AML: Fitness, Not Age, Predicts Intensive Chemotherapy Eligibility

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The current reliance on chronological age as a primary determinant for intensive chemotherapy (IC) eligibility in acute myeloid leukemia (AML) often excludes patients who may benefit from aggressive treatment. New data presented at EHA 2026 challenges this paradigm, demonstrating that comprehensive geriatric assessments (CGAs) and performance status provide a more accurate stratification of treatment tolerability and outcomes.1

KEY TAKEAWAYS

- The Pivot: Age alone is an insufficient criterion for intensive chemotherapy eligibility in AML; functional fitness is a superior predictor.
- The Data: Patients aged 70-75 with good performance status (ECOG 0-1) had similar rates of complete remission (CR) and early mortality as younger patients receiving IC.
- The Action: Clinicians should incorporate comprehensive geriatric assessments and validated fitness scales into routine AML treatment decision-making, irrespective of chronological age.

Acute myeloid leukemia (AML) disproportionately affects older adults, with a median age at diagnosis of 68 years.1 Intensive chemotherapy (IC) offers the best chance for long-term remission and survival, yet its use in older patients is often limited by concerns regarding treatment-related toxicity and early mortality.2 Historically, chronological age, particularly an arbitrary cutoff of 60 or 65 years, has been a significant factor in determining eligibility for IC. This practice has led to the under-treatment of fit older patients and the over-treatment of frail younger patients, highlighting a critical unmet need for more precise eligibility criteria.3

Re-evaluating Eligibility Criteria for Intensive Chemotherapy

A multicenter observational study, presented at EHA 2026, investigated the utility of comprehensive geriatric assessments (CGAs) and performance status scales in predicting outcomes for older AML patients considered for IC. The study enrolled 1,580 patients aged 60-80 years with newly diagnosed AML across 22 European centers.4 Patients were categorized into two main groups: those receiving IC and those receiving lower-intensity therapies (LIT), such as azacitidine or venetoclax-based regimens. Within the IC group, patients were further stratified by age (60-69 years vs. 70-80 years) and by baseline fitness parameters, including ECOG performance status (0-1 vs. 2-4), Charlson Comorbidity Index (CCI), and a validated frailty score derived from CGA components.4 The rationale for this stratification was to disentangle the independent effects of age and fitness on treatment outcomes, given the known heterogeneity in health status among older adults. The study aimed to provide evidence for a more individualized approach to treatment selection, moving beyond a sole reliance on chronological age.

The primary endpoints were complete remission (CR) rates, 30-day and 60-day mortality, and overall survival (OS). Secondary endpoints included incidence of grade 3-4 non-hematologic toxicities. The study found that among patients receiving IC, chronological age alone was not an independent predictor of treatment outcomes when accounting for fitness parameters. Specifically, patients aged 70-75 years with an ECOG performance status of 0-1 and a low frailty score (e.g., 4 on a 9-point scale) demonstrated CR rates of 68% (95% CI, 64-72%), which were comparable to those observed in younger patients (60-69 years) with similar fitness profiles (CR rate 72%, 95% CI, 69-75%; P=0.18).5 Furthermore, 30-day mortality rates for fit patients aged 70-75 receiving IC were 8% (95% CI, 6-10%), which did not differ significantly from the 30-day mortality rate of 6% (95% CI, 5-8%) in fit patients aged 60-69 (P=0.27).5 In contrast, patients aged 60-69 with an ECOG performance status of 2 or higher, or a high frailty score, experienced significantly higher 30-day mortality rates (18%, 95% CI, 15-21%) when treated with IC compared to their fitter counterparts (P0.001).6 This suggests that frailty, rather than age, is the dominant factor influencing early mortality and treatment tolerability. The incidence of grade 3-4 non-hematologic toxicities was also primarily associated with frailty scores and comorbidity burden, with no significant difference observed between age groups when fitness was controlled.6 These findings underscore the importance of a comprehensive assessment of a patient's physiological reserve and comorbidity burden, rather than relying on age as a proxy for these critical factors. The study's results support the integration of geriatric assessment tools into routine clinical practice for AML treatment decision-making.

The study’s limitations include its observational design, which inherently carries a risk of selection bias, despite efforts to adjust for confounding variables. The specific components and scoring of the frailty assessment varied slightly across participating centers, although a standardized algorithm was applied for data aggregation. This variability, while mitigated by standardization efforts, could introduce subtle inconsistencies in frailty classification. Additionally, the study did not include patients over 80 years of age, limiting the generalizability of these findings to the oldest old AML population. Future prospective randomized trials are warranted to definitively establish the superiority of fitness-based criteria over age-based criteria in guiding AML treatment decisions. Additionally, further research is needed to refine and standardize the optimal CGA tools for routine clinical practice in AML.

Readers seeking deeper insights into the assessment and management of acute myeloid leukaemia and other blood disorders may find the Oxford Handbook of Clinical Haematology invaluable.

CLINICAL IMPLICATIONS

The EHA 2026 data on AML treatment eligibility should prompt a critical re-evaluation of how we approach older patients. Continuing to use an arbitrary age cutoff for intensive chemotherapy is a disservice to fit individuals who could benefit from curative intent therapy. Clinicians must move beyond a superficial glance at a patient's birthdate and instead integrate comprehensive geriatric assessments and validated performance status scales into their decision-making algorithms. This requires a shift in clinical practice, potentially necessitating additional training for oncology teams in geriatric assessment methodologies, but it is a necessary evolution to optimize patient outcomes.

For the pharmaceutical industry, this evidence underscores the importance of developing and testing novel AML therapies in diverse patient populations, including those traditionally excluded from intensive regimens based solely on age. Clinical trials should stratify patients by fitness rather than age, ensuring that new agents

> are evaluated in the populations most likely to receive them in real-world practice. Guideline bodies, such as the European LeukemiaNet (ELN) and the National Comprehensive Cancer Network (NCCN), should consider updating their recommendations to explicitly endorse fitness-based assessments as the primary determinant for IC eligibility, providing clear guidance on which tools are most appropriate.
> Ultimately, this approach empowers patients by offering them treatment options based on their individual physiological capacity, not just their chronological age. It challenges the paternalistic notion that older patients are inherently too frail for aggressive treatment, instead advocating for personalized medicine that maximizes the chance of remission and improves quality of life. The data is clear: fitness, not age, should dictate the intensity of AML therapy. Ignoring this evidence risks perpetuating suboptimal care for a significant proportion of AML patients.

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