Taylor & Francis
Taylor & Francis Group

Expert Review of Hematology

ISSN: 1747-4086 (Print) 1747-4094 (Online) Journal homepage: www.tandfonline.com/journals/ierr20

Determining treatment pathways for older patients with acute myeloid leukemia: patient and clinician perspectives

Esther N. Oliva & Antonio Almeida

To cite this article: Esther N. Oliva & Antonio Almeida (2025) Determining treatment pathways for older patients with acute myeloid leukemia: patient and clinician perspectives, Expert Review of Hematology, 18:8, 595-604, DOI: 10.1080/17474086.2025.2521397

To link to this article: https://doi.org/10.1080/17474086.2025.2521397

© 2025 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

Published online: 22 Jun 2025.

Submit your article to this journal

Article views: 455

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=ierr20

EXPERT REVIEW OF HEMATOLOGY
2025, VOL. 18, NO. 8, 595–604
https://doi.org/10.1080/17474086.2025.2521397

Taylor & Francis
Taylor & Francis Group

CRITICAL PERSPECTIVES

OPEN ACCESS Check for updates

Determining treatment pathways for older patients with acute myeloid leukemia: patient and clinician perspectives

Esther N. Oliva[a] and Antonio Almeida[b,c]

[a]Hematology Department, London North West University Healthcare NHS Trust, London, UK; [b]Department of Hematology, Hospital da Luz, Lisbon, Portugal; [c]Faculdade de Medicina, Universidade Católica Portuguesa, Lisbon, Portugal

ABSTRACT

Introduction: Achieving remission and prolonging duration of response are the primary treatment objectives for patients with acute myeloid leukemia (AML). However, identifying the best approach for older patients poses a significant challenge. This review explores the treatment pathways for older patients, especially those not eligible for stem cell transplantation and emphasizes the importance of optimizing outcomes by actively involving patients in their care plans.

Areas covered: There is currently no clinical consensus on when to use intensive or less-intensive induction chemotherapy for older patients, and more empirical evidence is needed. Meanwhile, this decision must still account for patients' preferences and circumstances in addition to the benefits and risks of therapy. Survey data have shown that patients want to be involved in their treatment decisions and that higher patient engagement improves patient-reported quality of care and satisfaction. While the importance of patient engagement is widely recognized, clinicians can work toward bridging the gap between patients' preferred and perceived levels of involvement in their treatment decisions.

Expert opinion: Patient engagement in treatment decisions is particularly important for older patients with AML. Understanding patients' perspectives and expectations for clinical and quality-of-life outcomes is essential to tailoring the most appropriate and effective treatment plan.

ARTICLE HISTORY
Received 15 April 2025
Accepted 12 June 2025

KEYWORDS
Acute myeloid leukemia; intensive chemotherapy; patient-centered care; quality of life; shared decision-making; treatment

1. Introduction: the importance of patient-centered care for older people with AML

Acute myeloid leukemia (AML) accounts for around one-third of all leukemia cases in the United States [1]. While the expected median survival for patients with newly diagnosed AML has increased over the past few decades, 5-year survival rates remain relatively low at approximately 33% [2]. The median age of patients with newly diagnosed AML is 69 years [2], and advanced age is associated with unfavorable cytogenetics (51% among those ≥75 years), worsening Eastern Cooperative Oncology Group (ECOG) performance status [3], and the presence of mutational and epigenetic modification profiles similar to those associated with myelodysplastic syndromes [4,5].

The treatment pathway for all patients with AML is guided by assessment of their eligibility for intensive chemotherapy (IC), largely determined by age, cytogenetic and molecular data, and a comprehensive assessment of patient fitness, comorbidity burden, ECOG performance status, and frailty [6–9]. For patients who are eligible and considered appropriate for intensive therapy, IC is administered to induce disease remission, followed by either stem cell transplantation (SCT) or consolidation/maintenance chemotherapy to maximize the duration of response [10]. Older patients with AML, particularly those with unfavorable cytogenetics and a poor ECOG performance status, may have less benefit from IC and an increased risk of post-induction mortality [10]. Historically, less-intensive treatment options for patients for whom IC was considered inappropriate involved the use of low-dose cytarabine, or hypomethylating agents (HMAs; azacitidine [AZA] or decitabine) [11]. More recently, safe and effective venetoclax (VEN)- and HMA-based combination regimens have been introduced [12]. The effectiveness of these less-intensive combination regimens, and their relatively manageable side-effect profile, is challenging IC even for those older patients classified as fit for IC.

There remains a lack of consensus regarding the optimal therapeutic approach for older patients with AML, and an absence of clear, evidence-based protocols to support the choice of intensive or less-intensive regimens for these patients. In this context, decision-making is complex, and it is important to personalize treatment strategies to patients' needs and goals [7]. Engaging patients in their care plan has shown improved outcomes with greater patient-reported treatment satisfaction and quality of care [13,14]. Despite this, many older patients with AML report low awareness of treatment options and often feel powerless in how their own treatment decisions are made, despite preferring to have more input on their care plan and a more patient-centered treatment approach [15]. Furthermore, patients with AML prefer to receive treatments that allow increased time at home [16]. The World Health Organization encourages quality of life (QoL) considerations in healthcare as 'an individual's perception of

CONTACT Esther N. Oliva esther.oliva@nhs.net Hematology Department, London North West University Healthcare NHS Trust, London HA1 3UJ, UK

© 2025 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (http://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

Article highlights

- There is a lack of standardized guidance on the optimal treatment approach for older patients with acute myeloid leukemia (AML), particularly in relation to balancing patient preferences and clinical considerations when choosing intensive induction chemotherapy or less-intensive regimens.
- Assigning intensive or less-intensive treatment based on the fitness of older patients with AML can be challenging and is generally driven by patient and disease characteristics. Additional factors including treatment setting (such as hospitalization) and life situations (such as caregiver availability) can influence the treatment pathway and outcomes. Therefore, it is important to create an individualized care plan that incorporates patients' perspectives and circumstances.
- Shared decision-making between patients with AML and their physicians is important to address some of the challenges related to treatment selection and medical management, and can provide greater patient-rated quality of care, patient satisfaction with physician communication, and improved patient-reported outcomes.

their position in life in the context of culture and value systems [...] and in relation to their goals, expectations, standards, and concerns' [17]. As such, providing the best possible outcomes while optimizing QoL for patients with AML should be a priority for clinical care. To highlight the importance of clinical approaches to patient-centered care, this review focuses on the journey of older patients with AML who are ineligible for SCT, and the importance of patient engagement and consideration of patients' individual needs when determining the most appropriate AML treatment approach.

2. Fitness assessment in older patients with AML

Fitness assessment in patients with AML is important to determine suitability for intensive or less-intensive treatment regimens, and to identify the right treatment option for the right patient. Recent guidance from an expert panel of the European LeukemiaNet (ELN) [18] defined fitness as a 'comprehensive evaluation of age, performance status, comorbidities and functional capacity'. As such, fitness is generally determined by a range of patient and disease characteristics, including use of geriatric assessment tools such as the ECOG or Karnofsky performance scores and other functional status scoring systems, measures of comorbidity burden, mental health, polypharmacy, social support, and QoL [8]. The Italian Society of Hematology (SIE), Italian Society of Experimental Hematology (SIES), and Italian Group for Bone Marrow Transplantation (GITMO) is a consensus criteria for assessment of unfitness [19]. These 'Ferrara criteria' account for age, comorbidities, infection, cognitive impairment, and performance status, and have been validated in both the intensive and non-intensive treatment settings [19–22]. Age >75 years is included among the 9 criteria identified by Ferrara et al as indicative of unfitness for IC [19], while the ELN recommendations advise careful assessment of IC eligibility in this age group (including consideration of the patient's expectations for QoL, psychosocial factors, and treatment preferences) [18].

3. AML risk classification by genetics in older patients

Historically, AML has been classified into 1 of 3 risk-grading groups (favorable; intermediate; or adverse risk) according to criteria defined by the ELN in 2022, based on the presence or absence of cytogenetic abnormalities and gene mutations [10]. When retrospectively categorized by the ELN 2022 criteria, approximately 35% of all patients with newly diagnosed AML belonged to the favorable-risk group, 24% to the intermediate-risk group, and 41% to the adverse-risk group [23]. Notably, however, in a population of older patients with AML (aged ≥60 years), only 11% were classified as having favorable-risk, 11% intermediate-risk, and 78% adverse-risk disease (Table 1) [24]. The intermediate-risk group is the most heterogeneous in terms of clinical factors, as many patients are categorized as intermediate risk due to a lack of specific cytogenetic or molecular abnormalities required for inclusion in the favorable- or adverse-risk groups [25]. Patients in the adverse-risk group tend to be older men with lower white blood cell count and lower blood blasts, and subsequently lower remission rates, higher relapse rates, and shorter survival times [23].

Importantly, the ELN 2022 risk criteria were developed based on younger patients receiving IC, and did not discriminate survival outcomes between the intermediate- and adverse-risk groups for patients aged ≥60 years [10,23,26]. In 2024, the ELN published refined genetic-risk classifications for patients receiving less-intensive regimens [26,27]. According to the revised risk classifications (not applicable to those with prior HMA treatment), patients with mutated *NPM1*, *IDH2*, *IDH1*, *DDX41*, or other cytogenetic and molecular abnormalities, but who have *FLT3*-ITD^{neg}, wild-type *NRAS, KRAS*, and *TP53*, have a favorable risk classification [26]. Patients with *FLT3*-ITD^{pos} and/or *NRAS*^{mut} and/or *KRAS*^{mut}, with *TP53* wild-type, are considered to be at intermediate risk; while those with mutated *TP53* comprise the adverse-risk group [26]. Median overall survival (OS) was estimated at 23–39 months in the favorable-risk group, 12–13 months in the intermediate-risk group, and 5–8 months in the adverse-risk group [26].

4. AML treatment in older patients: intensive and less-intensive regimens

Treatment recommendations for patients with AML are generally similar between the 2022 ELN guidelines in Europe and the National Comprehensive Cancer Network® (NCCN®) (V.2.2025) in the United States [10,28]. Broadly, for patients for whom IC is considered appropriate, both recommend IC induction followed by appropriate consolidation therapy, and subsequent maintenance therapy. In patients for whom IC is not suitable or who decline IC, less-intensive treatment options are an option, or clinical trials may be preferred [10,28].

4.1. IC regimens

IC for patients with AML typically comprises the '7 + 3' regimen of cytarabine and daunorubicin [10]; addition of an FLT3 inhibitor to IC is recommended in patients with an *FLT3*

Table 1. Baseline characteristics of older patients with AML according to the beat-AML 2024 ELN-refined risk stratification model (Hoff et al. [24]).

Characteristic	All patients ($N = 595$)	Beat-AML 2024 ELN-refined model ($n = 579$)[a]			
		Beat-AML favorable ($n = 127$)	Beat-AML intermediate ($n = 238$)	Beat-AML adverse ($n = 214$)	*P*-value
Age, median (range), y	73 (60–92)	74 (60–89)	74 (60–92)	73 (60–89)	0.159
Female sex, n (%)	247 (42)	67 (53)	85 (36)	88 (41)	0.007
Ethnicity, n (%)[b]					
Hispanic	7 (1)	4 (3)	2 (1)	0 (0)	
Non-Hispanic	560 (94)	122 (94)	226 (94)	205 (96)	
Race, n (%)[b]					
White	463 (78)	97 (76)	190 (80)	165 (77)	0.871
African American	32 (5)	7 (6)	11 (5)	14 (7)	
Asian	15 (3)	5 (4)	6 (3)	4 (2)	
Multiple or other	43 (7)	9 (7)	15 (6)	16 (7)	
Cytogenetics, n (%)[b,c]					
Normal karyotype	198 (33)	88 (69)	86 (36)	19 (9)	<0.001
Complex karyotype	199 (33)	1 (0)	40 (17)	152 (71)	<0.001
Chromosome 5/5q abnormality	134 (23)	0 (0)	21 (9)	110 (52)	<0.001
Chromosome 7 abnormality	129 (22)	3 (2)	35 (15)	88 (41)	<0.001
Chromosome 17 abnormality	4 (1)	0 (0)	1 (0)	3 (1)	0.244
Core-binding factor	10 (3)	9 (7)	0 (0)	0 (0)	<0.001
KMT2A-rearrangement	18 (3)	6 (5)	6 (3)	6 (3)	0.496
Mutation, n (%)[d]					
TP53	175 (29)	3 (2)	7 (3)	160 (75)	<0.001
IDH2	112 (19)	42 (33)	64 (27)	3 (1)	<0.001
MLL2	98 (16)	19 (15)	8 (3)	69 (32)	<0.001
KRAS	40 (7)	7 (6)	2 (1)	29 (14)	<0.001
RUNX1	146 (25)	2 (2)	103 (43)	37 (17)	<0.001
DNMT3A	143 (24)	53 (42)	60 (25)	26 (12)	<0.001
TET2	139 (23)	24 (19)	73 (31)	37 (17)	0.002
ASXL1	137 (23)	7 (6)	94 (39)	33 (15)	<0.001
SRSF2	136 (23)	17 (14)	92 (39)	26 (12)	<0.001
NRAS	91 (15)	21 (17)	41 (17)	26 (12)	0.249
NPM1	90 (15)	74 (58)	9 (4)	3 (1)	<0.001
FLT3-ITD	71 (12)	29 (23)	29 (12)	8 (4)	<0.001
STAG2	62 (10)	3 (2)	49 (21)	10 (5)	<0.001
IDH1	54 (9)	21 (17)	23 (10)	10 (5)	0.001
BCOR	52 (9)	0 (0)	29 (12)	20 (9)	<0.001
U2AF1	49 (8)	0 (0)	32 (13)	15 (7)	<0.001
SF3B1	47 (8)	1 (1)	25 (11)	19 (9)	0.003
EZH2	35 (6)	3 (2)	23 (10)	7 (3)	0.003
ZRSR2	25 (4)	1 (1)	12 (5)	12 (6)	0.082

[a]The final model is restricted to patients with reported outcome data (579/595).
[b]Unknown values were not considered in *P*-value calculations and are excluded from the results.
[c]Mutations were considered present at any detectable VAF.
[d]Cytogenetics available for 588/595.
Abbreviations: AML, acute myeloid leukemia; ELN, European LeukemiaNet; VAF, variant allele frequency.

mutation, and patients with favorable-risk AML may benefit from the addition of gemtuzumab ozogamicin. Consolidation therapy for these patients is typically with intermediate-dose cytarabine with or without an FLT3 inhibitor or gemtuzumab ozogamicin (depending on receipt in the IC regimen). Following IC and consolidation therapy, guidelines recommend maintenance therapy consisting of an FLT3 inhibitor in patients with *FLT3* mutations, or oral azacitidine (Oral-AZA) in patients without *FLT3* mutations [10,28]. For older patients who are not candidates for SCT, maintenance therapy with Oral-AZA following IC has shown prolonged survival among those ≥55 years of age [10,29].

For patients with therapy-related AML or AML with myelodysplasia-related changes, CPX-351 (dual-drug liposomal cytarabine and daunorubicin) is a preferred option for IC in older patients aged ≥60 years, with consolidation therapy for 1–2 cycles at a reduced dose [10,28]. In patients with high-risk /secondary AML aged 60–75 years, a phase 3, open-label trial demonstrated improved OS with CPX-351 versus the 7 + 3 chemotherapy regimen [30], with the benefit of treatment observed primarily among those with AML with myelodysplasia-related mutations [31].

There are a limited number of trials demonstrating a clear benefit of IC among older patients with AML, and evidence to inform treatment decisions remains uncertain [32]. Patients >60 years of age receiving IC have shown complete response (CR) rates of 60–70% and a median OS of approximately 12 months [33–36]. Of note, several studies have shown that patients >65 years of age do not benefit from increasing the intensity of the standard 7 + 3 regimen [33,37]. IC is also generally associated with prolonged and severe treatment-related cytopenias, leaving older patients at considerable risk of morbidity and mortality due to infections and bleeding [38].

Studies of older patients with AML in remission have shown that the greatest decrements in physical function and QoL occur shortly after induction therapy [39–41]. In most cases, patients receiving IC are admitted to the hospital for approximately 4 weeks followed by up to 3 cycles of consolidation chemotherapy with supportive care (comprising approximately 3–5 days of chemotherapy, with visits for laboratory

tests and possible transfusions up to 3 times per week). At least 2–4 laboratory tests and office visits per month may be necessary if patients proceed to Oral-AZA maintenance therapy [42]. However, following the first 4 months of IC, it is estimated that patients are able to remain at home for 90% of the time after initiation of Oral-AZA treatment.

4.2. Less-intensive regimens

There have been significant advances in the development of less-intensive treatment regimens for patients with AML [7]. Prior to the introduction of the oral BCL-2 inhibitor, VEN, HMAs were the standard of care for the treatment of older patients with AML considered ineligible for IC [43]. Compared with AZA alone, the addition of VEN has shown improved clinical response (CR/CR with incomplete hematologic recovery [CRi], 66.4% vs 28.3%; $p < 0.001$) and median OS (14.7 vs 9.6 months; hazard ratio for death, 0.66; 95% confidence interval [CI], 0.52 to 0.85; $p < 0.001$), but with higher rates of hematologic adverse events (83% vs 69%) [12]. The use of VEN in combination with HMAs has since been approved for newly diagnosed patients ≥75 years of age or who have other medical conditions that prevent the use of IC [44,45], and is recommended in both NCCN and ELN guidelines [10,28]. Given the higher rates of hematologic adverse events when combined with VEN, there may be instances where HMA monotherapy is preferable such as in very frail patients [46]. Further, a recent study in a large cohort of patients with newly diagnosed disease showed median OS and response rates in patients with *TP53* mutated AML were similar in those treated with HMA and VEN or HMA monotherapy, meaning HMA monotherapy may be preferable [47]. Nonetheless, current guidelines only recommend HMA monotherapy in patients with contraindications to VEN, including those who are intolerant due to frailty or sensitivity to VEN toxicity [28]. VEN in combination with low-dose cytarabine may also be considered for patients who are ineligible for HMA treatment due to resistance or intolerance [10,28], although this regimen does not have regulatory approval in Europe [48].

In contrast to IC, although many patients receive the initial dosing of VEN+AZA in an inpatient setting, particularly due to potential adverse events such as tumor lysis syndrome, they can receive subsequent monthly cycles of VEN+AZA in an outpatient care setting in the context of suitability and close monitoring [49,50]. For some patients, VEN+AZA may also be initiated in the outpatient setting, with several retrospective or community-based studies supporting the feasibility and safety of this approach for selected patients [49–52]. Nonetheless, VEN-based regimens are associated with an increased risk of myelosuppression, febrile neutropenia, infections, and gastrointestinal toxicity, making appropriate inpatient and/or outpatient monitoring an important consideration in the treatment discussion [12,53–55]. Furthermore, real-world studies have shown that dose titrations of the combined drugs require an individualized approach, which is not well standardized [56,57]. It is estimated that approximately 25% of the time is spent in hospital following the first 4 months of treatment compared with patients who received IC and are now in remission [42].

5. Treatment decisions for older patients with AML: incorporating patient perspectives

Treatment decisions for older patients with AML need to account for multiple factors, including fitness, cytogenetic and gene mutation profile, and other clinical factors (Figure 1 [10,28,48,58–61]). Age-related comorbidities, polypharmacy, and increased frailty in older patients can increase

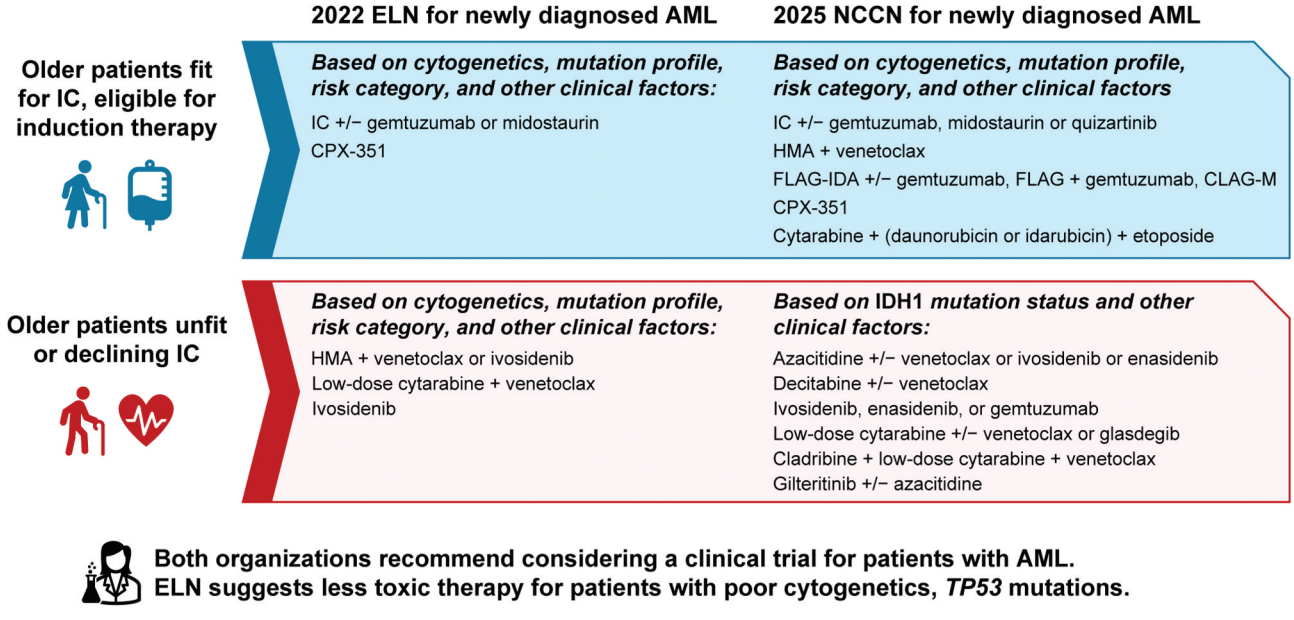

Figure 1. Summary of 2022 ELN and 2025 NCCN treatment recommendations for older patients with newly diagnosed AML [10,28,56][a].

[a]Treatment options are per guideline-recommendations and do not necessarily reflect regulatory approval for newly diagnosed AML. For example, the combination of low-dose cytarabine + venetoclax is not approved in Europe [46], and approvals for enasidenib (US [57]) and gilteritinib (US/Europe [58,59]) are in the relapsed/refractory (not first-line) setting.

Abbreviations: AML, acute myeloid leukemia; CLAG-M, cladribine, cytarabine, G-CSF, mitoxantrone; CPX-351, dual-drug liposomal cytarabine and daunorubicin; ELN, European LeukemiaNet; FLAG, fludarabine, cytarabine, G-CSF; FLAG-IDA, fludarabine, cytarabine, G-CSF, idarubicin; G-CSF, granulocyte colony-stimulating factor; HMA, hypomethylating agent; IC, intensive chemotherapy; NCCN, National Comprehensive Cancer Network.

the risk of experiencing treatment-related toxicity and complications, necessitating careful treatment selection and evaluation of suitability for IC [7]. Older patients also tend to have a more complex and unfavorable cytogenetic profile [7,8]. Additional factors, including treatment setting (hospitalization vs home), patient personality, and life situations (such as society or family roles, caregiver availability, and geographical factors), can further influence the treatment pathway and outcomes. Determining the suitability of older patients with AML for intensive or less-intensive treatment can thus present a significant challenge for clinicians, particularly in the absence of clear, evidence-based protocols to support decision-making.

Accounting for patients' perspectives is a critical part of decision-making for older patients with AML. Improved QoL, relief of symptoms, and extended survival have been reported as the most important factors in decision-making for patients with AML and their families, as well as by many treating physicians [62]. However, it should be noted that discrepancies between preferred and perceived levels of involvement in treatment decisions among cancer patients are highest for those who wanted a shared decision-making process but did not feel they had one with their physician (reported by a median of 42% of patients) [63]. Most patients with cancer report feeling overwhelmed or poorly informed during their clinical consultations, and older patients (>70 years) tend to want more information than younger patients [64]. Patients primarily seek information from their physicians regarding expectations for their treatment experience, potential side effects, and QoL during and after treatment [65].

Understanding the individual patient's expectations for how treatment decisions may impact their clinical outcomes and QoL is essential to tailoring the treatment plan in a shared decision-making process [66,67]. Beyond extending survival, patients want to live in 'good health' so they can have more time with their loved ones and pursue important life goals [62], with surveys showing that many older patients with AML prioritize QoL over quantity of life [68,69]. These patients often have clear life milestones and goals that should be considered in the context of potential treatment side effects to minimize disruptions to everyday life, such as time spent at home rather than in hospital [68,69]. Oral HMA therapies, which can be administered at home and may be preferred by patients who have difficulty traveling to the hospital or who opt for treatment at home due to personal circumstances, are now available. Oral decitabine/cedazurine is approved in Europe as induction therapy in patients with AML ineligible for standard induction chemotherapy [70], and Oral-AZA is approved as maintenance therapy in AML in the United States and Europe [71,72].

Patient involvement in treatment decisions is impacted by their often-limited understanding of treatment options and inaccurate perceptions of treatment side effects [62]. Physicians can support patients by educating them on their therapy options as part of a shared decision-making process, using relevant decision-aids and patient communication materials where available. Some patients may prefer a less-aggressive treatment approach resulting in discordance with their physician's treatment recommendations. For example, older patients with AML have reported giving the most value to treatments that reduce the duration of hospitalization and increase their QoL, whereas clinicians report valuing treatments that improve the chance of survival beyond 2 years [73]. While their priorities may not always align, both patients and physicians tend to perceive that the physician has the most influence in the decision-making process [62]. Importantly, physicians should remain conscious of this imbalance. For instance, by ensuring they maintain a clear understanding of the patient's priorities, selecting treatment that balances patient preferences with the potential for optimal clinical outcomes [74].

There is also an emotional impact associated with a diagnosis of AML that may interfere with patients' decision-making. In a study of older patients with newly diagnosed AML, patients felt shocked and overwhelmed by their diagnosis, powerless to make decisions, and rushed and unprepared to make treatment decisions [15]. These data emphasize the need to provide sufficient information and time for patients to participate meaningfully in decision-making. In the same study, while patients expressed a desire to follow their oncologist's treatment recommendations, they also reported a desire for ongoing involvement in their care [15]. Involvement in treatment decisions, for those patients who desire it, results in increased patient-rated quality of care, greater patient satisfaction with physician communication, and improved patient-reported outcomes [63,75,76]. Time constraints for both patients and physicians can hinder shared decision-making; however, pragmatic strategies could help to overcome this, such as sharing brief information during the initial consultation, and more detailed follow-up information via decision aids [77,78].

6. Hypothetical case studies

The following hypothetical case studies are intended to help readers consider specific aspects of patients' lives that may influence their participation and motivation behind treatment considerations in a shared decision-making process.

6.1. Case #1: 'Active family pillar'

A 75-year-old male was admitted to the emergency department following a copious nosebleed. His history included well-controlled arterial hypertension with no drinking or smoking habits. A complete blood count showed severe pancytopenia and circulating blasts. Following a complete hematologic assessment, bone marrow assessment showed a hypercellular marrow with 25% myeloblasts. The patient was diagnosed with AML not otherwise specified, with *NPM1*: wild-type, *FLT3*-ITD/TKD: negative, *TP53*: wild-type, *RUNX1*, *ASXL1*, *SRSF2*: negative, *IDH1* mutation detected, and cytogenetic abnormality trisomy 4. He is a retired but still active lawyer, the primary caregiver for his chronically ill spouse, and an engaged grandfather of two adopted children. He expresses a strong preference for minimizing hospitalization and rapidly returning to his active caregiving and professional roles. The patient was evaluated as fit for

IC based on ECOG performance status, absence of significant comorbidities, and preserved organ function. Due to the lack of a suitable donor, allogeneic transplant was deferred. Given his strong personal preference to avoid prolonged inpatient treatment and his caregiver responsibilities, the treatment plan needed to balance efficacy, tolerability, and time spent in hospital. Two primary therapeutic paths were discussed: Firstly IC (e.g. cytarabine/daunorubicin induction) followed by consolidation therapy and finally oral maintenance therapy, which would involve an initial hospital stay but potentially achieve deeper remission suitable for long-term disease control. Secondly, an outpatient-dominant regimen with AZA + ivosidenib, leveraging the presence of an *IDH1* mutation and providing a well-tolerated, mostly outpatient option, particularly suitable for older adults and those prioritizing QoL. The patient opted for the first regimen (IC), since this approach offered the highest likelihood of durable remission while preserving the patient's values – a short hospital stay, followed by a return to independence and home-based therapy.

6.2. Case #2: 'Independent and mobile'

A 71-year-old male presented with a one-month history of fatigue, pallor, recurrent infections, easy bruising, and occasional gum bleeds. Medical history included type 2 diabetes mellitus well-controlled with oral hypoglycemic agents, and history of smoking until 10 years prior. Following laboratory assessment, he was referred to a hematologist due to the findings of anemia, thrombocytopenia, and leukocytosis with circulating blasts. Bone marrow histology reported a hypercellular marrow with 40% blasts, cytogenetics: t(11q23), consistent with *KMT2A* rearrangement, *FLT3*-ITD/TKD: negative, *NPM1, IDH1/IDH2, TP53*: wild-type, other mutations tested (*RUNX1, ASXL1, SRSF2*): negative. The patient received a diagnosis of AML with *KMT2A* rearrangement with wild-type *NPM1* and was considered fit for IC. He is divorced and lives alone in a rural setting and describes himself as independent and mobile, with the ability to travel alone to his treatment center. He reported comfort in hospital-based care but wanted to retain some freedom for visiting distant family and maintaining his QoL throughout treatment. The patient was determined to be fit for IC based on preserved performance status, good organ function, and manageable comorbidities. The treatment team discussed potential therapeutic paths, considering both the unfavorable disease risk and patient preferences.

(1) Standard IC (e.g. 7 + 3) with inpatient induction followed by consideration of consolidation and/or maintenance therapy (e.g. Oral-AZA) following remission to minimize relapse risk and allow for flexible follow-up.
(2) Outpatient low-intensity regimens (e.g. HMA ± VEN), which were discussed but deprioritized due to the aggressive biology of *KMT2A*-rearranged AML and patient fitness for IC.

The patient expressed confidence in receiving hospital-based care during induction but placed high value on post-remission independence and flexibility. He declined SCT due to limited social support and geographic constraints but was receptive to oral maintenance options. This case underscores the importance of integrating disease biology with patient-centered goals in the treatment of AML. In older, fit patients with intermediate-to-adverse cytogenetic risk, short-course IC followed by oral maintenance offers a strategy that maximizes both therapeutic potential and respect for patient independence.

6.3. Case #3: 'Generally independent, with caregivers'

A 75-year-old female was admitted to the emergency department after a fall at home, which she attributed to dizziness. Her medical history was unremarkable, with the exception of a functional defect in her right knee due to arthritis, which caused some difficulty with mobility. Despite this, she remained independent at home and was able to manage day-to-day activities with the help of nearby family members who provided caregiver support when necessary. Upon laboratory testing, the patient was found to have severe anemia, mild thrombocytopenia, and leukopenia. A subsequent bone marrow biopsy confirmed a diagnosis of AML with *NPM1* mutation and an abnormal karyotype (monosomy 13, trisomy 8). Given her age and functional independence, she was considered fit for IC. The patient expressed a desire to receive treatment in a hospital environment for monitoring and surveillance but wished to avoid prolonged hospitalization. She also expressed concerns about her ability to manage frequent hospital visits due to her mobility issues and transportation needs, relying on caregiver support from nearby family. The patient was provided with two primary treatment options, each tailored to balance disease biology, efficacy, and patient preferences: IC followed by post-remission maintenance therapy, or VEN +AZA. Based on her clinical and personal considerations, this patient preferred the latter as a less-intensive chemotherapy regimen with more frequent outpatient hospital visits. Her treatment course must include a realistic plan for her regular transportation needs as she goes through the course of treatment, which may eventually require help from her nearby family. In this case, patient autonomy and family support were critical factors in decision-making, and the patient's choice of VEN+AZA reflects a personalized approach that prioritizes maintaining independence and family connections throughout their treatment journey.

6.4. Case #4: 'Conservative and concerned'

A 76-year-old male underwent a routine blood test as part of a regular checkup, revealing neutropenia and thrombocytopenia. Medical history was unremarkable. He was referred to the local hospital where bone marrow examination revealed the presence of 37% myeloid blasts. The patient was diagnosed with AML with *FLT3*-ITD, *NPM1*, and *DNMT3A* mutations, *TP53*: wild type, normal karyotype, and no additional molecular findings. He lives independently at home alone but requires regular help with domestic tasks from his children who live in the vicinity. The patient expressed concerns about the side effects of aggressive treatment, as well as the prospect of being hospitalized for prolonged periods. He also stressed the importance of

maintaining his independence and QoL, as much as possible in the context of his relatively advanced age. Given the *FLT3*-ITD, *NPM1*, and *DNMT3A* mutations, multiple treatment options were discussed in the context of his poor prognosis: 1. IC with the addition of a FLT-3 inhibitor (e.g. midostaurin or quizartinib), but given the patient's age and concerns about hospitalization, this was not deemed the best choice. 2. HMA+VEN, shown to be effective in older adults with AML, including those with *FLT3*-ITD mutations. The *FLT3*-ITD mutation typically signals a higher risk for relapse, suggesting the need for more aggressive therapy. However, this patient's age, preferences, and functional status led to the decision to pursue a less-intensive regimen with AZA and VEN, which can be administered on an outpatient basis and provides a good balance between disease control and QoL. This approach highlights the importance of considering not only biological factors but also the patient's goals and preferences when determining the appropriate treatment strategy. For older patients with AML, a less-intensive treatment regimen can offer a viable alternative to IC, preserving independence and QoL while still providing effective disease management. The logistical requirements of such a treatment plan should be considered with the caregivers, if possible, along with expectations for the treatment journey and potential outcomes.

7. Conclusion

Having a meaningful discussion of treatment options that consider the patient's life circumstances and preferences is particularly important for older patients with AML who are not eligible for SCT, especially for the decision to use intensive or less-intensive treatment. Physicians should consider the patient's perspective regarding their QoL while helping them to balance their preferences with the expected benefit-risk profile of their treatment options. To facilitate a truly informed decision, patients should be educated about their treatment options in a way that empowers rather than overwhelms them, providing clear and concise information that includes a discussion of the potential impact on their functional abilities, QoL, and clinical prognosis.

8. Expert opinion

The treatment of older patients with AML presents a complex challenge due to generally poor prognosis with high relapse rates, along with the need to balance clinical considerations with patient preferences. This complexity is compounded by the heterogeneity of AML and the diverse health profiles of older patients, who often present with comorbidities and varying levels of fitness [58]. Developing effective treatment plans to address this population may require a more comprehensive approach that considers both the disease complexity and the patient's preferences and QoL.

With a lack of standardized guidance on the optimal treatment approach for older patients with AML, the decision to assign intensive or less-intensive treatment can be challenging and is typically guided by patient and disease characteristics, such as genetic mutations, cytogenetic profiles, and overall health status [6–9]. For instance, intensive induction chemotherapy may offer higher remission rates but often comes with increased toxicity, which may not be tolerable for frail patients [33–36,38]. Conversely, less-intensive regimens, such as HMAs or low-dose cytarabine, are better tolerated but may result in lower remission rates and require frequent hospitalization for treatment regimens [7]. Additional factors including the treatment setting (e.g. hospitalization requirements) and the patient's life circumstances (e.g. caregiver availability) also significantly influence the treatment pathway and outcomes [7]. For example, patients without dedicated caregiver support may benefit from treatment in the hospital environment to ensure adequate monitoring and care, while for others, receiving treatment at home will allow them to maintain their independence and QoL.

The absence of a one-size-fits-all approach for treating older patients with AML underscores the importance of individualized care plans [58]. These plans should integrate not only clinical data but also the patient's values, goals, and QoL considerations. A decision-making process shared between patients and physicians is crucial in this context. This fosters better communication, enhances patient satisfaction, and aligns treatment choices with patient preferences, ultimately improving patient-rated quality of care and patient-reported outcomes [66,67].

Several developments are likely to shape the future of the treatment of older patients with AML. Advances in genomics and molecular profiling are paving the way for personalized medicine [79]. Identifying biomarkers that predict response to specific therapies could help tailor treatment plans more effectively. The availability of targeted agents, such as FLT3 inhibitors and IDH inhibitors, and newer agents, offers promising alternatives to traditional chemotherapy [80]. These therapies are generally less toxic and can be used in combination with other treatments. Emerging immunotherapeutic approaches also hold potential for improving outcomes in older patients with AML, aiming to harness the immune system to target leukemia cells more precisely [81]. While further research is needed, such therapies have the potential to benefit older patients with AML in future by reducing the potential for off-target toxicities.

We note that an urgent need remains for empirical evidence among older patients with AML to help optimize treatment approaches. Further, a better understanding of patient perspectives, fully capturing the diversity of the older patient population (including those with cognitive impairments or limited health literacy), is needed. Studies conducted in real-world settings are also required to provide insights into how different treatment regimens perform outside of clinical trials, where the large proportion of patients deemed ineligible for clinical trials may inform on treatment outcomes and guidelines, and help standardize care [82]. In addition, enhancing supportive care measures, such as managing treatment-related toxicities and addressing psychosocial needs, can improve the overall treatment experience and outcomes for older patients with AML.

Future research is likely to focus on developing comprehensive frailty assessment tools specifically for patients with AML to better stratify patients for intensive or less-intensive

treatments [83], and exploring combination therapies that integrate targeted agents with traditional regimens to maximize efficacy while minimizing toxicity [84]. While speculative at present, the role of artificial intelligence in predicting treatment outcomes and optimizing care plans also holds potential and warrants further study.

As these advancements unfold, they will help to address current gaps in the treatment of older patients with AML, offering more standardized and effective approaches that prioritize both clinical outcomes and patient well-being.

Funding

Writing and editorial support was funded by Bristol Myers Squibb, Princeton, NJ, USA.

Declaration of interest

EN Oliva has received royalties or holds licenses from Ryvu Therapeutics, Halia Therapeutics, and Servier; has received consulting fee from Daiichi Sankyo and Bristol Myers Squibb; has received honoraria from Sobi, Bristol Myers Squibb, Novartis, and Alexion Pharmaceuticals; has received meeting attendance support from Daiichi Sankyo and Sobi; and serves on the data safety monitoring or advisory boards for Daiichi Sankyo, Bristol Myers Squibb, Sobi, and Alexion Pharmaceuticals. A Almeida has received honoraria from Bristol Myers Squibb, Sobi, GSK, Novartis, and Gilead Sciences.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Siegel RL, Kratzer TB, Giaquinto AN, et al. Cancer statistics, 2025. CA Cancer J Clin. 2025;75(1):10–45. doi: 10.3322/caac.21871
2. SEER Cancer Stat Facts: Leukemia — Acute Myeloid Leukemia (AML). National Cancer Institute; [cited 2025 May 19]. Available from: https://seer.cancer.gov/statfacts/html/amyl.html
3. Appelbaum FR, Gundacker H, Head DR, et al. Age and acute myeloid leukemia. Blood. 2006;107(9):3481–3485. doi: 10.1182/blood-2005-09-3724
4. Figueroa ME, Skrabanek L, Li Y, et al. MDS and secondary AML display unique patterns and abundance of aberrant DNA methylation. Blood. 2009;114(16):3448–3458. doi: 10.1182/blood-2009-01-200519
5. Li JF, Cheng WY, Lin XJ, et al. Aging and comprehensive molecular profiling in acute myeloid leukemia. Proc Natl Acad Sci U S A. 2024;121(10):e2319366121. doi: 10.1073/pnas.2319366121
6. Deeg HJ. Not all patients with AML over 60 years of age should be offered early allogeneic stem cell transplantation. Blood Adv. 2022;6(5):1623–1627. doi: 10.1182/bloodadvances.2021004799
7. Babakhanlou R, Ravandi-Kashani F. Non-intensive acute myeloid leukemia therapies for older patients. Expert Rev Hematol. 2023;16(3):171–180. doi: 10.1080/17474086.2023.2184342
   • **This recent review provides a broad, comprehensive perspective on AML treatment options, including both intensive and less-intensive regimens, along with research on patient- and AML-related considerations.**
8. Cortes JE, Mehta P. Determination of fitness and therapeutic options in older patients with acute myeloid leukemia. Am J Hematol. 2021;96(4):493–507. doi: 10.1002/ajh.26079
   • **Cortes and Mehta provide a thorough, practical review of objective assessments of fitness for IC among older patients with AML.**
9. Venditti A, Cairoli R, Caira M, et al. Assessing eligibility for treatment in acute myeloid leukemia in 2023. Expert Rev Hematol. 2023;16(3):181–190. doi: 10.1080/17474086.2023.2185603
10. Döhner H, Wei AH, Appelbaum FR, 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):1345–1377. doi: 10.1182/blood.2022016867
    • **Update to the European LeukemiaNet (ELN) clinical practice recommendations for diagnosis and management of AML.**
11. Short NJ, Kantarjian H. When less is more: reevaluating the role of intensive chemotherapy for older adults with acute myeloid leukemia in the modern era. J Clin Oncol. 2021;39(28):3104–3108. doi: 10.1200/JCO.21.00960
12. DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. N Engl J Med. 2020;383(7):617–629. doi: 10.1056/NEJMoa2012971
13. Marzban S, Najafi M, Agolli A, et al. Impact of patient engagement on healthcare quality: a scoping review. J Patient Exp. 2022;9:23743735221125439. doi: 10.1177/23743735221125439
14. Morelli E, Mulas O, Caocci G. Patient-physician communication in acute myeloid leukemia and myelodysplastic syndrome. Clin Pract Epidemiol Ment Health. 2021;17(1):264–270. doi: 10.2174/1745017902117010264
15. Richardson DR, Mhina CJ, Teal R, et al. Experiences of treatment decision-making among older newly diagnosed adults with acute myeloid leukemia: a qualitative descriptive study. Support Care Cancer. 2024;32(3):197. doi: 10.1007/s00520-024-08397-3
    •• **Richardson and colleagues report findings from in-depth interviews with newly diagnosed older patients with AML, providing detailed insights into patients' perspectives on impact of AML and the treatment decision-making process.**
16. Richardson DR, Oakes AH, Crossnohere NL, et al. Prioritizing the worries of AML patients: quantifying patient experience using best-worst scaling. Psychooncology. 2021;30(7):1104–1111. doi: 10.1002/pon.5652
17. World Health Organization. WHOQOL: measuring quality of life. 2024 [cited 2024 Oct 17]. Available from: https://www.who.int/tools/whoqol
18. Venditti A, Palmieri R, Maurillo L, et al. Fitness assessment in acute myeloid leukemia: recommendations from an expert panel on behalf of the European LeukemiaNet. Blood Adv. 2025;9(9):2207–2220. doi: 10.1182/bloodadvances.2024013744
    •• **Recent consensus recommendations from an expert panel of the ELN on fitness assessment in patients with AML.**
19. Ferrara F, Barosi G, Venditti A, et al. Consensus-based definition of unfitness to intensive and non-intensive chemotherapy in acute myeloid leukemia: a project of SIE, SIES and GITMO group on a new tool for therapy decision making. Leukemia. 2013;27(5):997–999. doi: 10.1038/leu.2012.303
20. Palmieri R, Othus M, Halpern AB, et al. Accuracy of SIE/SIES/GITMO consensus criteria for unfitness to predict early mortality after intensive chemotherapy in adults with AML or other high-grade myeloid neoplasm. J Clin Oncol. 2020;38(35):4163–4174. doi: 10.1200/JCO.20.01392
21. Borlenghi E, Pagani C, Zappasodi P, et al. Validation of the "fitness criteria" for the treatment of older patients with acute myeloid leukemia: a multicenter study on a series of 699 patients by the Network Rete Ematologica Lombarda (REL). J Geriatr Oncol. 2021;12(4):550–556. doi: 10.1016/j.jgo.2020.10.004
22. Apolito V, Arrigo G, Vasseur L, et al. Validation of SIE/SIES/GITMO consensus criteria for unfitness to predict early mortality and survival in acute myeloid leukaemia patients treated with hypomethylating agents and venetoclax. Br J Haematol. 2023;203(4):e98–e101. doi: 10.1111/bjh.19022
23. Mrózek K, Kohlschmidt J, Blachly JS, et al. Outcome prediction by the 2022 European LeukemiaNet genetic-risk classification for

adults with acute myeloid leukemia: an alliance study. Leukemia. 2023;37(4):788–798. doi: 10.1038/s41375-023-01846-8

24. Hoff FW, Blum WG, Huang Y, et al. Beat-AML 2024 ELN-refined risk stratification for older adults with newly diagnosed AML given lower-intensity therapy. Blood Adv. 2024;8(20):5297–5305. doi: 10.1182/bloodadvances.2024013685
25. Awada H, Mustafa Ali MK, Thapa B, et al. A focus on intermediate-risk acute myeloid leukemia: sub-classification updates and therapeutic challenges. Cancers (Basel). 2022;14(17):4166. doi: 10.3390/cancers14174166
26. Döhner H, DiNardo CD, Appelbaum FR, et al. Genetic risk classification for adults with AML receiving less-intensive therapies: the 2024 ELN recommendations. Blood. 2024;144(21):2169–2173. doi: 10.1182/blood.2024025409

•• **This recent update to the ELN genetic risk classifications were specifically developed when data related to patients receiving less-intensive regimens were available, as the previous version was based on data from younger patients receiving IC.**

27. Döhner H, Pratz KW, DiNardo CD, et al. Genetic risk stratification and outcomes among treatment-naive patients with AML treated with venetoclax and azacitidine. Blood. 2024;144(21):2211–2222. doi: 10.1182/blood.2024024944
28. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.2.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. [cited 2025 May 19]. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.2.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved.

•• **Clinical practice recommendations from the National Comprehensive Cancer Network that are updated periodically as new evidence emerges.**

29. Wei AH, Döhner H, Pocock C, et al. QUAZAR AML-001 trial investigators. Oral azacitidine maintenance therapy for acute myeloid leukemia in first remission. N Engl J Med. 2020;383(26):2526–2537. doi: 10.1056/NEJMoa2004444

• **Primary findings from the QUAZAR AML-001 phase 3 clinical trial demonstrating the efficacy of maintenance therapy with Oral-AZA to improve OS and relapse-free survival while maintaining QoL measures among older patients with AML in remission after chemotherapy.**

30. Lancet JE, Uy GL, Cortes JE, 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):2684–2692. doi: 10.1200/JCO.2017.77.6112
31. Shimony SO, Murdock H, Keating J, et al. AML-MR mutations drive the benefit of CPX-351 over 7+3 in the pivotal phase 3 AML trial [abstract]. Blood. 2024;144(Suppl 1):60–61. doi: 10.1182/blood-2024-200413
32. Almeida AM, Ramos F. Acute myeloid leukemia in the older adults. Leuk Res Rep. 2016;6:1–7. doi: 10.1016/j.lrr.2016.06.001
33. Löwenberg B, Ossenkoppele GJ, van Putten W, et al. High-dose daunorubicin in older patients with acute myeloid leukemia. N Engl J Med. 2009;361(13):1235–1248. doi: 10.1056/NEJMoa0901409
34. Castaigne S, Pautas C, Terre C, 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):1508–1516. doi: 10.1016/S0140-6736(12)60485-1
35. Gardin C, Chevret S, Pautas C, et al. Superior long-term outcome with idarubicin compared with high-dose daunorubicin in patients with acute myeloid leukemia age 50 years and older. J Clin Oncol. 2013;31(3):321–327. doi: 10.1200/JCO.2011.40.3642
36. Pigneux A, Bene MC, Salmi LR, et al. Improved survival by adding lomustine to conventional chemotherapy for elderly patients with AML without unfavorable cytogenetics: results of the LAM-SA 2007 FILO trial. J Clin Oncol. 2018;36(32):3203–3210. doi: 10.1200/JCO.2018.78.7366
37. Pluta A, Robak T, Wrzesien-Kus A, et al. Addition of cladribine to the standard induction treatment improves outcomes in a subset of elderly acute myeloid leukemia patients. Results of a randomized Polish Adult Leukemia Group (PALG) phase II trial. Am J Hematol. 2017;92(4):359–366. doi: 10.1002/ajh.24654
38. Buckley SA, Othus M, Vainstein V, et al. Prediction of adverse events during intensive induction chemotherapy for acute myeloid leukemia or high-grade myelodysplastic syndromes. Am J Hematol. 2014;89(4):423–428. doi: 10.1002/ajh.23661
39. Alibhai SMH, Leach M, Kermalli H, et al. The impact of acute myeloid leukemia and its treatment on quality of life and functional status in older adults. Crit Rev Oncol Hematol. 2007;64(1):19–30. doi: 10.1016/j.critrevonc.2007.07.003
40. Alibhai SMH, Leach M, Gupta V, et al. Quality of life beyond 6 months after diagnosis in older adults with acute myeloid leukemia. Crit Rev Oncol Hematol. 2009;69(2):168–174. doi: 10.1016/j.critrevonc.2008.07.015
41. Alibhai SMH, Breunis H, Timilshina N, et al. Quality of life and physical function in adults treated with intensive chemotherapy for acute myeloid leukemia improve over time independent of age. J Geriatr Oncol. 2015;6(4):262–271. doi: 10.1016/j.jgo.2015.04.002
42. Atallah E. Low-intensity induction in acute myeloid leukemia. Always in the patients' best interest? Haematologica. 2023;108(4):949–950. doi: 10.3324/haematol.2022.281506
43. Gardin C, Dombret H. Hypomethylating agents as a therapy for AML. Curr Hematol Malig Rep. 2017;12(1):1–10. doi: 10.1007/s11899-017-0363-4
44. Maiti A, Rausch CR, Cortes JE, et al. Outcomes of relapsed or refractory acute myeloid leukemia after frontline hypomethylating agent and venetoclax regimens. Haematologica. 2021;106(3):894–898. doi: 10.3324/haematol.2020.252569
45. National Cancer Institute. Acute myeloid leukemia treatment (PDQ®)–Health professional version 2024. [cited 2024 Oct 24]. Available from: https://www.cancer.gov/types/leukemia/hp/adult-aml-treatment-pdq
46. Diekmann B, Timmerman M, Hempenius L, et al. New treatment opportunities for older patients with acute myeloid leukemia and the increasing importance of frailty assessment – an oncogeriatric perspective. J Geriatr Oncol. 2024;15(2):101631. doi: 10.1016/j.jgo.2023.101631
47. Shimony S, Garcia JS, Keating J, et al. Molecular ontogeny underlies the benefit of adding venetoclax to hypomethylating agents in newly diagnosed AML patients. Leukemia. 2024;38(7):1494–1500. doi: 10.1038/s41375-024-02230-w
48. VENCLYXTO® (venetoclax) summary of product characteristics. [cited 2025 May 22]. Available from: https://www.ema.europa.eu/en/documents/product-information/venclyxto-epar-product-information_en.pdf
49. Manda S, Anz BM 3rd, Benton C, et al. A phase 3b study of venetoclax and azacitidine or decitabine in an outpatient setting in patients with acute myeloid leukemia. Hematol Oncol. 2024;42(3):e3274. doi: 10.1002/hon.3274
50. Gat R, Miri N, Shai L, et al. Outpatient initiation of venetoclax-azacitidine for selected acute myeloid leukemia patients is feasible and safe: a real world single center analysis [abstract]. HemaSphere. 2023;7(Suppl):e4811210. doi: 10.1097/01.HS9.0000969188.48112.10
51. Palmer S, Patel A, Wang C, et al. Outpatient initiation of venetoclax in patients with acute myeloid leukemia. J Oncol Pharm Pract. 2023;29(7):1590–1598. doi: 10.1177/10781552221142872
52. Shallis RM, Weiss JJ, Winer ES, et al. Feasibility and safety of outpatient hypomethylating agent and venetoclax initiation with and without ramp-up for newly diagnosed acute myeloid leukemia: results from the consortium on myeloid malignancies and neoplastic diseases (COMMAND). Leuk Lymphoma. 2025 [online ahead of print]. 1–5. doi: 10.1080/10428194.2025.2496339
53. Wei AH, Montesinos P, Ivanov V, et al. Venetoclax plus LDAC for newly diagnosed AML ineligible for intensive chemotherapy: a phase 3 randomized placebo-controlled trial. Blood. 2020;135(24):2137–2145. doi: 10.1182/blood.2020004856

54. DiNardo CD, Lachowiez CA, Takahashi K, et al. Venetoclax combined with FLAG-IDA induction and consolidation in newly diagnosed and relapsed or refractory acute myeloid leukemia. J Clin Oncol. 2021;39(25):2768–2778. doi: 10.1200/JCO.20.03736
55. Jonas BA, Pollyea DA. How we use venetoclax with hypomethylating agents for the treatment of newly diagnosed patients with acute myeloid leukemia. Leukemia. 2019;33(12):2795–2804. doi: 10.1038/s41375-019-0612-8
56. Zhu LX, Chen RR, Wang LL, et al. A real-world study of infectious complications of venetoclax combined with decitabine or azacitidine in adult acute myeloid leukemia. Support Care Cancer. 2022;30(8):7031–7038. doi: 10.1007/s00520-022-07126-y
57. Cui J, Chen X, Li C, et al. Reduced duration and dosage of venetoclax is efficient in newly diagnosed patients with acute myeloid leukemia. Hematology. 2024;29(1):2293512. doi: 10.1080/16078454.2023.2293512
58. de Leeuw DC, Ossenkoppele GJ, Janssen JJWM. Older patients with acute myeloid leukemia deserve individualized treatment. Curr Oncol Rep. 2022;24(11):1387–1400. doi: 10.1007/s11912-022-01299-9
59. IDHIFA® (enasidenib) US prescribing information. [cited 2025 May 22]. Available from: https://packageinserts.bms.com/pi/pi_idhifa.pdf
60. XOSPATA® (gilteritinib) US prescribing information. [cited 2025 May 22]. Available from: https://astellas.us/docs/xospata.pdf
61. XOSPATA® (gilteritinib) summary of product characteristics. [cited 2025 May 22]. Available from: https://www.ema.europa.eu/en/documents/product-information/xospata-epar-product-information_en.pdf
62. LeBlanc TW, Russell NH, Hernandez-Aldama L, et al. Patient, family member and physician perspectives and experiences with AML treatment decision-making. Oncol Ther. 2022;10(2):421–440. doi: 10.1007/s40487-022-00200-9
63. Noteboom EA, May AM, van der Wall E, et al. Patients' preferred and perceived level of involvement in decision making for cancer treatment: a systematic review. Psychooncology. 2021;30(10):1663–1679. doi: 10.1002/pon.5750
64. Josfeld L, Keinki C, Pammer C, et al. Cancer patients' perspective on shared decision-making and decision aids in oncology. J Cancer Res Clin Oncol. 2021;147(6):1725–1732. doi: 10.1007/s00432-021-03579-6
65. Ankolekar A, Vanneste BGL, Bloemen-van Gurp E, et al. Development and validation of a patient decision aid for prostate cancer therapy: from paternalistic towards participative shared decision making. BMC Med Inform Decis Mak. 2019;19(1):130. doi: 10.1186/s12911-019-0862-4
66. Richardson DR, Crossnohere NL, Seo J, et al. Age at diagnosis and patient preferences for treatment outcomes in AML: a discrete choice experiment to explore meaningful benefits. Cancer Epidemiol Biomarkers Prev. 2020;29(5):942–948. doi: 10.1158/1055-9965.EPI-19-1277
67. Loh KP, Abdallah M, Kadambi S, et al. Treatment decision-making in acute myeloid leukemia: a qualitative study of older adults and community oncologists. Leuk Lymphoma. 2021;62(2):387–398. doi: 10.1080/10428194.2020.1832662
68. Booth A, Bell T, Halhol S, et al. Using social media to uncover treatment experiences and decisions in patients with acute myeloid leukemia or myelodysplastic syndrome who are ineligible for intensive chemotherapy: patient-centric qualitative data analysis. J Med Internet Res. 2019;21(11):e14285. doi: 10.2196/14285
69. Crawford R, Sully K, Conroy R, et al. Patient-centered insights on treatment decision making and living with acute myeloid leukemia and other hematologic cancers. Patient. 2020;13(1):83–102. doi: 10.1007/s40271-019-00384-9
70. INAQOVI® (oral decitabine/cedazuridine) summary of product characteristics. [cited 2025 May 22]. Available from: https://www.ema.europa.eu/en/documents/product-information/inaqovi-epar-product-information_en.pdf
71. ONUREG® (oral azacitidine) US prescribing information. [cited 2025 May 22]. Available from: https://packageinserts.bms.com/pi/pi_onureg.pdf
72. ONUREG® (oral azacitidine) summary of product characteristics. [cited 2025 May 22]. Available from: https://www.ema.europa.eu/en/documents/product-information/onureg-epar-product-information_en.pdf
73. Zhou M, Yang H, Song Y, et al. Patient and physician preferences for treatment of newly diagnosed acute myeloid leukemia (AML) in patients not candidates for intensive chemotherapy [abstract]. Blood. 2021;138(Suppl Supplement 1):4047. doi: 10.1182/blood-2021-145385
74. Harrison M, Milbers K, Hudson M, et al. Do patients and health care providers have discordant preferences about which aspects of treatments matter most? Evidence from a systematic review of discrete choice experiments. BMJ Open. 2017;7(5):e014719. doi: 10.1136/bmjopen-2016-014719
75. Brown R, Butow P, Wilson-Genderson M, et al. Meeting the decision-making preferences of patients with breast cancer in oncology consultations: impact on decision-related outcomes. J Clin Oncol. 2012;30(8):857–862. doi: 10.1200/JCO.2011.37.7952
76. Hahlweg P, Kriston L, Scholl I, et al. Cancer patients' preferred and perceived level of involvement in treatment decision-making: an epidemiological study. Acta Oncol. 2020;59(8):967–974. doi: 10.1080/0284186X.2020.1762926
77. Caverly TJ, Hayward RA. Dealing with the lack of time for detailed shared decision-making in primary care: everyday shared decision-making. J Gen Intern Med. 2020;35(10):3045–3049. doi: 10.1007/s11606-020-06043-2
78. Fisher KA, Tan ASL, Matlock DD, et al. Keeping the patient in the center: common challenges in the practice of shared decision making. Patient Educ Couns. 2018;101(12):2195–2201. doi: 10.1016/j.pec.2018.08.007
79. Duncavage EJ, Bagg A, Hasserjian RP, et al. Genomic profiling for clinical decision making in myeloid neoplasms and acute leukemia. Blood. 2022;140(21):2228–2247. doi: 10.1182/blood.2022015853
80. Bhansali RS, Pratz KW, Lai C. Recent advances in targeted therapies in acute myeloid leukemia. J Hematol Oncol. 2023;16(1):29. doi: 10.1186/s13045-023-01424-6
81. Subklewe M, Bücklein V, Sallman D, et al. Novel immunotherapies in the treatment of AML: is there hope? Hematology Am Soc Hematol Educ Program. 2023;2023(1):691–701. doi: 10.1182/hematology.2023000455
82. Derman BA, Belli AJ, Battiwalla M, et al. Reality check: real-world evidence to support therapeutic development in hematologic malignancies. Blood Rev. 2022;53:100913. doi: 10.1016/j.blre.2021.100913
83. Woods JD, Klepin HD. Geriatric assessment in acute myeloid leukemia. Acta Haematol. 2024;147(2):219–228. doi: 10.1159/000535500
84. Roman Diaz JL, Vazquez Martinez M, Khimani F. New approaches for the treatment of AML beyond the 7+3 regimen: current concepts and new approaches. Cancers (Basel). 2024;16(3):677. doi: 10.3390/cancers16030677