OHE Office of Health Economics

A MULTINATIONAL QUANTITATIVE STUDY

Patient preferences for treatment in relapsed/refractory acute leukemia

David Mott
Hannah Hussain
Jake Hitch
Sulayman Chowdhury
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ALAN
Acute Leukaemia Advocates Network

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David Mott
Office of Health Economics, London, UK

Hannah Hussain
Office of Health Economics, London, UK

Jake Hitch
University of Oxford, Oxford, UK

Sulayman Chowdhury
Office of Health Economics, London, UK

Samantha Nier
Acute Leukemia Advocates Network, Bern, Switzerland

Chris Skedgel
Office of Health Economics, London, UK

OFFICE OF HEALTH ECONOMICS &
ACUTE LEUKEMIA ADVOCATES NETWORK

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Corresponding Author:
David Mott
dmott@ohe.org

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Executive Summary

When acute leukemia relapses, treatment decisions can be complex. Patients may face trade-offs between survival benefits, side effects and how treatment is delivered. This study asked people with acute leukemia across five countries what matters most to them when making these choices.

How did we do it?

- We surveyed 267 patients in the UK, USA, France, Germany, and Italy.
- The survey included a task called a discrete choice experiment (DCE). In the DCE, patients made choices between different hypothetical treatment options.
- The treatments in the DCE were described in terms of how effective they are (the chance of responding, as well as the duration of the response), the impact on quality of life (during and after the treatment), and how the treatment is given (mode of administration).
- The DCE data were analyzed to identify the treatment priorities of people with acute leukemia in the event of a relapse.

What patients told us

The most important factor was how likely the treatments were to work

- The chance of responding to treatment was the most important characteristic by a significant margin.
- The second most important characteristic was quality of life during response, followed by the duration of response, and quality of life during treatment, respectively.
- Mode of administration was the least important characteristic overall — though it was very important to some people.

Different groups of patients had different treatment priorities

- We identified three distinct groups:
    - "Response-focused" (47%) — chance of response was by far their biggest priority compared to other characteristics.

- "Balanced decision-makers" (32%) — all characteristics except the mode of administration were important to this group.
- "Convenience + efficacy focused" (21%) — preferred to avoid hospital stays and prioritized a longer response duration.

Key messages

One size does not fit all

Many patients focus on the chance of the treatment working when making treatment choices. But other characteristics are important to some patients too — such as being able to avoid long hospital stays or maintaining good day-to-day quality of life. These differences remind us that treatment priorities are personal, and care should be flexible enough to reflect them.

Regional differences matter

Preferences were not the same everywhere. For example, patients in the United States placed greater weight on average on treatment convenience compared to European patients, preferring oral treatments or treatments received at outpatient appointments over hospital stays. Local health systems and cultural expectations may shape how patients think about their care.

Clinical trials should reflect patient priorities

Traditional trials often focus on survival or remission. While this is crucial, it does not fully capture patients' priorities. Intensive treatments may not be acceptable for all patients, particularly when benefits are uncertain. Incorporating patient preferences into trial design can help ensure that study outcomes are more patient-centered.

Decision-making should look beyond survival

When new therapies are assessed, the emphasis is often on clinical factors and, in some health systems, quality of life. Our findings highlight that patients also prioritize other factors — such as having fewer hospital visits and reduced treatment burden. Capturing these benefits ensures new treatments are valued for their real-world impact.

Evidence can inform patient advocacy

Patient advocates play a vital role in making sure the patient voice is heard in research, clinical care and policy. These results provide concrete evidence to show that what matters to patients may not always be reflected in current decision-making. Advocates can use this evidence to press for treatments, services and policies that better align with patient needs.

1. Introduction

Acute leukemia (AL) is an aggressive cancer of the white blood cells that progresses rapidly (Okikiolu, Dillon and Raj, 2021). There are two main types of AL, which differ in relation to the type of white blood cell that are affected. The first is acute myeloid leukemia (AML), which is the most common form in adults, and has a rare subtype called acute promyelocytic leukemia (APL) (Iyer et al., 2023; Döhner, Weisdorf and Bloomfield, 2015). The other is acute lymphoblastic (or lymphocytic) leukemia (ALL), which also has different subtypes, and is more common in children than in adults (Terwilliger and Abdul-Hay, 2017).

The different sub(types) of AL are associated with different clinical outlooks as well as different treatment options. However, there are broad similarities, in that most individuals initially have symptoms such as fatigue, increased bruising and bleeding, fever, shortness of breath, and repeated infections (Shephard et al., 2016). When AL is detected, treatment is typically provided rapidly due to the aggressive nature of AL and usually involves some combination of chemotherapy and targeted therapy and, for some, a stem cell or bone marrow transplant. Initial treatment is intensive and focused on achieving remission as soon as possible, which can be traumatic and often results in significant quality of life impacts for patients as well as their family members (Pemberton-Whiteley et al., 2023; Oliva et al., 2025).

While first-line therapies are often effective, some patients do not achieve remission (known as 'refractory disease') and some proportion of those that do may subsequently relapse. The outlook following relapse is considerably worse, with poor long-term survival rates and limited effective treatment options (Shahswar et al., 2025; Bataller et al., 2024). Given the trade-offs between survival benefits and treatment-related toxicity, treatment decisions in this context can be complicated.

The importance of patient preference research for informing decision-making has been highlighted in recent years (Mott, 2018; Bouvy et al., 2020; Benz, Saha and Tarver, 2020). It has been widely acknowledged that regulatory and reimbursement decisions can be informed by information on patients' preferences for different treatment options, provided that treatment decisions are, to some degree, "preference-sensitive".

Despite the relevance of patient preferences in this context, relatively little is known about the treatment preferences of people with AL. Richardson et al. (2020) used discrete choice experiment (DCE) methodology and found that people with AML in the USA prioritize treatments that offer a greater chance at remission, but that preferences differed depending on the age and gender of respondents. In a subsequent study Richardson et al. (2021) explored the priorities of people with AML in the USA using a best-worst scaling (BWS) exercise and found that the primary concerns of patients were death and long-term treatment side effects. Saini et al. (2023) found that people with AML in the USA, UK and Canada that had previously received a stem cell transplant prioritized post-transplant maintenance therapies that offered better quality of life, lower hospitalization durations, and a better chance of two-year relapse-free survival. More recently, a small pilot study by LoCastro et al. (2023) explored the preferences of older adults with AML in the USA across multiple timepoints. They found that preferences varied between patients that were on more intensive treatment compared to those on lower intensity treatments. Finally, Ashaye et al. (2022) found that adults with Philadelphia chromosome positive ALL in the USA prioritized overall survival and would be willing to accept an increased risk of a major cardiovascular event (e.g., heart attack, stroke) to achieve a higher level of overall survival.

While these studies have provided some insights into the priorities of people with AL, the majority have focused on AML, none have explored how preferences might differ across the broader AL population, and none have focused specifically on the relapsed/refractory setting. This study sought to

address this gap in the literature by examining the treatment preferences of people with AL in this setting.

2. Methods

2.1 Overview

This study comprised online surveys delivered to patients across six different study countries (UK, France, Germany, Italy, Spain, and USA). The online surveys contained multiple sections, with the DCE being the key component for addressing the objectives set out in the previous section. The online surveys, in all countries except the UK, were structured as in Figure 1.

FIGURE 1. SURVEY VERSIONS (EXCLUDING UK)

The UK survey was conducted first, independently of the others, with results published in Mott et al. (2024). The primary difference in the UK survey (relative to Figure 1) is that it did not include the best-worst scaling exercise, nor did it include cognition and tiredness bolt-on items alongside EQ-5D-5L. This report utilizes the UK dataset alongside the data from other countries.

2.2 Design of the DCE

DCE is a stated preference methodology that requires respondents to complete a series of tasks containing hypothetical choices between different alternatives. The alternatives are described using a set of attributes, the levels of which vary between tasks. In this study, the alternatives were treatments for AL, in the event of a relapse. The remainder of this subsection provides details on how the attributes and levels were identified, the experimental design of the DCE, and the pre-testing.

2.2.1 Determining attributes and levels

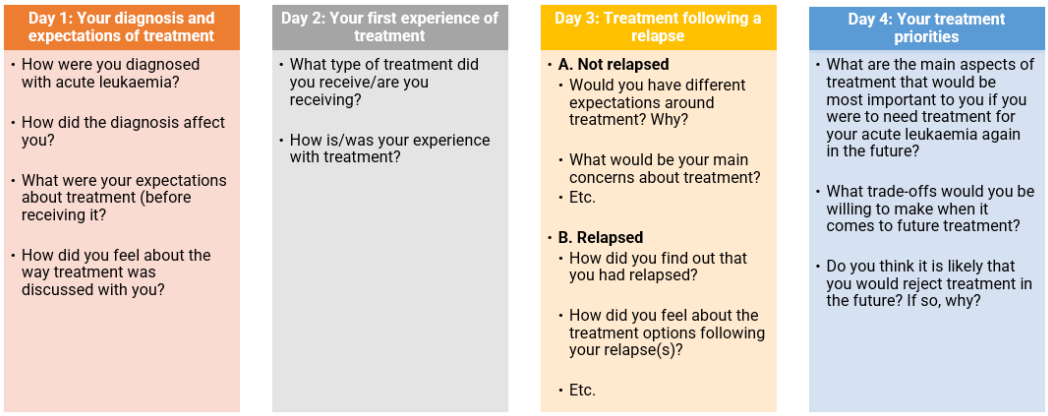
To determine appropriate attributes for the DCE, we began by conducting background research. This consisted of a targeted literature review of past preference studies in AL as well as a review of the characteristics of current/forthcoming treatments in the relapsed/refractory setting.

This background research was subsequently supplemented with formative qualitative research with people with AL (Hollin et al., 2020). We conducted two online bulletin boards (OBBs), with patients recruited via Leukemia Care, a UK-based leukemia charity and member of the Acute Leukemia Advocates Network (ALAN).

OBBs are an alternative to focus groups and involve participants responding to questions from the study team and, if desired, engaging in discussions with other participants, in a virtual forum-style setting (Cook et al., 2019; Bohorquez et al., 2024). Two separate OBBs were conducted, one for people with AML or APL (n=12) and one for people with ALL (n=9), in part to explore whether there were any significant differences in the treatment characteristics that matter to people with different AL subtypes.

Each OBB was live for six days in total. During the first three days, questions were added by the study team about participant's diagnosis experience and their initial expectations around treatment (day 1), their first-line treatment experience (day 2), and any experience or expectations around later lines of treatment (day 3). On the fourth day, participants were asked about their priorities in a future relapse scenario. The structure of each OBB is presented in Figure 2.

FIGURE 2. STRUCTURE OF EACH OBB



The OBBs were left open for a further two days to enable further discussion amongst the groups. Whilst the OBBs were open, members of the study team observed the messages and occasionally posted follow-up questions to encourage further debate. On average, participants posted 22 messages each on the OBB over the course of the six days. Participants were reimbursed for their time.

The insights from the background research and the OBBs were considered by the study team with input from the Acute Leukemia Advocates Network's (ALAN) steering committee and the project's advisory groups (consisting of both a patient advisory group and an academic advisory group). It was decided to create a single DCE design with the attributes and levels detailed in Table 1, which are intentionally broad to cover the wide range of treatments available across different acute leukemia subtypes.

TABLE 1. ATTRIBUTES AND LEVELS FOR THE DCE

Attribute	Levels
Mode of administration	• Injections (requiring an inpatient hospital stay) followed by tablets (taken at home) • Injections (at regular outpatient hospital appointments) and tablets (taken at home) • Tablets (taken at home)
Quality of life whilst receiving treatment (quality of life during treatment)	• 0 • 25 • 50

Chance of responding to treatment (chance of response)[1]	• 20% • 35% • 50% • 65% • 80% • 95%
Duration of the response to treatment (duration of response)[1]	• 6 months • 9 months • 12 months • 15 months • 18 months
Quality of life whilst responding to treatment (quality of life during response)	• 25 • 50 • 75

[1]Respondents were told that when they stop responding (or if they do not respond at all), they'd move to "supportive/palliative care" whereby symptoms would be managed but the leukemia would not be treated.

It was agreed to define the concept of quality of life using a 0 to 100 scale whereby 100 is the best imaginable and 0 is the worst imaginable quality of life. To help illustrate this, we described quality of life using the five dimensions of the EQ-5D-5L, given its brevity and its use in health technology assessment internationally (Herdman et al., 2011). To increase familiarity with EQ-5D-5L ahead of the DCE tasks, it was decided that all respondents would complete the EQ-5D-5L questionnaire prior to beginning them.

2.2.2 Experimental design

There were two alternatives (treatments) in each task, and given the breadth of the research question, these were 'unlabeled' (Treatment A and Treatment B). Furthermore, given that the treatment outlook in the relapsed/refractory setting can be poor, it was agreed to include an opt-out "no active treatment" alternative alongside the two treatment alternatives, which represented a move to "supportive/palliative care". The experimental design sought to produce a subset of treatments based on the attributes and levels in Table 1 such that we could explore their relative importance.

A d-efficient design containing 24 rows was produced using Ngene and split into two blocks. As such, respondents each completed 12 choice tasks.

Constraints were used to encourage respondents to make trade-offs during the task. In any DCE task the biggest possible difference in the chance of response between the two treatments could not exceed 30%, and for duration of response the difference could not exceed six months. Furthermore, for any treatment, quality of life during response could not be lower than quality of life during treatment, as this may have been perceived as unrealistic.

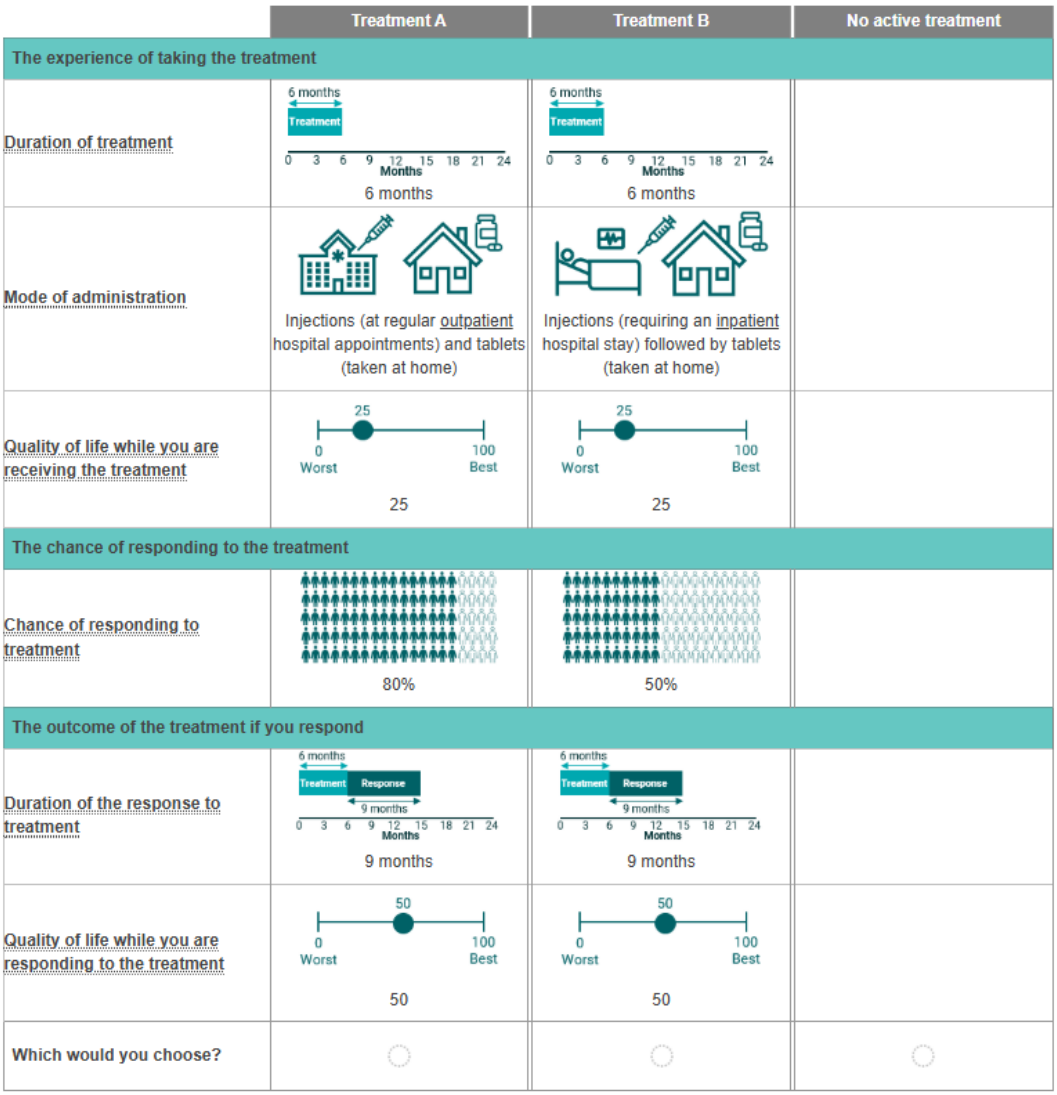
The order in which the tasks were presented, as well as the order of the two treatment options were randomized to minimize biases, including left-right bias ("no active treatment" was always on the right-hand side). Prior to completing the 12 choice tasks, respondents were shown a simple practice task where one treatment that had better (or equivalent) characteristics was compared to the other.

2.2.3 Pre-testing

Ten cognitive "think aloud" pre-testing interviews were conducted with people with AL living in the UK (Campoamor et al., 2024). The interviews were conducted over a three-week period: five interviews were conducted in week one, week two was reserved for initial survey revisions, and the final five interviews were conducted in week three.

A range of revisions were made to the survey following both sets of five interviews. This included the addition of a 'fixed' attribute (i.e., one that does not vary/is not part of the experimental design) for duration of treatment, which was set at six months. This was added because some participants misunderstood duration of response to mean the duration of treatment. Furthermore, the ordering of the attributes was revised to be more intuitive, the icons for duration of response were revised, and broad subheadings were introduced (the experience of taking the treatment; the chance of responding to treatment; and the outcome of the treatment if you respond). An example DCE task with the final formatting can be seen in Figure 3.

FIGURE 3. DCE TASK EXAMPLE



2.3 Recruitment

Adults with AL of any (sub)type were eligible to participate in the study. In the UK, all recruitment was conducted via Leukemia Care. In all other countries, recruitment was conducted via a specialist patient recruitment agency. We aimed to recruit 100 people with AL in the UK, USA and across the EU4 (France, Germany, Italy and Spain).

2.4 Ethics approval

Ethical approval for this study provided by the Economics Research Ethics Committee at City St George's, University of London (formerly City, University of London), via two applications with IDs: ETH2223-2151 and ETH2425-0034.

2.5 Statistical analysis

The DCE choice data were analyzed within a random utility maximization framework and several different models were used for different purposes. As is conventional, the first model used was a multinomial logit (MNL) model. However, this model does not account for variation in people's preferences (known as preference heterogeneity), and as such more complex models were subsequently employed for full sample analyses (Vass et al., 2022).

To produce a single aggregate set of results for the full sample, a mixed logit model was used because it can account for preference heterogeneity. In this model, the effect of each attribute level is estimated as an average across the whole sample, allowing for differences in preferences between respondents. We started by assuming that preferences for all attribute levels could vary randomly (with normal distributions) across people and then simplified the model by fixing any attributes that did not show any evidence of preference heterogeneity. The final model was estimated using simulation with 5,000 Halton draws.

While the mixed logit model allows for random preference heterogeneity, the typical (main effects) version of this model does not provide insights into the extent to which people with different characteristics (e.g., younger vs. older; women vs. men) may have different preferences. Thus, to enable a closer examination of preference heterogeneity across the full sample, latent class models were used. These models look for groups (called 'classes') of people in the data that share similar preferences. The number of classes is pre-specified (by the analyst) and therefore it is typical to test models with different numbers of classes, and to select the best performing model using statistical criteria (predominantly the Bayesian Information Criterion [BIC]). Upon doing this, it was determined that the optimal model, balancing information with complexity, for our data had three classes. We explored how different personal characteristics, such as age, gender, AL type, years since

diagnosis, relapse history could predict the people that might belong to each class. In the final predictive model, we retained only those variables that were statistically significant predictors of class membership in at least one class.

Finally, as the relative complexity of mixed logit and latent class models can obscure simple patterns within subgroups, we conducted exploratory subgroup analyses using MNL models.

All models produce coefficients, also known as part-worth utilities or preference weights, which cannot be directly interpreted. Therefore, for ease of interpretation, coefficients were used to generate relative attribute importance (RAI) scores. RAI scores indicate the relative importance of each attribute on a 0-100% scale, with higher scores indicating higher importance. These are calculated by dividing the utility range for each attribute by the full utility range (for all attributes). Furthermore, trade-offs, known as marginal rates of substitution (MRS), were calculated using the latent class model results using the chance of response attribute as the 'numeraire'. This means that the MRS illustrate how much chance of response respondents would (on average) be willing to forgo to receive a favorable change in another attribute (e.g., a 3-month increase in duration of response). Confidence intervals around the RAI scores and MRS estimates were estimated using the Delta method (Mott, Chami and Tervonen, 2020). All analyses were conducted in Stata SE version 15.

3 Results

The recruitment target for Spain was not met, and therefore it was dropped from the analysis. As such, the European data were combined to create an 'EU3' group comprising France, Germany, and Italy.

Overall, 267 people with AL responded to the surveys, of which 95 were from the UK, 88 from the USA, and 84 from the EU3. Their characteristics are detailed in Table 2. Across the full sample, the mean age was 55.6 years (SD=12.3) and 60% of the sample were female (n=159). Most respondents were white (n=218; 82%) and had completed high school (n=228; 85%). Furthermore, a small majority of respondents had a degree or equivalent qualification (n=137; 51%). The mean age at diagnosis was 51.2 years (SD=13.7) and the mean time since diagnosis was 4.3 years (SD=5.9). The majority of respondents had AML (n=165; 62%), just over a quarter had ALL (n=73; 27%) and 11% had APL (n=28).

Just under half of respondents reported not being on any active treatment (n=122; 46%), and significant proportions of respondents reported being on maintenance therapy (n=45; 17%) or consolidation therapy (n=37; 14%). In terms of relapse history, half of respondents reported never having relapsed (n=134; 50%), while a significant proportion reported experiencing one relapse (n=71; 27%). Furthermore, more than half of respondents reported having had a transplant in the past (n=145; 54%).

There were differences in the characteristics of respondents across countries/regions. Respondents in the USA were older on average (mean=59.7; SD=8.8) compared with those in the UK (mean=53.6; SD=13.7) and EU3 (mean=53.4; SD=12.7). Time since diagnosis was also shortest in the USA (mean=3.0 years; SD=2.5) and longest in the UK (mean=6.2 years; SD=8.5). The distribution of leukemia type varied: nearly half of the USA sample had ALL (n=40; 46%), whereas AML dominated in the UK (n=60; 64%) and EU3 (n=71; 85%).

Figure 4 presents the preference weights, and Figure 5 the resulting RAI scores, from the full sample mixed logit model. The chance of response

attribute was the single most important attribute (RAI=62.2%), and each increase in this attribute was associated with an increase in utility. All other attributes were far less important, ranging from 6.6% (mode of administration) to 13.7% (quality of life during response).

The preference weights show that, for quality of life during response, a score of 75 is much preferable to a score of 25 or 50. In contrast, for quality of life during treatment, a score of 50 did not offer any more utility than a score of 25. The duration of response preference weights indicated that durations greater than one year are preferred, but that 3-month increases in duration are not valued equally (e.g., an increase to 18 months from 15 months is not as good as an increase from 12 months to 15 months). In terms of mode of administration, receiving treatment as tablets taken at home is preferable to receiving injections at outpatient appointments, and both are preferable to an inpatient stay at hospital.

TABLE 2. DEMOGRAPHIC AND CLINICAL INFORMATION

	Full Sample (n=267)	UK (n=95)	USA (n=88)	EU 3 (n=84)
Age (Mean (SD))	55.6 (12.3)	53.6 (13.7)	59.7 (8.8)	53.4 (12.7)
Gender				
Male	108 (40%)	39 (41%)	36 (41%)	51 (61%)
Female	159 (60%)	56 (59%)	52 (59%)	33 (39%)
Ethnicity				
White	218 (82%)	93 (98%)	43 (49%)	82 (98%)
Black	17 (6%)	1 (1%)	16 (17%)	0 (0%)
Asian	7 (3%)	0 (0%)	7 (8%)	0 (0%)
Mixed	1 (<1%)	0 (0%)	0 (0%)	1 (1%)
Other	13 (5%)	1 (1%)	11 (13%)	1 (1%)
Hispanic/Latino*	11 (4%)	-	11 (13%)	-
Education				
Completed high school	228 (85%)	69 (73%)	88 (100%)	71 (85%)
Has degree or equivalent	137 (51%)	50 (53%)	40 (46%)	47 (56%)
Marital status				
Married/ civil partnership	139 (52%)	42 (44%)	57 (65%)	40 (48%)
Not married	89 (33%)	14 (15%)	31 (35%)	44 (52%)
Other	39 (15%)	39 (41%)	0 (0%)	0 (0%)
Responsible for children				
Yes	74 (28%)	25 (26%)	26 (30%)	23 (27%)
No	192 (72%)	70 (74%)	62 (70%)	60 (72%)

	Full Sample (n=267)	UK (n=95)	USA (n=88)	EU 3 (n=84)
Not reported	1 (<1%)	0 (0%)	0 (0%)	1 (1%)
Leukemia type				
ALL	73 (27%)	22 (23%)	40 (46%)	11 (13%)
AML	165 (62%)	60 (64%)	34 (39%)	71 (85%)
APL	28 (11%)	12 (13%)	14 (16%)	2 (2%)
Age at diagnosis				
(Mean (SD))	51.2 (13.7)	47.4 (15.3)	56.7 (8.8)	49.8 (14.4)
Years since diagnosis				
(Mean (SD))	4.3 (5.9)	6.2 (8.5)	3.0 (2.5)	3.6 (4.0)
Current treatment				
None	122 (46%)	54 (57%)	32 (36%)	36 (43%)
Induction therapy	9 (3%)	2 (2%)	6 (7%)	1 (1%)
Consolidation therapy	37 (14%)	6 (6%)	10 (11%)	21 (25%)
Maintenance therapy	45 (17%)	11 (12%)	21 (24%)	13 (16%)
Awaiting transplant	10 (4%)	1 (1%)	9 (10%)	0 (0%)
Recently transplant	27 (10%)	14 (15%)	6 (7%)	7 (8%)
CAR-T/ gene therapy	7 (3%)	1 (1%)	2 (2%)	4 (5%)
Don't know/not sure	6 (2%)	2 (2%)	2 (2%)	2 (2%)
Other	4 (1%)	4 (4%)	0 (0%)	0 (0%)
Relapse history				
Not yet achieved	36 (13%)	9 (10%)	15 (17%)	12 (14%)
remission	134 (50%)	66 (69%)	21 (24%)	47 (56%)
Never relapsed	71 (27%)	18 (19%)	33 (38%)	20 (24%)
One relapse	23 (9%)	2 (2%)	16 (18%)	5 (6%)
Two relapses	3 (1%)	0 (0%)	3 (3%)	0 (0%)
More than two relapses				
Transplant history				
None	122 (46%)	44 (46%)	52 (59%)	26 (31%)
One	134 (50%)	49 (52%)	30 (34%)	55 (66%)
Two	8 (3%)	1 (1%)	4 (5%)	3 (3%)
More than two	3 (1%)	1 (1%)	2 (2%)	0 (0%)

FIGURE 4. PREFERENCE WEIGHTS (MIXED LOGIT MODEL)

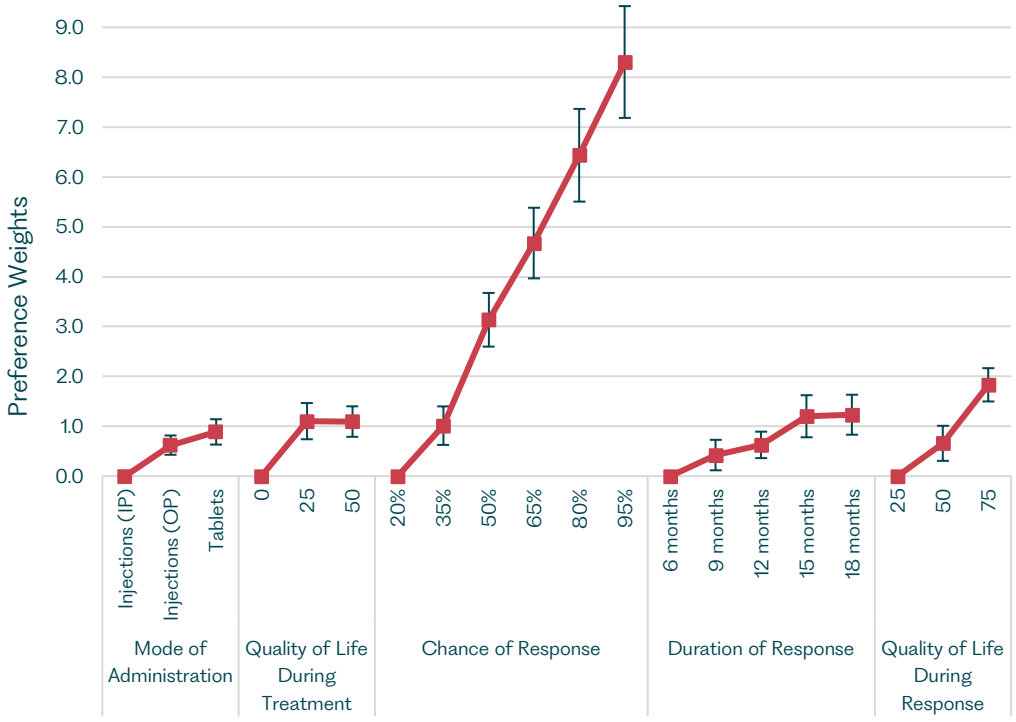


FIGURE 5. RAI SCORES (MIXED LOGIT MODEL)

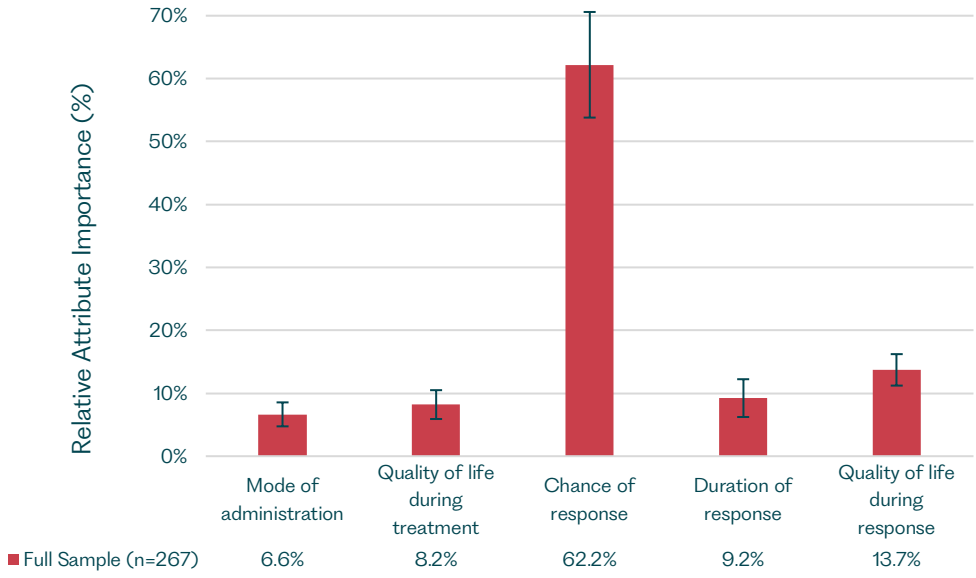


Table 3 presents the model output from the latent class model. In this model, to limit the number of attribute levels, we analyzed the numeric variables as continuous rather than categorical variables as in the MNL. Figure 6 presents the RAI scores from the same model. The latent class modelling identified three distinct preference groups within the full sample.

The largest group, Class 1, with a class share of 47%, were "chance of response focused" and predominantly made choices based on the chance of response attribute. For these respondents, the RAI score of chance of response was 77%. All other attributes were statistically significant, but were much smaller, suggesting that treatment efficacy was their key concern.

In contrast, Class 2, with a class share of 21%, were "convenience and efficacy focused". In this group, duration and chance of response were highly influential (RAI scores of 40% and 30%, respectively). Furthermore, mode of administration was also very important (RAI=23%). In contrast, quality of life during treatment was not important at all (RAI score not statistically significantly different from zero), and quality of life during response was not particularly important (RAI=6%).

Finally, Class 3, with a class share of 32%, were "balanced decision-makers". In this group, all attributes were important except for mode of administration. The most important attribute was chance of response (RAI=49%), followed by quality of life during response (RAI=24%), quality of life during treatment (RAI=15%) and duration of response (RAI=10%).

The class membership variables revealed that those more recently diagnosed and those that had relapsed in the past were more likely to be in class 1 (chance of response-focused), and those in the USA were less likely, compared to class 3 (balanced decision-makers). Furthermore, those in the USA and those with ALL were more likely to belong in class 2 (convenience and efficacy focused), compared to class 3 (balanced decision-makers).

TABLE 3. LATENT CLASS MODEL RESULTS

		Class 1 (Share: 46.7%)	Class 2 (Share: 21.5%)	Class 3 (Share: 31.8%)
DCE variables	Mode of administration Outpatient	0.338** (0.138)	1.226*** (0.218)	0.203 (0.142)
	Mode of administration Tablets	0.463*** (0.135)	2.144*** (0.320)	0.136 (0.158)
	Quality of life during treatment	0.019*** (0.004)	0.001 (0.005)	0.030*** (0.005)
	Chance of response	0.147*** (0.012)	0.037*** (0.009)	0.065*** (0.009)
	Duration of response	0.050** (0.022)	0.310*** (0.047)	0.085*** (0.028)
	Quality of life during response	0.025*** (0.004)	0.011** (0.005)	0.048*** (0.005)
Class membership	Years since diagnosis	-0.201*** (0.058)	-0.051 (0.051)	—
	Lives in USA	-1.278** (0.495)	1.092** (0.542)	—
	Relapsed before	0.913** (0.458)	-0.215 (0.556)	—
	Has ALL	-0.007 (0.386)	0.912** (0.453)	—
	Constant	1.145*** (0.357)	-1.073** (0.512)	—

Notes: Standard errors in parentheses. Significance levels: *** p<0.01, ** p<0.05, * p<0.1.

FIGURE 6. RAI SCORES (LATENT CLASS MODEL)

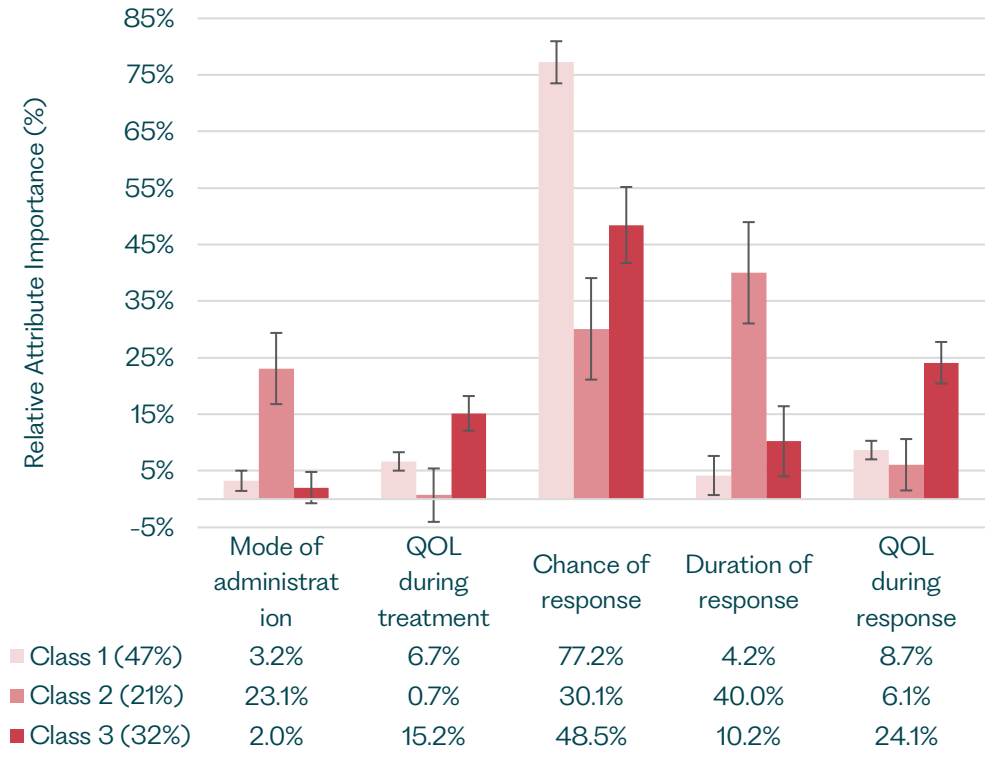


FIGURE 7. MARGINAL RATES OF SUBSTITUTION (LATENT CLASS MODEL)

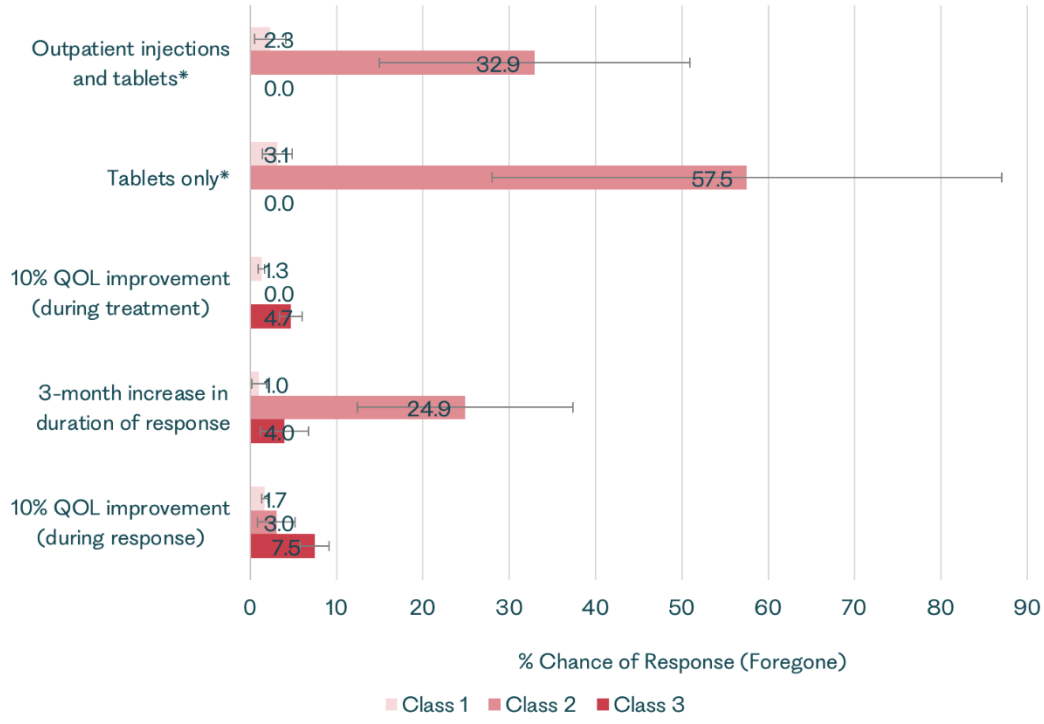
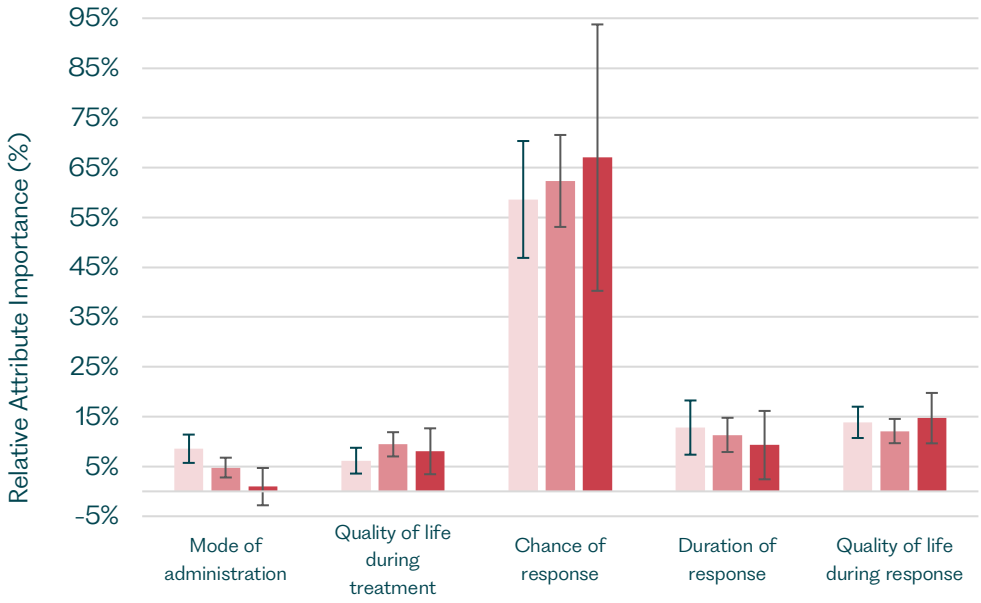


Figure 7 illustrates the trade-offs (MRS) from the latent class model results. Given the importance of chance of response in class 1 (chance of response focused), respondents in this group would not be willing to trade-off any meaningful % chance of response for improvements in other attributes. For example, to achieve a 10% improvement in quality of life during response, people in this group would only be willing to forgo a 1.7% chance of response.

In contrast, chance of response was less important in class 2 (convenience and efficacy focused) compared to the other two classes. Therefore, people in this class would be willing to forgo a significant chance of response for improvements in some of the other attributes. For example, people in this group would be willing to forgo a 58% chance of response in order to receive a treatment that is given via tablets (taken at home), compared to a treatment that requires an inpatient hospital stay.

Finally, in class 3 (balanced decision-makers), respondents would typically not be willing to trade-off much chance of response for improvements in other attributes. However, they would be willing to forgo a 7.5% chance of response in order to receive a 10% improvement in quality of life during response.

FIGURE 8. RAI SCORES, BY ACUTE LEUKAEMIA SUBTYPE (MNL MODELS)



	Mode of administration	Quality of life during treatment	Chance of response	Duration of response	Quality of life during response
ALL (n=112)	8.6%	6.2%	58.6%	12.8%	13.9%
AML (n=127)	4.8%	9.4%	62.3%	11.3%	12.1%
APL (n=28)	0.9%	8.0%	67.0%	9.3%	14.7%

Figure 8 illustrates the RAI scores from three separate models, one for each type of acute leukemia (ALL, AML, and APL). Overall, the pattern of results is very similar between the three groups. The only statistically significant difference observed relates to mode of administration, which was not considered important by those with APL.

FIGURE 9. RAI SCORES, BY COUNTRY/REGION (MNL MODELS)

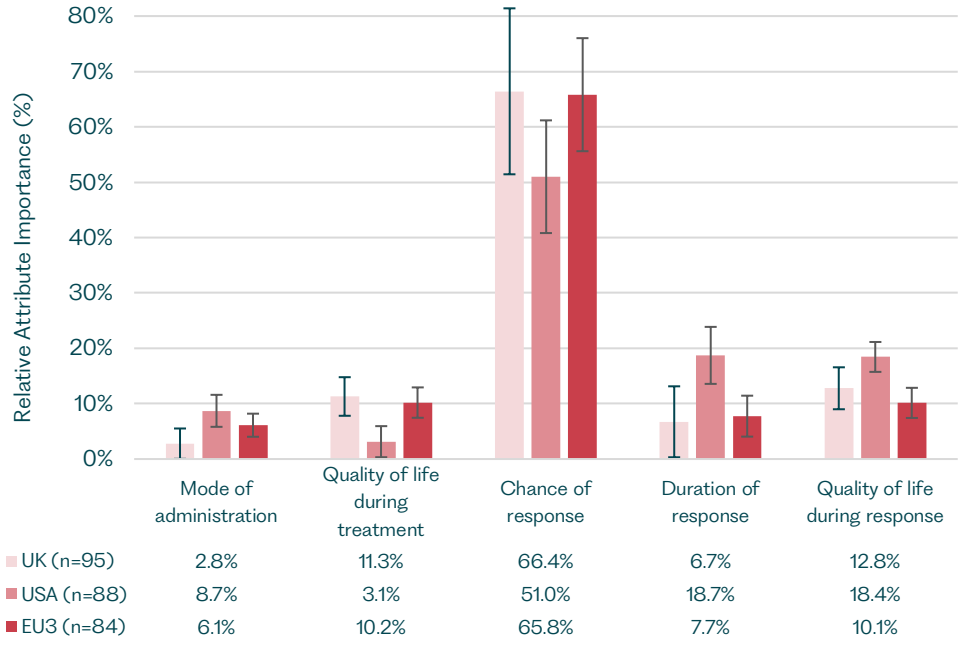


Figure 9 illustrates the RAI scores from three separate models, one for the UK, one for the USA, and one for the EU3. While the RAI scores for the UK and EU3 are broadly similar, with confidence intervals overlapping for all attributes (indicating that any differences are not statistically significant), the results in the USA differ substantially. For example, chance of response and quality of life during treatment are considerably less important in the USA, with all other attributes more important.

This aligns with the latent class model results, where people from the USA were less likely to be in class 1 (chance of response focused) and more likely to be in class 2 (convenience and efficacy focused).

4 Discussion

4.1 Summary of results

These results build on the UK results, published in Mott et al. (2024). The UK-only results showed two main patterns: 1) that chance of response dominates as the most important treatment characteristic in the relapsed/refractory treatment context; and 2) that there is significant preference heterogeneity across the acute leukemia patient population. Regarding the latter, more specifically, we found that there were two groups of respondents in the UK that shared similar preferences. The first was a group that prioritized chance of response almost exclusively, and people that had ALL or APL, and/or were diagnosed more recently were more likely to be in this group. In contrast, the second group cared about all treatment characteristics (though chance of response was still the most important), and people that had AML and/or were diagnosed longer ago were more likely to be in this group.

The results in this report incorporate the UK data and include further data collected from people with AL in the USA, France, Germany, and Italy. When all the data are combined, the results remain similar to the original findings from the UK alone. That is, while all treatment characteristics are important to some extent, the chance of responding to treatment is the most important characteristic by a significant margin. Duration of response is of a similar overall importance compared to the UK alone, though the analysis in this report indicates that there may be diminishing returns to additional months of response, perhaps given that the range of durations in the DCE were all relatively short (6-18 months).

There are also similarities in relation to the preference heterogeneity observed in the analysis in this report. The latent class analysis identified three distinct groups of preferences. Two of these groups were similar to those identified in the UK analysis: the “chance of response-focused” group (class 1), and the “balanced decision-makers” group (class 3). The combined class share for these two groups in this analysis was 79%, indicating that most respondents across the full sample would fit within one of these two groups and, as per the UK analysis, those that were diagnosed more recently were more likely to be in the “chance of response focused” group. This suggests that those that had

more recently been through the trauma of an AL diagnosis are more focused on treatment efficacy. Furthermore, in this analysis, we also found that those that had experience of a relapse were more likely to be in the "chance of response focused" group. It perhaps makes sense that those that had not experienced a relapse before and whose diagnosis was longer ago would be relatively less focused on the efficacy of treatment in this context, as more time had passed and their expectations about experiencing a future relapse may be lower.

Class 2, though, is distinct to this broader analysis. Respondents in the USA were significantly less likely to be in the "chance of response-focused" group (Class 1) and were much more likely to be in the third, more unique, class identified in the present analysis; we refer to them as the "convenience and efficacy focused" group (Class 2). In this group, both chance and duration of response were highly important, with the duration just as, if not more, important than the chance. Furthermore, this group had strong preferences in relation to mode of administration; a pattern that was not observed within the UK-only sample. Respondents in this group not only had a strong preference for treatment that is solely administered at home (tablets), but also strongly preferred injections delivered via outpatient appointments (with tablets taken at home), compared to receiving treatment via an inpatient hospital stay. The extent of the preferences for mode of administration was substantial, with the MRS indicating that these respondents would be willing to accept a treatment with a better mode of administration that offered a significantly lower chance of response.

Healthcare in the USA is well known to be amongst the most expensive in the world, especially when hospital stays are involved (Papanicolas, Woskie and Jha, 2018), so it may be the case that the USA respondents whose preferences aligned with this group were particularly averse to treatments requiring a hospital stay based on the financial implications. While there may still be financial implications for those in the UK and EU3, these are perhaps more likely to be indirect, such as inability to work, travel-related costs, and so on, which may be why these respondents were relatively less likely to be in this group. Equally, it could be that some respondents consider treatments requiring inpatient stays as less attractive for other reasons, such as the impact on their families, and/or an assumption that the treatment would be more intensive. All this being said, it is worth noting that the class share of the

"convenience and efficacy focused" group was only 21%, indicating that it is a minority of respondents — who were spread across the entire sample (not just the USA) — that held these preferences.

To directly examine differences in preferences across the sample, we ran some exploratory subgroup analyses. Unlike the UK-specific analysis, significant differences in preferences by AL (sub)type were not observed in this full sample. The only exception is that people with APL did not consider mode of administration to be important (the RAI score was not statistically significantly different from zero). However, the sample size for this group was particularly low (n=28) and this result should therefore be taken with caution. In contrast, this analysis did point towards differences in preferences between regions. As expected, given the latent class results, people with AL in the USA had different preferences to those in the UK and EU3. In summary, people in the USA were less concerned about chance of response and quality of life during treatment, and were more concerned about duration of response, mode of administration, and quality of life during response. Those in the UK and EU3 had very similar preferences to one another on average, with the only exception being mode of administration, which was less important in the UK compared to the EU3.

In conclusion, the results of this study show that, while people with AL largely prioritize treatments with a higher chance of response, a large proportion consider a wider range of factors, including quality of life and mode of administration. As such, while there is a clear need for clinically effective treatments in the relapsed/refractory settings to be prioritized, it is important that the broader impact on people with AL is not disregarded. Furthermore, it is important to note that preferences may differ across regions, and treatments that are well suited to people in one country may not be as well suited to people in another.

4.2 Strengths and limitations

In this study, we developed a DCE to explore the preferences of people with AL for treatments in the event of a relapse. Our design process followed best practice guidance, including conducting formative qualitative research and conducting 'think aloud' pre-testing interviews. Furthermore, our study design

was informed by patient and academic advisory groups at key stages, and with the assistance of a patient network and organization (ALAN and Leukemia Care) throughout.

However, the study is not without its limitations. We set out to explore the preferences of people with AL across the UK and EU4 as well as the USA, however, we were unable to recruit sufficient numbers in Spain. Given the severity and relative rarity of acute leukemia, it can be particularly difficult to recruit people to participate in online surveys, and this proved to be the case for this study. In anticipation of this, we did not set quotas for different patient characteristics across regions and therefore the samples varied significantly between them; for example, 85% of patients in the EU3 had AML compared to 39% in the USA. While the lack of quotas facilitated recruitment, the variation in respondents somewhat limits our ability to make meaningful comparisons between the different regions. It is also worth noting that, across our full sample, the average age of our study participants is relatively low compared to typical diagnosis age. For example, the average age across our sample was 56, whereas the median age at diagnosis for AML (of which 62% of the sample had) is around 69 (Krayem, Frisch and Horowitz, 2025). It may be the case that people that are willing to participate in online research are likely to be younger, on average, than the broader patient population and, as a result, our results might not be fully generalizable.

5 Conclusion

This study shows that, when considering treatment in the event of a relapse, people with AL largely prioritize treatments that offer a higher chance of response. However, the results highlight substantial differences in preferences, both across patient subgroups and between regions, reflecting the diverse needs and priorities of people with AL.

These findings have several implications. For clinicians, they highlight the importance of discussing treatment options not only in terms of survival prospects, but also in relation to quality of life both during and after treatment, since patients may weigh these aspects differently. For researchers and those involved in clinical trial development, they reinforce the need to capture outcomes beyond survival such as quality of life and treatment burden, so that studies capture what patients truly value. For regulators and payers, the results emphasize the importance of considering patient preference evidence when assessing new therapies, ensuring that value is judged not only by clinical efficacy but also by real-world impact. Finally, for patient advocates, this evidence provides a foundation for pressing for care pathways and policies that reflect the diverse priorities of people living with AL.

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ALAN is hosted under the umbrella of the Leukemia Patient Advocates Foundation (LePAF), a patient-led non-profit foundation based in Switzerland. As a foundation we connect leukemia patient organizations on all continents to strengthen advocacy work. The mission is to improve the lives and survival of patients affected by leukemia as well as their relatives by supporting leaders in providing help and support.

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