AML: Fitness, Not Age, Predicts IC Eligibility at EHA 2026

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The management of Acute Myeloid Leukemia (AML) in older adults presents a persistent clinical dilemma, with chronological age often serving as a primary, albeit imperfect, criterion for intensive chemotherapy (IC) eligibility. Data presented at EHA 2026 indicates that a comprehensive geriatric assessment (CGA) and performance status provide a more accurate stratification of treatment benefit and toxicity risk than age alone, suggesting a shift towards individualized fitness-based eligibility.

KEY TAKEAWAYS

- The Pivot: Age alone is an insufficient criterion for intensive chemotherapy eligibility in AML; comprehensive fitness assessments are superior.
- The Data: Patients aged 70-75 with good performance status (ECOG 0-1) and no major comorbidities demonstrated similar overall survival (OS) and complete remission (CR) rates to younger patients receiving IC.
- The Action: Clinicians should integrate validated fitness scales and comorbidity indices into routine AML assessment, particularly for older patients, to avoid undertreatment.

Acute Myeloid Leukemia (AML) predominantly affects older individuals, with a median age at diagnosis of approximately 68 years.1 Intensive chemotherapy (IC) regimens, typically involving an anthracycline and cytarabine, offer the best chance for complete remission and long-term survival.2 However, concerns regarding treatment-related mortality and morbidity in older patients have historically led to age-based exclusion from IC, often without a nuanced assessment of physiological reserve. This practice has resulted in a significant proportion of older, fit patients being denied potentially curative treatment, while some frail younger patients may receive therapy they cannot tolerate.3 The EHA 2026 presentation directly addresses this disparity by evaluating the utility of fitness criteria beyond chronological age. The rationale for this study stems from a growing understanding that physiological age, rather than chronological age, is a more accurate predictor of tolerance to aggressive therapies and subsequent outcomes in various oncological settings. This is particularly relevant in AML, where treatment decisions carry significant risks and potential benefits.

What the study did

The presented analysis pooled data from several prospective trials and real-world registries, encompassing N=3,870 patients with newly diagnosed AML.4 The cohort included patients aged 60-80 years, stratified by age (60-69, 70-75, >75 years) and by a composite fitness score. This score integrated Eastern Cooperative Oncology Group (ECOG) performance status, the Charlson Comorbidity Index (CCI), and a modified Geriatric Assessment (GA) score, which

included assessments of instrumental activities of daily living (IADL) and cognitive function.4 Patients were categorized as 'fit,' 'intermediate-fit,' or 'unfit' based on these composite scores, irrespective of their chronological age. The primary endpoints were overall survival (OS) and complete remission (CR) rates following IC. Secondary endpoints included early mortality (30-day and 60-day) and incidence of grade 3 or higher non-hematologic toxicities.4 The specific IC regimens generally followed standard 7+3 induction protocols, though minor variations existed across contributing studies, reflecting real-world clinical practice. Patient characteristics such as cytogenetics and molecular mutations were also collected and considered in subgroup analyses, although the primary focus remained on fitness and age.

The study demonstrated that among patients aged 70-75 years, those classified as 'fit' (ECOG 0-1, CCI ≤2, intact IADL and cognitive function) achieved a complete remission rate of 68% (95% CI, 64-72%) following IC, which was comparable to the 72% (95% CI, 69-75%) observed in fit patients aged 60-69 years.5 The median overall survival for fit patients aged 70-75 was 14.5 months (95% CI, 12.8-16.2 months), not significantly different from the 16.1 months (95% CI, 14.7-17.5 months) in fit patients aged 60-69 years (Hazard Ratio [HR] for mortality: 1.08; 95% CI, 0.95-1.23; P=.24).5 These results suggest that chronological age alone does not dictate treatment outcomes for physiologically robust older individuals.

Conversely, patients aged 60-69 years classified as 'unfit' (ECOG ≥2, CCI >2, or significant IADL/cognitive impairment) experienced a significantly lower CR rate of 42% (95% CI, 38-46%) and a median OS of 6.3 months (95% CI, 5.1-7.5 months).6 This 'unfit' younger cohort had a 30-day mortality rate of 18% (95% CI, 15-21%), which was higher than the 12% (95% CI, 10-14%) observed in fit patients aged >75 years (HR for 30-day mortality: 1.56; 95% CI, 1.25-1.95; P).6 The incidence of grade 3 or higher non-hematologic toxicities was primarily driven by fitness status rather than age. Fit patients, regardless of age, had lower rates of severe infections, mucositis, and cardiac events compared to unfit patients. For instance, severe infection rates were 35% in fit patients aged 70-75 versus 58% in unfit patients aged 60-69.6 These findings underscore the importance of comprehensive fitness assessments in identifying patients at higher risk of treatment-related complications, irrespective of their birth year.

The study's limitations include its retrospective component from registry data, which may introduce selection bias, and the heterogeneity in specific GA tools used across different contributing studies. While the composite fitness score aimed to standardize assessment, variations in data collection could influence outcomes. For example, the precise instruments used to assess IADL or cognitive function might have differed, potentially leading to subtle inconsistencies in fitness categorization. Furthermore, the study did not specifically evaluate the impact of novel AML therapies, which have emerged in recent years, on fitness-based treatment decisions. Future prospective trials are warranted to validate these findings with a uniformly applied, standardized fitness assessment tool. Nevertheless, the consistent trend across multiple datasets strengthens the argument for a fitness-based approach.

CLINICAL IMPLICATIONS

The EHA 2026 data on AML eligibility for intensive chemotherapy is a timely reminder that medicine, at its best, treats the patient, not the number on their birth certificate. For too long, chronological age has been a blunt instrument, denying potentially life-saving treatment to physiologically robust individuals simply because they crossed an arbitrary age threshold. This analysis provides compelling evidence that a comprehensive geriatric assessment, incorporating performance status and comorbidity indices, is a superior predictor of

treatment tolerance and outcome. It is time for guideline bodies, such as the NCCN and ELN, to formally integrate these fitness criteria into their recommendations, moving beyond age-centric algorithms that risk both undertreatment and overtreatment.

The implications for clinical practice are clear: a more thorough, individualized assessment is required. This will necessitate dedicated resources for geriatric oncology assessments, which may pose an initial logistical challenge for busy oncology units. However, the long-term benefits of improved patient selection, reduced futile treatments, and enhanced quality of life for those who can benefit from IC outweigh these initial hurdles. Pharmaceutical companies developing novel AML therapies, particularly those targeting older or unfit populations, should also take note. The definition of 'unfit' is evolving, and trials designed around age cut-offs may inadvertently exclude a significant proportion of patients who could benefit from intensive approaches, or conversely, include patients who are truly too frail for any intensive regimen.

Ultimately, this shift benefits patients by ensuring access to appropriate care. It empowers clinicians to make more informed decisions based on a holistic view of patient health, rather than relying on an arbitrary number. The data underscores that physiological age, not chronological age, should dictate treatment intensity in AML. This is not a radical concept, but a return to fundamental medical principles, now supported by robust evidence.

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