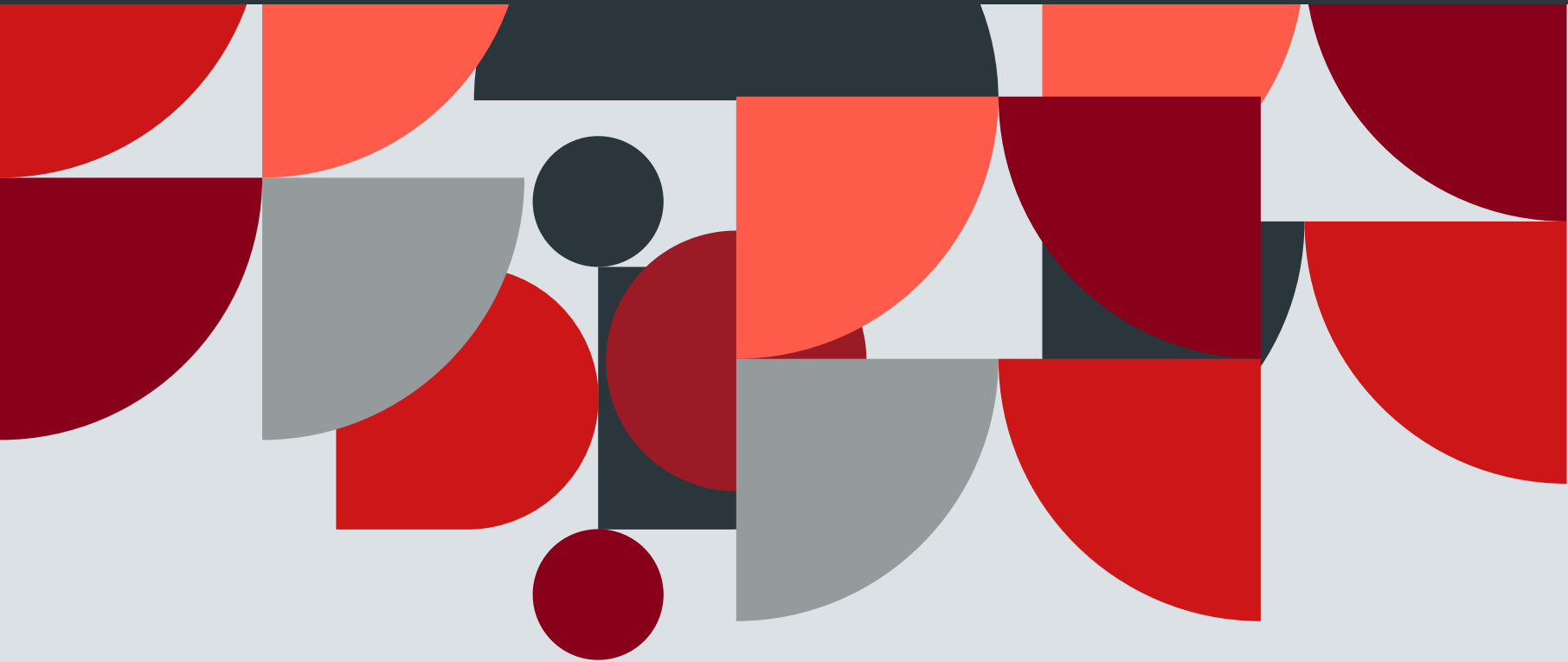




FITNESS ASSESSMENT IN ACUTE MYELOID LEUKEMIA

RECOMMENDATIONS FROM AN EXPERT PANEL ON BEHALF OF EUROPEAN LEUKEMIA NET

For Physicians
March 2025



Venditti A, Palmieri R, Maurillo L, Röhlig C, Wierzbowska A, de Leeuw DC, Efficace F, Curti A, Ngai LL, Tettero JM, Adès L, Almeida AM, Bullinger L, Dennis M, Esteve J, Ferrara F, Heuser M, Huls GA, Lübbert M, Mehta P, Montesinos P, Pabst T, Récher C, Rossi G, Russell NH, Sierra J, Stauder R, Vey N, Walter RB, Wang ES, Nier S, Martins CG, Ossenkoppele GJ. FITNESS ASSESSMENT IN ACUTE MYELOID LEUKEMIA: RECOMMENDATIONS FROM AN EXPERT PANEL ON BEHALF OF EUROPEAN LEUKEMIA NET. Blood Adv. 2025 Feb 6;bloodadvances.2024013744. doi: 10.1182/bloodadvances.2024013744. Epub ahead of print. PMID: 39913928.

GENERAL DEFINITIONS

The diverse intensities of available treatments emphasize the necessity of recognizing additional fitness levels extending beyond the conventional categories of “fit,” “unfit,” and “frail.”



Therefore, **patients should be considered “eligible” for a specific treatment strategy** based on clinical fitness and biological factors, with a clear explanation of the treatment approach and the provision of alternative options.

02

Ineligibility for intensive chemotherapy (IC) does not necessarily exclude eligibility for AlloSCT in patients achieving CR, following non-intensive treatment.

04

Antileukemic therapy should be considered for mitigating disease-related symptoms, even if a curative intent is unattainable



Several parameters including **age, performance status (PS), comorbidities, and a comprehensive geriatric assessment**, concur to influence a patient’s ability to tolerate AML-directed therapies.

01



Therefore, a **comprehensive, patient-centered evaluation** of these factors should be conducted before initiating any therapeutic program.



Eligibility for intensive treatment does not automatically mean a patient is eligible for a AlloSCT, as their health status may change during treatment. **Regular reassessment is essential.**

03



Decisions regarding symptom management should be informed by **patient preferences and quality-of-life (QoL) objectives**, ensuring they align with **individual values and expectations.**





COMPONENTS OF FITNESS

While fitness for IC declines with aging, age as a single parameter should not be considered as the sole criterion to define patients' fitness.



Doctors should also consider **overall health, energy levels, QoL, life expectancy and personal circumstances and preferences.**

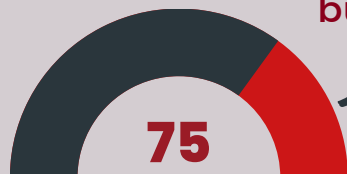


PS plays a crucial role in the definition of fitness.

Nevertheless, considering its subjective nature and limited sensitivity, a **geriatric assessment is particularly useful for patients with a PS >2 to inform decision about treatment intensity.**

For patients with a **PS >3**, the decision between active treatment and supportive therapy alone **should be made on a case-by-case basis.**

07 Given that only a small proportion of patients aged > 75 years can benefit from IC and considering the lack of clinical trials focusing exclusively on intensively treated patients in this age group, **careful evaluation of eligibility for IC is needed for patients over 75.**



It is crucial to also consider the **patient's QoL expectations, psychosocial circumstances, and willingness to undergo IC.**



09 Patient's **self-reported physical and social functioning, as well as QoL before illness onset**, should be considered an important parameter when evaluating fitness.



Treatment decisions should be always **individualized and made in partnership with patients** after careful consideration of all **patient- and disease-related characteristics** that may affect efficacy or tolerability of any therapeutic intervention.



OVERALL HEALTH AND GENETICS

Although an agreement was not reached, 67% of the panelists concurred that **no clear contraindications exist to treating adverse risk, older, fit patients with adverse-risk profiles using IC.**

The lack of consensus on this issue stems from unsatisfactory results when treating patients with adverse risk with either intensive or non-intensive approaches.



11 **Patients unfit for active therapy should be tested for mutations that could be susceptible to targeted monotherapy** before being considered for supportive therapy alone.



Involving specialists, such as **psychiatrists or psychologists**, for targeted support may be beneficial.



Psychiatric comorbidities and cognitive disorders should be carefully assessed to inform therapeutic decisions, as they may affect patient compliance with therapy and increase the risk of complications.



Since **time-to-treatment initiation does not appear to impact short- or long-term patient outcomes**, a comprehensive fitness and biological assessment should be performed before starting therapy. For patients with clinically stable disease, treatment **can safely be delayed for up to three weeks from diagnosis.**

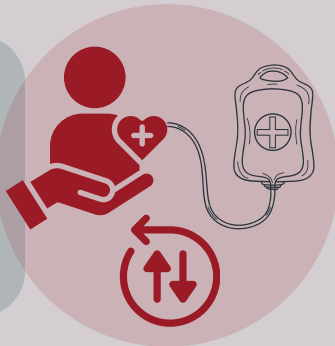
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Patients should be informed that the time spent on comprehensive assessments is critical for tailoring the most effective treatment plan.



Fitness level attribution should be performed after appropriate supportive therapy when general condition impairments are suspected to be due to disease burden rather than pre-existing conditions.

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Fitness improvement or worsening should be **addressed dynamically** throughout therapy, in both responding and nonresponding patients, to modulate treatment intensity as appropriate.



WHEN TO ASSESS OVERALL HEALTH AND GENETIC FACTORS



Patients and caregivers should be **kept informed about how fitness changes may affect treatment adjustments**, ensuring they understand the rationale behind modifications in therapy intensity.



17

Biological reassessment should be performed **at disease relapse** to assist in the choice of salvage therapy.



18



Social support, provided through a multidisciplinary approach involving professionals beyond physicians, should be offered **to all patients from the beginning of therapy, regardless of treatment intensity.**



QUALITY OF LIFE AND SOCIAL SUPPORT



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Although there is insufficient evidence to consider QoL as a measure of fitness, **any anti-leukemic treatment significantly impacts patient's QoL.**

Therefore, the extent of such an impact should be **considered and discussed with patients** when making therapeutic decisions and **monitored throughout treatment.**

Although social support is not a component of fitness, it may impact the success of a therapeutic program.

Accordingly, **patient's social support should be intensified** when considering any therapeutic interventions, **especially in the absence of caregivers.**



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Although not reaching a consensus, 67% of the panelists agreed that **early palliative care (EPC) should be standard of care**, even for patients receiving IC, to improve QoL and treatment outcome.

EPC should be integrated at diagnosis, **tailored to the patient's goals, preferences, and expectations, with a focus on symptom management and psychosocial support.**





Guiding questions for Physicians



Consider:



- **Age**
- **Existing medical conditions**
- **Overall physical strength**
- How **independent** you are in your daily life
- **Memory, mood, and mental well-being**
- **Nutrition** and the risks of weight loss
- **Medications** someone is taking
- **Support** from family and caregivers
- Personal **circumstances**
- Personal **preferences**



- “Can we discuss how your **overall health and the specifics of your leukemia** should influence the treatment choices we consider?”
- “Would you like to discuss **different treatment options** and what might work best for you?”
- “Do you have any questions about **why waiting a short time before treatment begins is considered safe** and beneficial for your overall care?”
- “Are you open to **genetic testing** to help us better understand how your body might respond to different treatment options for AML?”



- “What are your **main concerns or priorities** when choosing your treatment?”
- “What are your **preferences** for treatment, and how can we tailor it to **fit your goals and well-being**?”



- “Would you like to discuss how your overall condition affects your **eligibility for a stem cell transplant**?”
- “Would you like to discuss how **less intensive treatment** could still lead to a stem cell transplant?”



- “Would you be open to **genetic testing** to help us understand if targeted therapies could be an option for you?”
- “Given your overall health and age (>75), would you be open to exploring **more intensive treatment options**, even if there’s some uncertainty about their effectiveness?”
- “How do you feel about trying newer, **less intensive treatments** that might help slow the disease and improve your quality of life?”



- “Do you understand that **your treatment plan might change depending on how your health evolves** during treatment? How can I help you **stay informed** throughout the process?”



- “How would you **describe your physical abilities, quality of life, daily activities and social life before you were diagnosed**?”



Guiding questions for Physicians



- “What are your **main goals and priorities** for your treatment, **even if curing the leukemia isn’t possible?**”
- “Would you like to discuss how active treatment options, even if a cure isn’t possible, **could help manage your symptoms, improve comfort, and potentially extend your life?**”



- “How are you feeling **emotionally and mentally**, and do you think any changes in your **energy levels or mood** are impacting your ability to care for yourself?”
- “Would you be open to working with a mental health specialist, such as a **psychiatrist or psychologist**, to support you during your treatment?”



- “How can we **best support you and your family** with your **emotional and social well-being** throughout your treatment?”
- “Do you have a **support system in place**, and is there anything additional we can do to help ensure you have the support you need during your treatment?”



- “Are there any challenges — such as **transportation, daily activities, financial struggles or lack of emotional support** — that might make it harder for you to continue treatment? How can we help address these?”



- “How do you feel about the **potential impact of this treatment on your daily life and overall well-being?**”
- “Are there any specific **symptoms or side effects** that are making it harder for you to maintain your usual activities or quality of life?”
- “Would you like to discuss **alternative treatment options** that might better align with your personal preferences and lifestyle?”



- “How can we personalize **palliative care** to best align with your preferences and help improve your quality of life throughout treatment?”