

Untangling Complexities of Acute Myeloid Leukemia Review Series

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Acute myeloid leukemia (AML) is the most common acute leukemia in adults, comprising 1% of all cancers [1]. Major improvements in pathophysiological insights, in part due to the use of novel technologies, have revolutionized the diagnostic, prognostic, and therapeutic landscape of AML [2]. In the last few years, new diagnostic classification systems and prognostic algorithms were introduced [3–5] based on our enhanced understanding of the interplay of biology and clinical outcome. Our ability to measure small numbers of diseased cells (measurable residual disease) improved and influenced clinical decisions on a daily basis [6, 7]. Importantly, at least 12 agents or combination therapies were recently approved for AML [8–19]. These advances allow individualization of therapy, thereby leading to better outcomes in patients with AML. Such therapeutic advances require a comprehensive assessment of both patients and their diseases.

We present a series of reviews on various controversies in AML which should aid clinicians in optimizing care (Fig. 1). After a comprehensive review of AML pathophysiology, we present a review of new AML classification systems, noting similarities and

differences between the two classifications. A major issue vexing clinicians, how to integrate measurable residual disease measurement into daily practice, is discussed in detail. The therapeutic landscape is covered in treatises reviewing optimal post-remission approaches and both immunotherapy and non-immunotherapeutic advances in advanced disease. We provide a focus on two important and challenging populations with AML, older patients and those harboring TP53 mutations. Finally, we present a review on the controversial topic of prophylactic antibiotic therapy in AML. We hope that our review series will serve as a tool kit to help clinicians resolve the uncertainty and complexity inherent in modern AML management.

This review series is dedicated to the recently deceased Prof. Ben-Bassat, a pioneer and a leader in Israeli hematology, who served as the editor-in-chief of *Acta Haematologica* for several decades. We have therefore included an obituary written by the current editor-in-chief, Prof. Pia Raanani.

Conflict of Interest Statement

R.M.S. reports consulting fees from Abbvie, Aptevio, Aprea, Arog, BMS, CTI Pharma, Curis Oncology, Epizyme, GSK, Hermavant, Ligand Pharma, Lava Therapeutics, Redona Therapeutics, and Takeda. S.S. has no COI to declare.

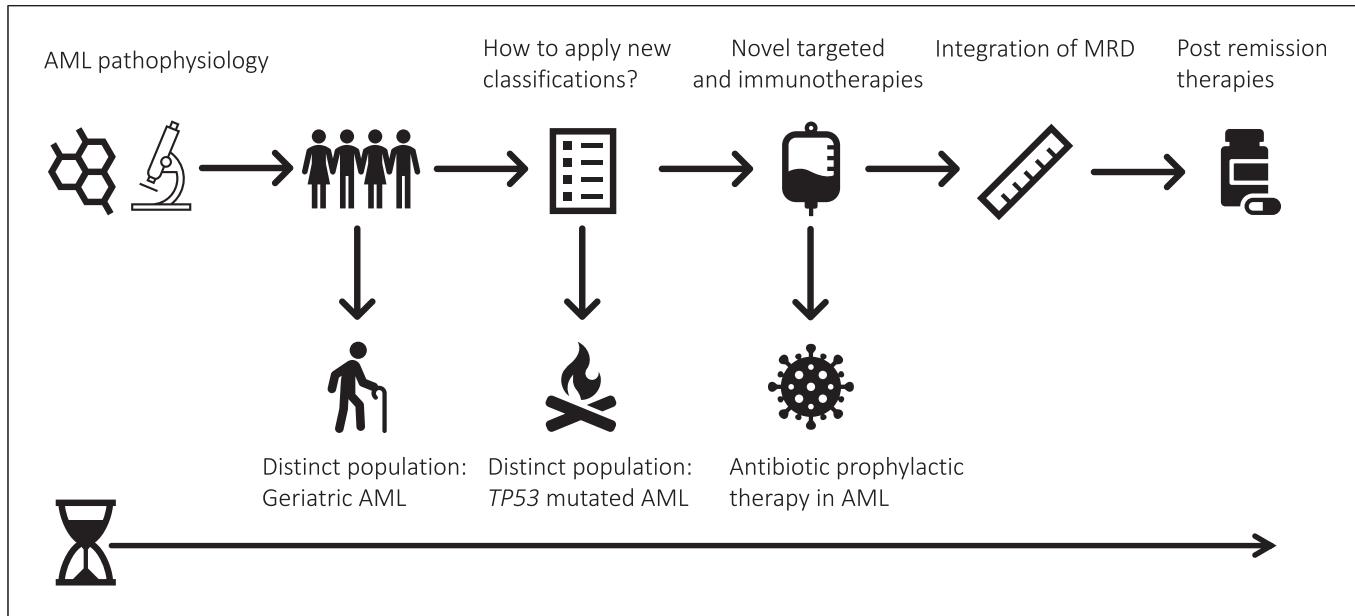


Fig. 1. Untangling controversies in AML review topics, selected topic in the review series. AML, acute myeloid leukemia; MRD, measurable residual disease.

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Author Contributions

S.S. conceived and wrote the editorial. R.M.S. conceived and edited the editorial.

References

- SEER data base: cancer stat facts: leukemia – acute myeloid leukemia (AML). (Internet). (cited 2023 June 11). Available from: <https://seer.cancer.gov/statfacts/html/amyl.html>.
- Shimony S, Stahl M, Stone RM. Acute myeloid leukemia: 2023 update on diagnosis, risk-stratification and management. *Am J Hematol*. 2023;98(3):502–26.
- Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, et al. The 5th edition of the world health organization classification of haematolymphoid tumours: myeloid and histiocytic/dendritic neoplasms. *Leukemia*. 2022;36(7):1703–19.
- Arber DA, Orazi A, Hasserjian RP, Borowitz MJ, Calvo KR, Kvasnicka HM, et al. International consensus classification of myeloid neoplasms and acute leukemias: integrating morphologic, clinical, and genomic data. *Blood*. 2022;140(11):1200–28.
- Döhner H, Wei AH, Appelbaum FR, Craddock C, Dinardo CD, Dombret H, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. *Blood*. 2022;140(12):1345–77.
- Heuser M, Freeman SD, Ossenkoppele GJ, Buccisano F, Hourigan CS, Ngai LL, et al. 2021 Update on MRD in acute myeloid leukemia: a consensus document from the European LeukemiaNet MRD Working Party. *Blood*. 2021;138(26):2753–67.
- Dillon LW, Gui G, Page KM, Ravindra N, Wong ZC, Andrew G, et al. DNA sequencing to detect residual disease in adults with acute myeloid leukemia prior to hematopoietic cell transplant. *JAMA*. 2023;329(9):745–55.
- DiNardo CD, Jonas BA, Pullarkat V, Thirman MJ, Garcia JS, Wei AH, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. *N Engl J Med*. 2020;383(7):617–29.
- Montesinos P, Recher C, Vives S, Zarzycka E, Wang J, Bertani G, et al. Ivosidenib and azacitidine in IDH1-mutated acute myeloid leukemia. *N Engl J Med*. 2022;386(16):1519–31.
- Stein EM, DiNardo CD, Polley DA, Fathi AT, Roboz GJ, Altman JK, et al. Enasidenib in mutant IDH2 relapsed or refractory acute myeloid leukemia. *Blood*. 2017;130(6):722–31.
- DiNardo CD, Stein EM, de Botton S, Roboz GJ, Altman JK, Mims AS, et al. Durable re-missions with ivosidenib in IDH1-mutated relapsed or refractory AML. *N Engl J Med*. 2018;378(25):2386–98.
- Watts JM, Baer MR, Yang J, Prebet T, Lee S, Schiller GJ, et al. Olutasidenib alone or with azacitidine in IDH1-mutated acute myeloid leukaemia and myelodysplastic syndrome: phase 1 results of a phase 1/2 trial. *Lancet Haematol*. 2023;10:e46–58.
- Lancet JE, Uy GL, Cortes JE, Newell LF, Lin TL, Ritchie EK, et al. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol*. 2018;36(26):2684–92.
- Castaigne S, Pautas C, Terré C, Raffoux E, Bordessoule D, Bastie J-N, et al. Effect of gemtuzumab ozogamicin on survival of adult patients with de-novo acute myeloid leukaemia (ALFA-0701): a randomised, open-label, phase 3 study. *Lancet*. 2012;379(9825):1508–16.
- Wei AH, Döhner H, Pocock C, Montesinos P, Afanasyev B, Dombret H, et al. Oral azacitidine maintenance therapy for acute myeloid leukemia in first remission. *N Engl J Med*. 2020;383(26):2526–37.

- 16 Stone RM, Mandrekar SJ, Sanford BL, Laumann K, Geyer S, Bloomfield CD, et al. Midostaurin plus chemotherapy for acute myeloid leukemia with a FLT3 mutation. *N Engl J Med.* 2017;377(5):454–64.
- 17 Erba HP, Montesinos P, Kim HJ, Patkowska E, Vrhovac R, Žák P, et al. Quixartinib plus chemotherapy in newly diagnosed patients with FLT3-internal-tandem-duplication-positive acute myeloid leukaemia (QuANTUM-First): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* 2023; 401(10388):1571–83.
- 18 Perl AE, Martinelli G, Cortes JE, Neubauer A, Berman E, Paolini S, et al. Gilteritinib or chemotherapy for relapsed or refractory FLT3-mutated AML. *N Engl J Med.* 2019; 381(18):1728–40.
- 19 Cortes JE, Heidel FH, Hellmann A, Fiedler W, Smith BD, Robak T, et al. Randomized comparison of low dose cytarabine with or without glasdegib in patients with newly diagnosed acute myeloid leukemia or high-risk myelodysplastic syndrome. *Leukemia.* 2019;33(2):379–89.