



Patient, Family Member and Physician Perspectives and Experiences with AML Treatment Decision-Making

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ABSTRACT

Introduction: Treatment decisions in older adults with acute myeloid leukemia (AML) are challenging, particularly for those who are not candidates for intensive chemotherapy (IC), and the trade-offs patients, their families and physicians consider when choosing a treatment

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option are not well understood. This qualitative research explored the value of extending survival and the treatment decision-making process from a multi-stakeholder perspective.

Methods: Overall, 28 patients with AML (≥ 65 years old, unsuitable for IC), 25 of their relatives and 10 independent physicians from the US, UK and Canada took part in one-on-one, 60-minute qualitative interviews.

Results: Across all stakeholders, improved health-related quality of life (HRQoL), extended survival and relief of AML symptoms were rec-

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ognized as most important in AML treatment decision-making. However, extending survival in ‘good health’ was more important than extending survival alone, particularly because of the extra time it gives patients and their relatives together, and allows patients to achieve important goals. Patients’ limited understanding of available treatment options, paired with incorrect perceptions of treatment side effects, impacted their involvement in the treatment decision-making process. Patients and physicians perceived physicians to have the most influence in the decision-making process despite their priorities not always aligning.

Conclusion: These findings illustrate the importance of having structured discussions which explicitly assess patients’ goals and their understanding and expectations of treatments and also the need for patient friendly resources about the lived experience of AML and available treatment options. These measures will help to ensure that patients are fully involved in the shared decision-making process.

Keywords: Acute myeloid leukemia; AML; Decision-making; Qualitative interviews; Treatment

Key Summary Points

Every day matters to enable patients with acute myeloid leukemia (AML) to spend more time with family/friends and do hobbies, but not at the sacrifice of good health

Incorrect perceptions and limited understanding about treatment options may limit patients’ treatment acceptance resulting in worse outcomes

Patients consider physicians to have the most influence in treatment decision-making; however, priorities and treatment goals of patient and physicians do not always align

INTRODUCTION

Acute myeloid leukemia (AML) is one of the more common blood cancers, characterized by peripheral blood and bone marrow myeloblast proliferation, leading to bone marrow failure and rapid death without treatment. AML primarily affects older adults, with a median age of almost 70 years [1, 2]. Previous research indicates that older patients with AML have substantial misperceptions about their prognosis and often feel distressed, overwhelmed, and uninformed about available treatments, yet are faced with the urgent need to make these potentially life defining decisions [3–8].

With the recent introduction of several new drugs [9], treatment decisions for patients with AML have become even more challenging, with difficult risk-to-benefit assessments to be made when deciding among multiagent intensive chemotherapy (IC), non-intensive chemotherapy (NIC) [3, 10] or best supportive care (BSC; e.g., blood product transfusions) alone [11–13]. Consideration must be given, for example, to likelihood of achieving complete remission (CR) and disease-free survival versus experiencing substantial toxicities or even early death. In recent years, it has been acknowledged that traditional survival endpoints in oncology clinical trials overlook disease- or treatment-related events that impact patients’ wellbeing. For this reason, health-related quality of life (HRQoL) has been recognized as an important endpoint and predictor of outcomes in AML [14], with worsening HRQoL potentially offsetting the value of prolonging survival. For example, one study found that, while patients with AML highly valued the chance at CR, they were willing to forgo small increases in the probability of remission to improve other outcomes, notably long-term side effects [15]. Other treatment factors, including treatment delivery and convenience, may also play a significant role.

However, for older patients with AML, there are other factors that contribute to a poorer prognosis including physical frailty, a higher incidence of comorbidities and adverse cytogenetic abnormalities, and an increased risk for

treatment-related morbidity and mortality [16–18]. As such, for older patients with AML (particularly those who are over the age of 75 years and have significant comorbidities), IC is not considered a suitable treatment option [19]. Thus, for this population, treatment options are narrowed, adding further complexity to treatment decision-making. Despite this, there is very little published in the literature on the treatment decision-making process in older patients with AML who are unsuitable for IC, including the factors that influence decision-making, the trade-offs these patients are willing to make and patients' expectations about treatment outcomes—particularly from a multi-stakeholder perspective. The current research aimed to substantiate and build on the current literature by exploring the value of extending survival in older patients with AML who are unwilling or unsuitable to receive IC and the associated complex, multifactorial decision-making process and inter-stakeholder dynamics from the perspective of patients, their relatives and physicians.

METHODS

Study Design

This was a non-interventional, cross-sectional, qualitative interview study involving patients with AML as well as their relatives and independent physicians recruited in the United States (US), United Kingdom (UK) and Canada.

To support a patient-centered approach and ensure the perspectives of different stakeholders were considered, four physicians with expertise in AML and four patient advocates formed a steering committee (SC) to provide input and consultation at key stages throughout the research. Figure 1 presents an overview of the study design.

Sample

It was planned that a total of 10 physicians (not part of the SC) and 25 patients (and their

relatives) would be recruited to take part in this study.

Physicians specialized in treating adults with AML (> 10 cases per year, with ≥ 3 cases where the patient was unsuitable for IC) based in the US, Canada and UK were recruited via research recruitment agencies and were not physicians of the participating patients.

Patients and relatives were recruited as dyads to facilitate comparisons between patient and relatives' perspectives. In the US, patients were recruited by a recruitment agency via referrals from physicians working in hematology and/or oncology (any site names/locations were blinded to the authors). In the UK and Canada, patients were recruited via physician referrals from The Russell Centre for Clinical Haematology at Nottingham University Hospitals NHS Trust (Nottingham, UK), Bristol Haematology & Oncology Centre at University Hospitals Bristol NHS Foundation Trust (Bristol, UK) and Princess Margaret Cancer Center (Toronto, Canada) facilitated by authors NHR and DM.

Eligible patients were ≥ 65 years old, had a physician-confirmed diagnosis of AML according to the World Health Organization (WHO) 2016 Classification [20] and were unsuitable or unwilling to receive IC. Suitability for IC was determined by the recruiting physician who considered factors such as poor performance status, significant comorbidities and adverse cytogenetics/molecular genetics. [21]

Relatives were referred by the patient and had to be ≥ 18 years old and have frequent contact with the patient.

A quota sampling approach was employed for the patient sample to ensure representation of key demographic and clinical characteristics [22], including age, time since diagnosis and treatment option. However, due to the rarity of the condition and how unwell patients were, these were target quotas only (i.e., flexible).

Ethics

The study was approved by relevant ethical review agencies in the US, Canada and the UK. Written informed consent was obtained prior to the collection of any data.

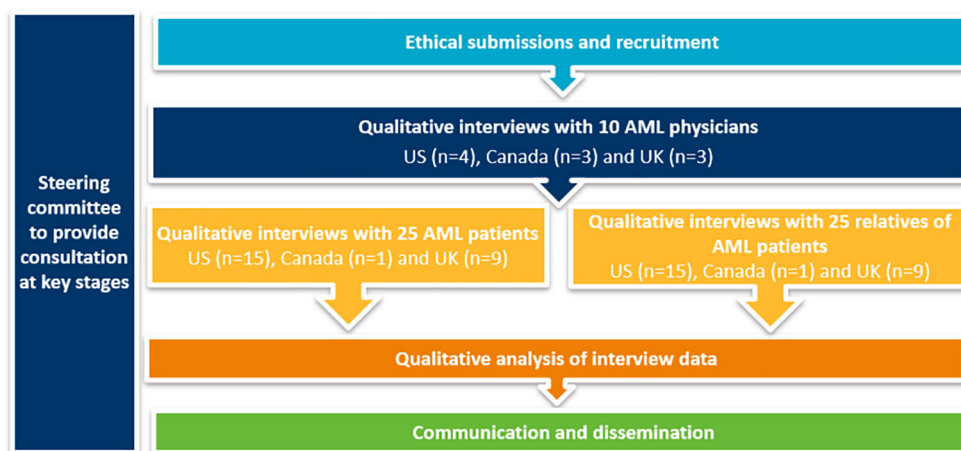


Fig. 1 Overview of study design

Interview Process and Content

Each participant took part in a single, one-on-one, 60-minute interview conducted via telephone or video conference with a trained interviewer with extensive expertise in qualitative techniques (JS and LO). Interviews were conducted between April 2019 and December 2020.

A semi-structured interview guide, developed based on findings from a literature review [10] and with SC input, was used for each participant group to ensure all topics of interest were discussed. The interviews were conducted using a concept elicitation (CE) technique where open-ended, exploratory questions were asked to elicit spontaneous, unbiased responses about the participant's experience, followed by more focused questions on topics that may not have naturally emerged during the interview [23, 24].

The patient interviews explored the AML journey and the value of living longer, specifically, key milestones that patients had achieved since diagnosis and hoped to achieve in future (e.g., family weddings or travel). The interviews also explored the treatment decision-making process and the role of the various stakeholders (e.g., how information was provided and what treatment options were discussed). The interviews with relatives explored similar topics but from the relatives' perspective. The physician interviews covered these topics and also the

clinical management of patients who were unsuitable for IC.

As part of the interview, all participants completed a quantitative questionnaire where they rated the importance of various factors in AML treatment decision-making from 0 (not important) to 3 (very important).

Data Analysis and Sample Size Considerations

In qualitative research, sample size is typically determined based on the goal to achieve 'concept saturation' (a point at which no new concepts are likely to emerge with further interviews). Research suggests that, in a relatively homogeneous population, approximately 85% of all concepts will be elicited after 10 interviews and > 90% of all concepts after 15 interviews; as such, a planned sample size consisting of 10 physicians and 25 patients/relatives was considered sufficient [25, 26].

The interviews were recorded and transcribed verbatim. Transcripts were analyzed via Thematic Analysis methods in ATLAS.ti [27] by authors JS and LO (and overseen by authors LM, CP and AG). Using an agreed code list to ensure consistency, participant quotes pertaining to the research objectives were assigned corresponding concept codes. New codes were also organically added, and previously analyzed transcripts were reanalyzed to ensure new codes

were applied across all transcripts [28, 29]. Data were then converted into a filterable Microsoft Excel data extraction spreadsheet using the statistical software R/RStudio to facilitate calculation of discrete frequency counts of the number of participants reporting each concept code [30, 31].

While the analysis did not rely solely on frequency counts, they can be useful supplementary data, alongside descriptions of emergent themes and supportive patient quotes, to understand the relative importance and relevance of concepts. This information is particularly valuable when devising evidence-based recommendations for patient care [32].

Consolidated Criteria for Reporting Qualitative Research (COREQ)

The reporting of the study adhered to criteria in the COREQ qualitative research checklist [33].

RESULTS

Sample Characteristics

Twenty-eight patients with AML, 25 of their relatives and 10 physicians from the US, UK and Canada participated in final interviews. The demographic and clinical characteristics of the patient sample are summarized in Table 1. Due to recruitment challenges, patients on the various treatment options were not proportionately represented across countries, with most of the US patients having untreated AML while all UK and Canadian patients were currently or had previously been treated with active therapy. Characteristics of participating relatives are summarized in supplemental data Table 1. Characteristics of the physicians who took part in the interviews are described in Table 2. On average, physicians had experience of treating patients with leukemia for 17.3 years and were seeing 22 patients with AML per month, with on average 10 of these patients considered not to be suitable to receive IC, as determined by the physician.

Interview Findings

To align with the two key topics explored during the interviews, the results have been presented in two key sections: the value of extended life and the treatment decision-making process. Within each section, the keytheme(s) have been pulled out and presented as sub-sections.

Value of Extended Life

Every Day Matters to Enable Patients to Spend More Time with Family/Friends and Do Hobbies During the interviews, all patients and relatives were asked about life milestones (goals, events or activities) they/their family member had achieved since diagnosis or hoped to achieve in the future. The life milestones discussed pertained to five high-level domains of HRQoL, which broadly align with categories of life goals described by Pinqart et al. [34] most notably: social goals (focusing on maintaining or enhancing social relationships), leisure goals (focusing on meaningful and self-rewarding activities) and health-related goals (focusing on maintaining or improving physical health). Other domains included activities of daily living (ADL) and important dates.

As illustrated in Fig. 2, almost all patients and relatives mentioned social goals when discussing life milestones that they/their family member hoped to achieve (patients $n = 27/28$, 96.4%; relatives $n = 23/25$, 92.0%), indicating their importance. Patients and relatives described wanting to spend time with family/friends, while others discussed wanting to do particular activities with family, such as meals out or at home, or travel/vacations. Example quotes in support of the key findings are summarized in Table 3.

Patients and relatives also discussed leisure goals they/their family member hoped to achieve in the future (patients $n = 24/28$, 85.7%; relatives $n = 21/25$, 84.0%). This included going on walks, watching TV, reading, games and crafts, going to the cinema, gardening, doing some sport/exercise, travel/vacations and listening to music.

Table 1 Demographic and clinical characteristics of patient sample, broken down by country ($n = 28$)

Characteristic		US ($n = 15$)	UK ($n = 9$)	Canada ($n = 4$)	Total ($n = 28$)
Patient-reported demographic characteristics					
Age (years)	Mean (range)	72.2 (65–80)	75.3 (68–81)	77.5 (72–83)	74.0 (65–83)
Sex, n (%)	Male	5 (33.3%)	6 (66.7%)	4 (100.0%)	15 (53.6%)
	Female	10 (66.7%)	3 (33.3%)	–	13 (46.4%)
Race, n (%)	White/Caucasian	8 (53.3%)	9 (100.0%)	4 (100.0%)	21 (75.0%)
	Black/African American/ Caribbean/Black British	6 (40.0%)	–	–	6 (21.4%)
	Multi-racial	1 (6.7%)	–	–	1 (3.6%)
Living status, n (%)	Living with others	15 (100.0%)	8 (88.9%)	3 (75.0%)	26 (92.9%)
	Living alone	–	1 (11.1%)	1 (25.0%) ^e	2 (7.1%)
Highest level of education, n (%)	Postgraduate education	–	2 (22.2%)	–	2 (7.1%)
	Certificate programme	1 (6.7%)	1 (11.1%)	–	2 (7.1%)
One UK patient had missing data	College or university degree	4 (26.7%)	–	4 (100.0%)	8 (28.6%)
	Some years of college	1 (6.7%)	–	–	1 (3.6%)
	High school diploma/GED ^a	6 (40.0%)	–	–	6 (21.4%)
	GCSE level ^b	–	4 (44.4%)	–	4 (14.3%)
	Some high school	3 (20.0%)	–	–	3 (10.7%)
Activity over the past month, n (%)	Normal with no limitations	–	1 (11.1%)	1 (25.0%)	2 (7.1%)
	Not my normal self, but able to be up and about with fairly normal activities	4 (26.7%)	6 (66.7%)	2 (50.0%)	12 (42.9%)
	Not feeling up to most things, but in bed or chair less than half the day	6 (40.0%)	2 (22.2%)	–	8 (28.6%)
	Able to do little activity and spend most of the day in bed or chair	3 (20.0%)	–	2 (50.0%)	4 (14.3%)
	Pretty much bed ridden, rarely out of bed	2 (13.3%)	–	–	2 (7.1%)

Table 1 continued

Characteristic		US (<i>n</i> = 15)	UK (<i>n</i> = 9)	Canada (<i>n</i> = 4)	Total (<i>n</i> = 28)
Physician-reported clinical characteristics					
Time since AML diagnosis in months	Mean (range)	5.8 (3–10)	8.2 (3–19)	6.9 (2–15)	6.9 (2–19)
Treatment options	Currently on NIC	-	8 (88.9%)	3 (75.0%)	11 (39.3%)
	Discontinued NIC	1 (6.7%)	1 (11.1%)	1 (25.0%)	3 (10.7%)
	Currently on BSC	1 (6.7%)	-	-	1 (3.6%)
	None	13 (86.7%)	-	-	13 (46.4%)
Reason for unwillingness or unsuitability for IC determined by physician, <i>n</i> (%) ^c	Too unwell for	8 (53.3%)	-	2 (50.0%)	10 (35.7%)
	Significant comorbidities	5 (33.3%)	3 (33.3%)	-	8 (28.6%)
	Patient unwilling to receive IC	5 (33.3%)	-	2 (50.0%)	7 (25.0%)
	Older age	-	7 (77.8%)	-	7 (25.0%)
	Avoiding hospitalization during Covid-19 pandemic	-	2 (22.2%)	-	2 (7.1%)
	Current treatment, <i>n</i> (%)	Dexamethasone	1 (6.7%)	-	-
Hydroxyurea		1 (6.7%)	-	-	1 (3.6%)
Cytarabine (low dose)		-	5 (55.6%)	1 (25.0%)	6 (21.4%)
Azacitidine		-	3 (33.3%)	2 (50.0%)	5 (17.9%)
^d BCT-100		-	1 (11.1%)	-	1 (3.6%)
Venetoclax		-	3 (33.3%)	3 (75.0%)	6 (21.4%)
Previous treatment, <i>n</i> (%)	Azacitidine	1 (6.7%)	-	1 (25.0%)	2 (7.1%)
	Venetoclax	-	-	1 (25.0%)	1 (3.6%)
	Dexamethasone	1 (6.7%)	-	-	1 (3.6%)
	Cytarabine (low dose)	-	1 (11.1%)	-	1 (3.6%)
	Lenalidomide	-	1 (11.1%)	-	1 (3.6%)
	Midostaurin	-	-	1 (25.0%)	1 (3.6%)

^aGED = General Educational Development (high-school level diploma awarded in the US)

^bGCSE = General Certificate of Secondary Education (certificate acquired in education in the UK, usually around age 15)

^cPhysicians could select multiple options

^dBCT-100 = pegylated human recombinant arginase

^eOne patient had live-in staff

To a lesser extent, patients and relatives also described hoping to achieve health-related goals (e.g., better health, longer survival), maintain activities of daily living (e.g., daily chores, housework) and reach important dates (e.g., family occasions). Patients described being limited in some activities because of poor health and/or coronavirus disease 2019 (COVID-19) pandemic restrictions.

These responses resonated with the physicians, who described patients wanting to achieve important dates ($n = 7/10$, 70%), such as family occasions and public holidays, mostly to spend more time with family ($n = 5/10$, 50%).

Patients' Outlook and Expectations About the Future May Be Impacted by Treatment Experience During the interviews, patients and their relatives had mixed expectations for the future. Patients and relatives had negative expectations and worries about their/their relative with AML's physical health including deteriorating health, treatment not working or even imminent death, and this remained a key concern over time. However, there were positive expectations related to time being spent with family, with patients and relatives both describing upcoming family events and visiting family members who may have lived further away.

Among patients who had no prior exposure to AML treatment, outlook for the future became more negative over time. Few patients ($n = 4/13$, 30.8%) recalled experiencing negative expectations about the future at diagnosis, while most ($n = 10/13$, 76.9%) did express negative outlooks at the time of the interview. Conversely, patients with AML treatment experience appeared to have an increasingly positive outlook. Most of these patients ($n = 11/14$, 78.6%) recalled feeling negative about the future at diagnosis, whereas at the time of the interview, most ($n = 9/14$, 64.3%) felt hopeful about future events.

Furthermore, among those with treatment experience, positive expectations were more frequently reported among those diagnosed ≥ 6 months prior to interview ($n = 6/7$, 85.7%) compared to those

diagnosed < 6 months prior to interview ($n = 3/7$, 42.8%). This was also supported by findings from physician interviews, where seven ($n = 7/9$ asked, 77.8%) physicians noted that patients' feelings changed over time depending on treatment success.

Treatment Decision-Making Process

The Shock of Diagnosis May Impact Patients' Understanding of the Various Treatment Options Most patients discussed their emotional reactions when first diagnosed, which most commonly included feeling shocked ($n = 19$), concerned/worried ($n = 13$) and overwhelmed ($n = 10$). All physicians ($n = 10$) reported discussing NIC treatments with patients unsuitable for IC. While patients confirmed that they discussed treatment with their physician, most patients ($n = 15/28$, 53.6%) did not articulate a difference between IC, NIC and BSC during the interview, but were not directly asked if they understood the distinctions. The remaining patients ($n = 13/28$, 46.4%) were directly asked whether they had been made aware of the difference between various treatment options (e.g., IC vs NIC, NIC vs BSC). Most patients ($n = 9/13$, 69.2%) explained that they had been provided with some materials, such as leaflets, which provided some treatment-related information. However, despite this, understanding of treatment options was limited. The remaining four patients ($n = 4/13$, 30.8%) reported personally seeking out treatment information.

Extending Survival in Good Health is More Important Than Extending Survival Alone Figure 3 presents the proportion (%) of patients, relatives and physicians who rated each factor as 'very important' in the quantitative questionnaire. Overall, improved HRQoL (patients: 92.6%, relatives: 96.0%, physicians: 70.0%), extended survival (patients: 89.3%, relatives: 88.0%, physicians: 80.0%) and relief of symptoms (patients: 88.9%, relatives: 88.0%, physicians: 60.0%) were most commonly rated as 'very important' in AML treatment decision-making. However, patients and their relatives further described certain trade-offs they made or would be willing to make when deciding

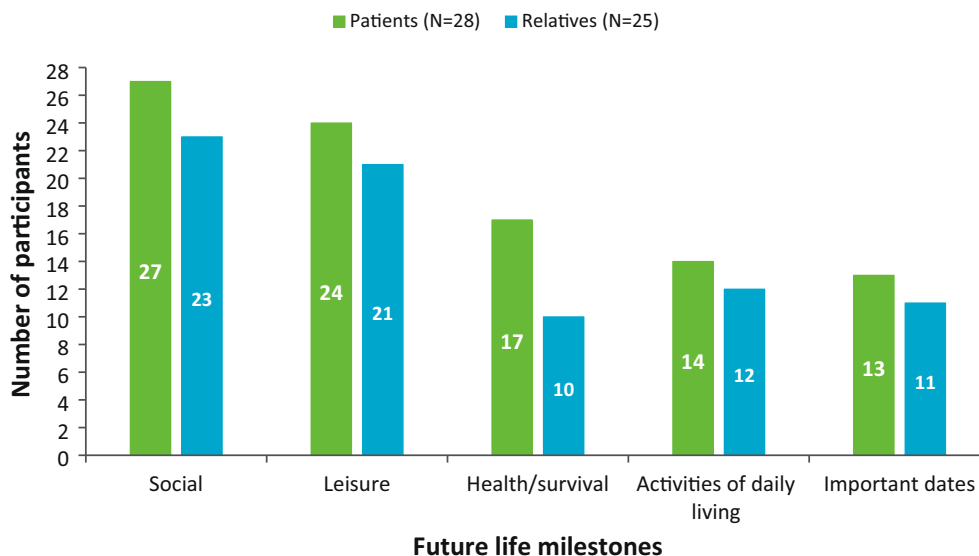
Table 2 Physician characteristics ($n = 10$)

Characteristic	US ($n = 4$)	UK ($n = 3$)	Canada ($n = 3$)	Total ($n = 10$)
Current job role, n (%)				
Hematologist	-	2 (66.7%)	3 (100%)	5 (50.0%)
Hematologist and oncologist	4 (100%)	1 (33.3%)	-	5 (50.0%)
Current work setting, n (%)^a				
Hospital	1 (25.0%)	3 (100%)	2 (66.7%)	6 (60.0%)
Academic	2 (50.0%)	1 (33.3%)	2 (66.7%)	5 (50.0%)
Private practice	2 (50.0%)	1 (33.3%)	-	3 (30.0%)
Outpatient	2 (50.0%)	1 (33.3%)	2 (66.7%)	1 (10.0%)
Number of patients seen per month, n (%)				
Mean	243.8	190	200	215.7
Range	125–400	120–250	150–250	120–400
Number of patients with AML seen per month				
Mean	23	21.7	21.7	22.2
Range	12–40	15–30	10–40	10–40
Number of patients with AML seen per month who are unsuitable for IC				
Mean	11.3	9.3	7.7	9.6
Range	7–15	8–1	3–15	3–15
Length of time treating patients with leukemias (years)				
Mean	15.3	15	22.3	17.3
Range	7–27	5–20	17–25	5–27
Frequency of patients seen with AML receiving NIC				
Once per week	1 (25.0%)	2 (66.7%)	1 (33.3%)	4 (40.0%)
Twice per week	-	-	1 (33.3%)	1 (10.0%)
Once every 2 weeks	-	1 (33.3%)	1 (33.3%)	2 (20.0%)
Once per month	2 (50.0%)	-	1 (33.3%)	3 (30.0%)
Frequency of patients seen with AML receiving BSC				
Once per week	2 (50.0%)	-	-	2 (20.0%)
Twice per week	-	-	1 (33.3%)	1 (10.0%)
Once every 2 weeks	-	3 (100.0%)	1 (33.3%)	4 (40.0%)
Once per month	2 (50.0%)	-	1 (33.3%)	3 (30.0%)
Proportion of patients with AML unsuitable for IC				
Mean proportion	50.0	40.0	31.7	41.4
Range	45–55	30–60	20–40	20–60

Table 2 continued

Characteristic	US ($n = 4$)	UK ($n = 3$)	Canada ($n = 3$)	Total ($n = 10$)
Proportion of patients with AML who receive BSC who were unsuitable for IC				
Mean proportion	77.5	60.0	61.7	67.5
Range	75–80	50–70	35–80	35–80

^aPhysicians could select multiple options

**Fig. 2** Overview of future life milestones

whether to pursue treatment. Overall, patients across all treatment options ($n = 19/28$, 67.9%) and their relatives ($n = 15/25$, 60.0%) most frequently reported that QoL was more important than extended survival.

Conversely, a smaller proportion of patients reported that they would be willing to tolerate side effects if survival could be extended ($n = 7/28$, 25.0%), though most of these patients were already on NIC ($n = 5/7$, 71.4%). The perceptions and reality of side effects are discussed below.

Incorrect Perceptions of Treatment Side Effects May Limit Treatment Acceptance and Result in Worse Outcomes As detailed in Fig. 3, side effects were rated as ‘very important’ by a greater proportion of patients ($n = 15/25$ who

answered, 60.0%) and their relatives ($n = 16/25$, 64.0%) compared to physicians ($n = 4/10$, 40.0%). Furthermore, side effects were rated as ‘very important’ by a greater proportion of patients not on treatment ($n = 9/13$, 69.2%) and their relatives ($n = 12/13$, 92.3%) compared to those with experience of NIC ($n = 5/11$ who answered, 45.5%) and their relatives ($n = 3/11$, 27.3%).

Patients with no treatment experience ($n = 9/13$, 69.2%) and their relatives ($n = 7/13$, 53.8%) reported a fear of side effects being the primary reason for opting not to pursue AML treatment. Specifically, many of these patients ($n = 6/13$, 46.2%) were worried that side effects would be worse than their AML symptoms. Although it was not clear whether patients were distinguishing between the side effects of IC

Table 3 Key findings and supporting quotes

Key findings	Supporting quotes
Every day matters to enable patients to spend more time with family/friends and do hobbies	<p data-bbox="788 302 1406 365"><i>‘Just hoping to spend a little bit of time with my friends and my family until I’m out.’</i> (US patient not on treatment)</p> <p data-bbox="788 386 1406 527"><i>‘Just being able to be with him. We will sit opposite each other across the kitchen table and drink copious amounts of tea...and just talk for hours.’</i> (Relative of UK patient on NIC)</p> <p data-bbox="788 548 1406 716"><i>‘I think that a lot of people are kind of focused on family get-togethers and seeing their families and that kind of thing can be organized. I think they want enough time for family members to come home and visit them.’</i> (Canadian physician)</p> <p data-bbox="788 737 1406 800"><i>‘I still do go for walks, shorter walks of course.’</i> (Canadian patient on NIC)</p> <p data-bbox="788 821 1406 926"><i>‘I need to have a daily routine and the easiest is for me to sit in front of the television and watch the news.’</i> (US patient not on treatment)</p>
The shock of diagnosis may impact patients’ understanding of the various treatment options	<p data-bbox="788 947 1406 1052"><i>‘When the doctor told me what I have cancer that—blood cancer that’s shocking. Everybody gets shocked.’</i> (US patient not on treatment)</p> <p data-bbox="788 1073 1406 1178"><i>‘...we were both very much overawed by everything... we... couldn’t remember hardly anything when we came out.’</i> (UK patient on NIC)</p> <p data-bbox="788 1199 1406 1325"><i>‘We were given a lot of brochures about leukemia in general, about diet, and about all sorts of side effects of medication and so on and so forth. So, lots of literature.’</i> (Canadian patient on NIC)</p>
Treatment may have a positive impact on patients’ outlook and expectations about the future	<p data-bbox="788 1346 1406 1451"><i>‘We’re hoping to have a big party ... that we can all get together... And she gets graduation... We’ve got things to look forward to like that.’</i> (UK patient, discontinued NIC)</p> <p data-bbox="788 1472 1406 1577"><i>‘My outlook on life has changed... I’m not as optimistic and as positive as I used to be before...I pray a lot.’</i> (US patient not on treatment)</p> <p data-bbox="788 1598 1406 1692"><i>‘They realize that things are progressing in a bad or good way, and they change their expectation based on how they feel the disease is responding or progressing.’</i> (UK physician)</p>

Table 3 continued

Key findings	Supporting quotes
Extending survival in good health is more important than extending survival alone	<p data-bbox="826 317 1449 384">“You don’t want longer survival if the quality of life is down.” (Canadian patient, discontinued NIC)</p> <p data-bbox="826 405 1449 506">“My opinion on it is that I would rather have a shorter life but a better quality of life.” (Relative of Canadian patient on NIC)</p> <p data-bbox="826 527 1449 663">“...if I can’t really enjoy my life to the fullest, and certain things, certain basic criteria aren’t met, well, I don’t want to be an invalid in a chair or in the bed. I, I just don’t want that.” (US patient not on treatment)</p>
Incorrect perceptions of treatment side effects may limit treatment acceptance and result in worse outcomes	<p data-bbox="826 684 1449 785">“That’s one of the reasons why I’m not getting treatment... the side effects can be worse than actually where I’m at with the disease now.” (US patient not on treatment)</p> <p data-bbox="826 806 1449 907">“I don’t want the side effect to rule my everyday life. I don’t want to be stuck at the toilet throwing up all day because the chemo has made me so sick.” (US patient not on treatment)</p> <p data-bbox="826 928 1449 1104">“I had heard one patient that was getting treatment, and they were saying, it made them sicker than the cancer, so how they felt, the cancer was, you know, making them feel sick but nothing like the chemo, not even close, not even close at all.” (US patient not on treatment)</p> <p data-bbox="826 1125 1449 1226">“People that say, well this is a horrible thing to go through, I haven’t experienced that at all... I don’t have the unpleasant side effects” (Canadian patient on NIC)</p> <p data-bbox="826 1247 1449 1461">“I was aware from what I read, from the brief materials that I received that there were chances of some side effects, certainly diarrhea, constipation, and so on I’ve experienced regularly, I’ve become accustomed to them, that’s just sort of, normal procedure now. Other side effects, there have been really no side effects.” (Canadian patient on NIC)</p>

Table 3 continued

Key findings	Supporting quotes
<p>Patient and physician priorities are not always the same, potentially resulting in a misalignment of treatment goals</p>	<p><i>‘I think my personal opinion is that there’s no place I’d rather be than home. I don’t want to languish someplace in a hospital or hospice.’</i> (US patient not on treatment)</p> <p><i>‘I have a lot of patients with like venetoclax that have the neutropenic fever. They get in the hospital for a few days and then they’re gone...it’s not that much different than staying in the housing facilities. So, I don’t think it’s a great concern.’</i> (US Physician)</p> <p><i>‘...Even if the chemo did work, she could succumb to another infection from her immune system being battered from the chemotherapy.’</i> (Relative of US patient not on treatment)</p> <p><i>‘...The disease itself causes infection...they can usually be managed.’</i> (Canadian physician)</p>
<p>Patients consider physicians to have the most influence in treatment decision-making</p>	<p><i>‘I think we have to go in with a certain treatment in mind because patients have no clue as to what you’re talking about, you could explain it to them, but they’re going to ultimately, 90% of the time or more, leave it up to me because they didn’t go to medical school. They didn’t study leukemia.’</i> (US physician)</p> <p><i>‘As I said, I sort of put my faith in the doctor and sort of followed his lead at that point.’</i> (Canadian patient on NIC)</p>

and NIC, patients generally perceived side effects as severe ($n = 9/13$, 69.2%) and mentioned nausea/vomiting, pain, hair loss, multiple organ failure and death. Four patients further described being influenced by seeing or hearing about other cancer patients who suffered from side effects.

Although two patients’ experiences of side effects resulted in them discontinuing NIC ($n = 2/14$, 14.3%), most patients with experience of NIC ($n = 9/14$, 64.3%) reported a small number of side effects that had little impact on their life, including fatigue, reduced appetite, generally feeling unwell, nausea and injection site irritation. Nausea ($n = 5$) and risk of infection ($n = 3$) were the treatment side effects most frequently reported by physicians.

Patient and Physician Priorities Are Not Always the Same, Potentially Resulting in a Misalignment of Treatment Goals There was evidence of other differences in priorities between physicians and patients and their relatives such as the possibility of being hospitalized, risk of infection and location of care (Fig. 3).

The possibility of being hospitalized was rated as ‘very important’ by a greater proportion of patients ($n = 14/27$ who answered, 51.9%) and relatives ($n = 16/25$, 64.0%) than physicians ($n = 1/10$, 10.0%). Most patients and relatives described how hospitalization was to be avoided because it meant being away from home or because it indicated being seriously ill. Others considered it beneficial because it afforded access to medical care. In contrast,

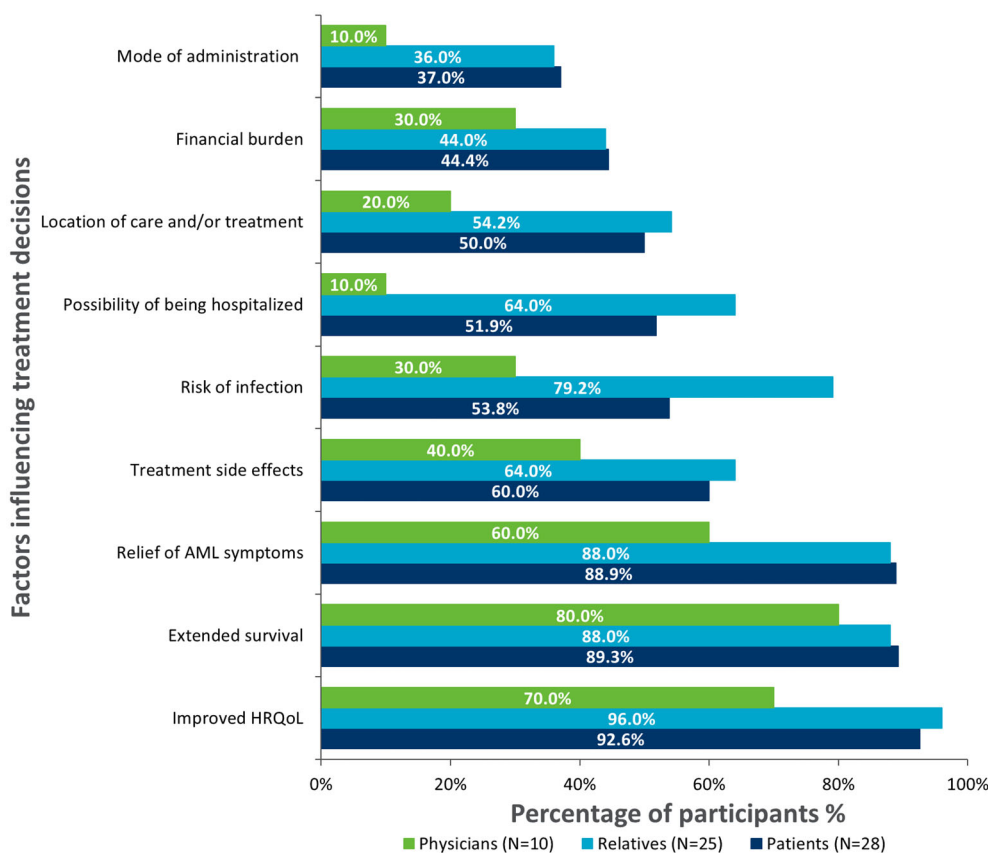


Fig. 3 Treatment factors rated ‘very important’ by patients, relatives and physicians when making AML treatment decisions

physicians tended to view hospitalization as a standard and necessary part of treatment.

The risk of infection was also rated as ‘very important’ by a greater proportion of patients ($n = 14/26$ who answered, 53.8%) and relatives ($n = 19/24$, 79.2%), compared to physicians ($n = 3/10$, 30.0%). Patients and relatives commented on susceptibility to infection further impacting quality of life. In contrast, most physicians explained that infections are usually caused by the disease, rather than treatment, and can be managed.

Finally, location of care was rated as ‘very important’ by a greater proportion of patients ($n = 13/26$ who answered, 50.0%) and their relatives ($n = 13/24$, 54.2%) compared to physicians ($n = 2/10$, 20.0%) because of the desirability of having easily accessible treatment closer to home or at home.

Patients Consider Physicians to Have the Most Influence in Treatment Decision-Making During the interview, all participants (patients, their relatives and physicians) discussed a shared treatment decision-making process involving the physician(s)/hematologist(s), the patient, family members (including spouses, children or other family members) as well as other healthcare professionals (nurses, pharmacists and support workers). Participants also discussed who had the most influence on treatment decision-making (Fig. 4). All physicians asked ($n = 6/6$, 100.0%) and most patients asked ($n = 20/23$, 74.1%) stated that it was the physician who had the most influence due to their knowledge and experience, while most of the relatives asked ($n = 15/23$, 65.2%) thought it was the patient. A small proportion of patients ($n = 2/27$, 7.4%) said that the decision was joint between them and a family member.

DISCUSSION

The overall objective of this study was to characterize the experiences of patients with AML who were unwilling or unsuitable for IC and to better understand the treatment decision-making process from the perspective of patients, their relatives and physicians and how this links to the perceived value of extended survival. The key findings from this study were that:

- Every day mattered to enable patients with AML to spend more time with family/friends and do hobbies, but not at the sacrifice of good health;
- Patients' incorrect perceptions and limited understanding about treatment options may limit treatment acceptance and result in worse outcomes;
- Patients consider physicians to have the most influence in treatment decision-making; however, patient and physicians' priorities and treatment goals do not always align.

First, the findings of this study showed that extending survival in good health was valuable for both patients and their family, particularly in terms of the opportunity to spend more time together, ability to do daily activities and attain meaningful goals and milestones. These findings are supported by previous research where cancer patients discussed the importance of spending time with family [34, 35] and maintaining a 'normal life,' which included engaging in hobbies and remaining active [36]. As a novel finding, this study indicated that patients and physicians' priorities did not always align when making treatment decisions, for example, regarding the perceived importance of the possibility of being hospitalized and the risk of infection. These findings have an important implication for the AML treatment decision-making process, highlighting the need for structured patient-physician discussions to allow the physician to align recommended treatments and plans with the patient/family's goals and expectations. Tools to facilitate this could include discussion guides for both the physician and the patient, which may include topics and questions to cover (e.g., goals and

important considerations) and techniques to enhance engagement of the patient.

Second, this study illustrated that older AML patients had limited understanding of the different treatment options. No standard treatment approach exists for older patients with AML; those who are unsuitable for IC are typically offered NIC or BSC [37, 38]. Despite physicians reporting that they discussed various treatment options with their patients, most patients in this study did not articulate or had limited understanding about the difference between IC, NIC and BSC. Patients noted the overwhelming shock upon diagnosis [39–41], which can make it difficult to process complex information about treatment options [5, 41] and to feel involved in treatment decision-making [42]. Several patients also described inflated concerns regarding the treatment side effects based on their experiences with family/friends on other chemotherapies. Since NIC in AML is less intensive than many typical solid tumor chemotherapy regimens, it is important to recognize that patients with AML may have pre-conceived perceptions about the side effects of NIC that could limit treatment acceptance [10] and lead to worse outcomes. Physicians should carefully consider how information is delivered, explicitly assessing patient and family understanding and expectations with attention to correct false assumptions. The highlighted lack of patient understanding also calls for the need for more accessible, patient-friendly resources, such as videos, blogs/vlogs and brochures. For example, education videos and vlogs can be effective and powerful tools for patients by facilitating knowledge and providing accounts of the "real lived" experience that can mitigate misconceptions (e.g. about different treatment pathways) and provide useful tips to enhance coping skills and self-care. Ensuring the resources are patient-centered and involve input from patients is critical. Given the influence of other patients' experiences, it might also be useful to provide opportunities for peer support and education between patients who have had a similar diagnosis or are on the same treatment path.

Finally, this study illustrated that involvement during treatment decision-making is

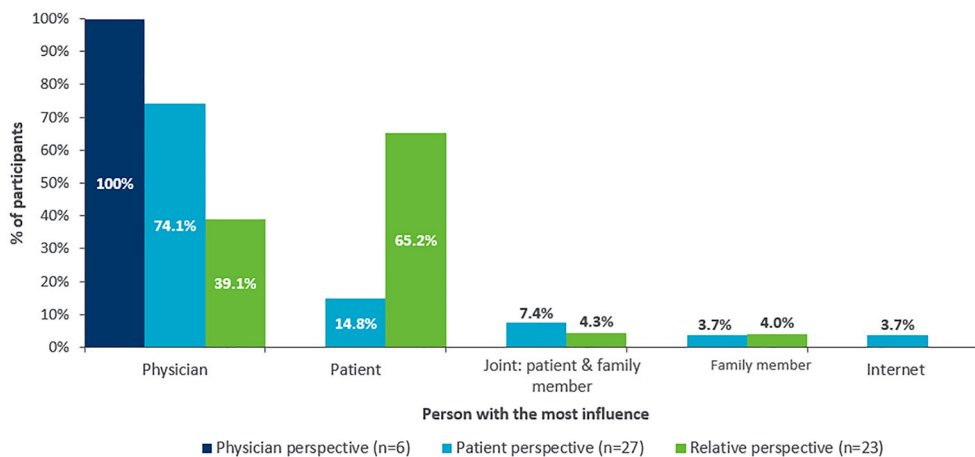


Fig. 4 Who had the most influence in treatment decision-making?

further complicated by who the different stakeholders perceived to have the most influence in the decision. There was consensus among physicians and patients that the physician had the most influence, demonstrating the importance of the physician acting as a facilitator to engage the patient. This is especially vital in the current landscape of increasing numbers of available therapies and the patients' limited understanding of the treatment options available to them. By actively creating space for the patient to voice their own concerns and questions, the physician can ensure that the process achieves the oncology gold standard of shared decision-making.

While the qualitative study design of this research provided considerable depth of insight regarding varied stakeholder perspectives of AML and the treatment decision-making process, it is necessary to acknowledge some limitations. First, while the overall sample size was considered sufficient for qualitative research, it is important to acknowledge that the data are based on a small number of participants, therefore limiting the generalizability of the findings. Additionally, while the overall sample was demographically and clinically diverse, samples within each country were less so. There was no representation of black African or multi-racial ethnicities in the UK or Canadian samples, education levels were higher in the UK and Canadian samples, and all Canadian patients

were male. In terms of treatment paths, there was just one patient on BSC and patients with untreated AML were represented in the US sample only. Of note, the low treatment uptake in the US sample is supported by the Surveillance Epidemiology and End Results (SEER)-Medicare database, which reported that approximately 50% of older US AML patients remain untreated for reasons that are not well understood [43]. It is also important to acknowledge that the access and funding of healthcare are different in the US compared to the UK and Canada, and this may have influenced patients' treatment decision-making. Given some of the other differences in the US, UK and Canadian samples (including representation of patients on different treatment options), no comparisons were made at the country level. Finally, no information about patients' remission status was collected, and recruitment for the study was also prolonged by the global COVID-19 pandemic, although, the data collected from interviews was rich and descriptive and allowed for the exploration of patients on different treatment paths. Patients recruited and interviewed during the COVID-19 pandemic were also able to effectively differentiate between any limitations to their HRQoL as and when this was due to their AML experience or to COVID-19.

CONCLUSION

In conclusion, this qualitative study illustrates the complexities associated with treatment decision-making in older patients with AML who are unsuitable for IC and how patient priorities (such as every day HRQoL) do not always align with physicians' priorities. The misalignment in stakeholder priorities and the perceived weighty influence of physicians must encourage physicians to strive for structured discussions about diagnosis and treatment with their patients, allowing them the space and opportunity to be informed and to discuss their goals and concerns surrounding receiving treatment at an emotionally challenging time. Additionally, future research efforts should focus on the development of patient-centric resources to ensure patients and their families are supported to make fully informed decisions.

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Timothy J Bell, Francois Peloquin, Diana Merino Vega and Lucy Morgan were working at their listed affiliations at the time the research was conducted.

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Compliance with Ethics Guidelines. This study was performed in line with the principles of the Declaration of Helsinki. In the US, the study was approved by a centralized independent Institutional Review Board WIRB (#1-1173688-1). In Canada, ethical approval was obtained from a local IRB University Health Network Research Ethics Board (reference 19-5579). In the UK, ethical approval was obtained from the National Health Service (NHS) Research Ethics Committee and Health Research Authority (reference 19/EM/0337), followed by localized approval from the relevant research and development departments. Written informed consent was obtained prior to the collection of any data.

Data Availability. All the relevant data has been reported in the manuscript and supplementary files. The datasets generated during

and/or analyzed during the current study are not publicly available due to participants consenting to data being published in aggregated form and full interview recordings/transcripts only being available to the project team responsible for conducting the research.

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