according to interviewed caregivers, who said transfusions were necessary but decisions about them often were deferred to clinicians. Cited as relevant barriers: difficulties in recognizing that death was imminent, hope for miracles, and the necessity of accepting that life was ending. **American Journal of Hospice and Palliative Medicine.**

American Cancer Society:

<https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html>

BMJ:

<https://www.bmj.com/content/375/bmj.n2026>

JNCCN:

<https://jnccn.org/view/journals/jnccn/19/1/article-p16.xml>

Nature Communications:

<https://www.nature.com/articles/s41467-021-26551-x>

Science Daily:

<https://www.sciencedaily.com/releases/2021/07/210720160814.htm>

Leukemia & Lymphoma:

<https://www.tandfonline.com/doi/abs/10.1080/10428194.2021.2005046?journalCode=ilal20>

Blood:

<https://pubmed.ncbi.nlm.nih.gov/33910230/>

Annals of Translational Medicine:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7859772/>

JNCCN:

<https://jnccn.org/view/journals/jnccn/19/11/article-p1272.xml>

American Journal of Hospice and Palliative Medicine:

<https://journals.sagepub.com/doi/abs/10.1177/10499091211013290>