





Patient Preferences for Treatment in Relapsed/Refractory Acute Leukemia in the United Kingdom: A Discrete Choice Experiment

David John Mott ¹, Jake Hitch ^{1,2}, Samantha Nier ³, Zack Pemberton-Whiteley^{3,4}, Chris Skedgel ¹

¹Office of Health Economics, London, UK; ²Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK; ³Acute Leukemia Advocates Network, Bern, Switzerland; ⁴Leukemia Care, Worcester, UK

Correspondence: David John Mott, Email dmott@ohe.org

Background: Acute leukemia is a cancer of the white blood cells which progresses rapidly and aggressively. There are two types: acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). The latter has a rare subtype: acute promyelocytic leukemia (APL). For some patients, following first-line treatment, remission is not achieved (“refractory disease”), and for others the leukemia returns after achieving remission (“relapse”). For these individuals, outcomes are typically poor. It is, therefore, important to understand patients’ treatment priorities in this context.

Methods: Building upon formative qualitative research, an online survey containing a discrete choice experiment (DCE) was designed to explore patients’ treatment preferences in the relapsed/refractory setting. The DCE attributes were mode of administration; quality of life during treatment; chance of response; duration of response; and quality of life during response. Each respondent completed twelve scenarios containing two hypothetical treatments. Participants were eligible if they lived in the United Kingdom and had a diagnosis of acute leukemia. The data were analysed using a latent class model.

Results: A total of 95 patients completed the survey. The latent class analysis identified two classes. For both, chance of response was the most important attribute. For class 1, every attribute was important, whereas for class 2, the only important attributes were quality of life (during treatment and response) and chance of response. A greater proportion of respondents would fall into class 1 overall, and those with ALL or APL and those more recently diagnosed were more likely to be in class 2.

Conclusion: Our results indicate that patients are strongly concerned about the chance of response, as well as quality of life (to a lesser extent), when faced with different treatment options in the relapsed/refractory setting. However, there is significant preference heterogeneity within the patient population, and other treatment characteristics also matter to many.

Keywords: acute leukemia, hematology, oncology, patient preferences, discrete choice experiment

Introduction

Acute leukemia is a cancer of the white blood cells which progresses rapidly and aggressively. There are different types of acute leukemia, classified by the type of white blood cells that are affected, all of which are relatively rare compared to other types of cancer.^{1–3} Acute myeloid leukemia (AML) is the most common type of leukemia in adults, of which there is a rare subtype called acute promyelocytic leukemia (APL) which accounts for around 15% of AML cases.^{1–4} Acute lymphoblastic leukemia (ALL), also commonly called acute lymphocytic leukemia, is the most common type of leukemia in children and is most common before age 15 and after age 50.^{1–3} As with AML, there are also subtypes of ALL.

Whilst there are many (sub)types of acute leukemia, each with differing outlooks, there are many similarities in the symptoms that people experience and the types of treatment available.⁵ Most individuals experience symptoms as some combination of fatigue, fever, shortness of breath, bone or joint pain, repeated infections, unexplained weight loss, and increased bruising and bleeding.⁵ Acute leukemia is typically detected via blood tests, and, upon diagnosis, it is important

that treatment is provided quickly due to its rapid progression. Treatment options vary by (sub)type as well as patient age and/or general condition but typically involve some combination of chemotherapy, radiotherapy, immunotherapy, targeted therapy, and (for those eligible) stem cell or bone marrow transplants.^{2,3} Initial, or “first-line”, treatment is usually intensive and focused on achieving remission (where the bone marrow and blood cell counts return to normal) as quickly as possible. For patients, the experience of diagnosis and first-line treatment is traumatic and often results in long-term side effects due to the aggressive nature of many of the treatment options, which can have a significant impact on quality of life.^{6,7}

Unfortunately, not all patients will achieve a complete remission with first-line treatment (referred to as “refractory” disease). Furthermore, for around 50% of people with AML⁸ and 50% of adults with ALL that achieve remission,⁹ the acute leukemia later returns (referred to as a “relapse”). For other groups of patients, the relapse rate is significantly lower, such as children with ALL (around 10–20%)¹⁰ and those with APL (around 5–10%).⁴ The outlook for those with relapsed or refractory acute leukemia is often poor as many treatment options are less effective compared to first-line treatments,^{4,8–10} though there are some exceptions.¹¹

In recent years, there has been a drive to better understand patients’ preferences to inform decision-making.^{12–15} Patient preference studies can be conducted using a wide range of both qualitative and quantitative approaches.¹⁶ Quantitative evidence on patients’ preferences for different treatment characteristics may be particularly useful for informing regulatory and reimbursement decisions,^{17,18} as indicated by the Food and Drug Administration (FDA) in the United States (US)¹⁹ and the National Institute for Health and Care Excellence (NICE) in England and Wales,²⁰ amongst other agencies.^{21,22}

Only a small number of quantitative patient preference studies using stated preference methods have been published in the context of acute leukemia to date. Two relatively broad studies have been conducted in the US to explore the preferences of people with AML. The first study,²³ which used best-worst scaling methodology, found that the two primary worries of patients were death and long-term treatment side effects. The second study,²⁴ which used discrete choice experiment (DCE) methodology, found that patients prioritise treatments that offer a greater chance at remission, but that age and gender may impact treatment preferences. A further two studies were conducted in narrower contexts, ie, in groups of patients with a specific subtype of acute leukemia or with a specific treatment experience. Ashaye et al²⁵ elicited preferences from people in the US with Philadelphia chromosome positive ALL using a DCE. They found that overall survival was the most important aspect of first-line treatment and that many (particularly younger) patients would be willing to accept an increased risk of a major cardiovascular event (eg, heart attack, stroke) for a better level of overall survival. Saini et al²⁶ elicited preferences from people with AML in the US, United Kingdom (UK) and Canada that had previously received a stem cell transplant. They found that quality of life, duration of hospitalisation, and chance of two-year relapse-free survival were the most important characteristics of maintenance therapies (post-transplant) from the patient perspective.

Whilst the published studies provide some insight into the treatment preferences of people with acute leukemia, many gaps in the literature remain. For example, no studies have focused on the broader population of people with acute leukemia (ie, incorporating all types), which could enable a better understanding of how preferences differ by (sub)type. Furthermore, no studies have focused specifically on the relapsed/refractory setting, where outcomes are typically poorer, and preferences may therefore vary significantly. Our study aimed to address this gap in the literature by conducting the first preference study in the relapsed/refractory setting.

Methods

Study Overview

Patient preferences were elicited using a DCE, which was delivered as part of an online survey. DCE is a stated preference methodology whereby respondents are asked to make a series of hypothetical choices between different alternatives, providing insight into preferences for the characteristics of the alternatives and the trade-offs that respondents are willing to make.²⁷ In this case, the alternatives were treatments for relapsed/refractory acute leukemia, and respondents were people from the UK that have had a diagnosis of acute leukemia of any (sub)type (referred to as

“people with acute leukemia” hereafter for brevity). In addition to the DCE, participants were asked a range of demographic and clinical status questions.

Ethical approval for the study was granted by a Research Ethics Committee at City, University of London (ETH2223-1008), and all participants provided consent before participating in the research activities. Two advisory groups supported the study throughout by providing guidance and reviewing study materials: an Academic Steering Group and a Patient Advisory Group.

Recruitment

Adults with acute leukemia living in the UK were recruited via Leukemia Care (<https://www.leukemiacare.org.uk>), a leukemia charity and member of the Acute Leukemia Advocates Network (ALAN; <https://www.acuteleuk.org>). Participants recruited to take part in the online bulletin boards or cognitive pilot interviews (see below) were remunerated, whereas respondents to the online survey were not.

DCE: Identifying Attributes and Levels

The first stage of the DCE design was to identify the attributes of relapsed/refractory treatments that are of greatest relevance and importance to patients. As a first step, a targeted literature review of past preference studies in acute leukemia was conducted. Alongside this, the characteristics of current and forthcoming relapsed/refractory treatments were reviewed and collated.

Whilst the reviews provided some initial insights into the important treatment characteristics in this setting, it has long been acknowledged that DCEs should be informed by qualitative research with the relevant patient population(s).^{28,29} We therefore organised a qualitative online bulletin board (OBB) study.³⁰ OBBs are an alternative to face-to-face focus groups and are increasingly used in qualitative research.^{31–33} We conducted two OBBs, one for people with AML or APL (n = 12), and another for people with ALL (n = 9). This arrangement was, in part, set up to test whether it would be appropriate to design a single DCE for both populations. The OBBs were each live for six days in total. On each of the first three days, posts were added by the study team containing questions about the participants’ experience in being diagnosed with acute leukemia and expectations around treatment, their experience with first-line treatment and their experience or expectations around later lines of treatment, respectively. On the fourth day, participants were asked to consider what their priorities would be should they need treatment again in future (ie, in the event of a relapse). Following this, the OBBs were live for another two days (over the weekend) to enable any further discussion amongst the group. Over the course of six days, participants on average posted 22 messages each on the OBB.

The insights from the literature reviews and the OBBs were subsequently considered in detail by the study team, with input from ALAN’s steering committee and the project’s advisory groups. It was decided that a single DCE design for all acute leukemia patients would be appropriate. On the basis of comments in the OBBs and guidance from the project’s advisory groups, the set of attributes and levels detailed in [Table 1](#) was derived.

The EQ-5D-5L questionnaire was used as a framework for the quality of life attributes.³⁴ Respondents were introduced to the concept of quality of life on a numerical scale, given examples of different EQ-5D-5L profiles, and then asked to complete the EQ-5D-5L questionnaire themselves, prior to completing the DCE. Furthermore, to aid comprehension of the attribute levels, icons were used for every attribute.

DCE: Experimental Design

It was agreed that the DCE should be unlabelled, contain two treatment alternatives, and include an opt-out alternative (“no active treatment”). A d-efficient experimental design was produced using Ngene (ChoiceMetrics, Sydney, Australia) containing 24 rows in total, which were split into two blocks, such that each respondent completed 12 choice scenarios. Several constraints were implemented to reduce attribute dominance and encourage trade-offs. Specifically, chance and duration of response were constrained such that the difference between the levels of these attributes could not exceed 30% or 6 months, respectively, between the alternatives in each scenario, to encourage trade-offs and avoid dominant alternatives. Quality of life whilst responding was also constrained to ensure that it was never lower than quality of life during treatment, ie, it was not possible for quality of life to decline after treatment ended, but whilst someone was

Table 1 Attributes and Levels

Attribute	Levels
Mode of administration	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • 0 • 25 • 50
Chance of responding to treatment (chance of response)	<ul style="list-style-type: none"> • 20% • 35% • 50% • 65% • 80% • 95%
Duration of the response to treatment (duration of response)	<ul style="list-style-type: none"> • 6 months • 9 months • 12 months • 15 months • 18 months
Quality of life whilst responding to treatment (quality of life during response)	<ul style="list-style-type: none"> • 25 • 50 • 75

Note: Shortened attribute names in parentheses.

responding. Prior to completing the 12 choice scenarios, participants saw a practice task where one alternative dominated the other (had equivalent or more favourable attribute levels for each attribute). The order of the alternatives within the choice scenarios was randomised to avoid left–right bias.

DCE: Piloting

A total of 10 cognitive “think aloud” pilot interviews were conducted with people with acute leukemia.³⁵ The interviews were conducted over three weeks, with an initial block of five interviews conducted in week one, followed by a week for survey revisions, with a final block of five interviews conducted in week two. In week one, some participants misinterpreted the “duration of response” attribute as “duration of treatment” and struggled to distinguish between the quality of life attributes, which appeared to partly be due to the ordering of the attributes. Therefore, in week two, a fixed attribute indicating the duration of treatment (six months for all treatments) was added to the presentation of each alternative, the ordering of the attributes was revised, the duration of response icons were revised, and broad subheadings were introduced. In the week three interviews, comprehension of the survey was much improved, and only a small number of minor revisions were suggested, which were subsequently implemented before the full launch. An example choice scenario with the final formatting can be seen in [Figure 1](#).

Statistical Analysis

The DCE data were analysed using a random utility maximisation framework, with all attributes continuously coded except for mode of administration (which was dummy coded).³⁶ A conditional logit model was initially used; however, as there were *a priori* expectations of preference heterogeneity within the sample given the different types of acute leukemia, more flexible models were subsequently estimated.³⁷ These included mixed logit models, and a series of latent class models with varying numbers of classes.³⁶ A latent class model was preferred for illustrating preference heterogeneity, and based on Bayesian Information Criterion, the preferred model specification was a two-class model.

	Treatment A	Treatment B	No active treatment
The experience of taking the treatment			
<u>Duration of treatment</u>	<p>6 months Treatment 0 3 6 9 12 15 18 21 24 Months 6 months</p>	<p>6 months Treatment 0 3 6 9 12 15 18 21 24 Months 6 months</p>	
<u>Mode of administration</u>	<p>Injections (requiring an <u>inpatient</u> hospital stay) followed by tablets (taken at home)</p>	<p>Injections (at regular <u>outpatient</u> hospital appointments) and tablets (taken at home)</p>	
<u>Quality of life whilst you are receiving the treatment</u>	<p>25</p>	<p>25</p>	
The chance of responding to the treatment			
<u>Chance of responding to treatment</u>	<p>50%</p>	<p>35%</p>	
The outcome of the treatment if you respond			
<u>Duration of the response to treatment</u>	<p>6 months Treatment Response 0 3 6 9 12 15 18 21 24 Months 6 months</p>	<p>6 months Treatment Response 0 3 6 9 12 15 18 21 24 Months 6 months</p>	
<u>Quality of life whilst you are responding to the treatment</u>	<p>50</p>	<p>75</p>	
<u>Which would you choose?</u>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Figure 1 Example choice scenario.

Relative attribute importance (RAI) scores were estimated by dividing the utility range for each attribute (based on the estimated parameters) by the total utility range, and confidence intervals for these scores were estimated via the delta method. To explore the effect of respondent characteristics on class membership, various respondent characteristics were included within the latent class models to explore whether they had an impact. To explore the trade-offs that respondents were willing to make, marginal rates of substitution were estimated between the most preferred attribute and other attributes, with confidence intervals estimated via the delta method.³⁸ All analyses were conducted in Stata v15 (StataCorp, Texas, USA).

Results

A total of 95 people with acute leukemia completed the online survey and provided DCE responses that could be analysed (three participants opted-out of all choice scenarios and were therefore excluded from the analysis). Table 2 provides an overview of the characteristics of the 95 respondents included in the analysis.

Table 2 Respondent Characteristics

	Total N = 95	AML N = 61	ALL N = 22	APL N = 12	p-value
Age (mean)	53 (14)	54 (13)	53 (15)	46 (15)	0.14
Age at diagnosis (mean)	48 (15)	49 (13)	46 (19)	42 (14)	0.31
Years since diagnosis (mean)	5 (7)	5 (5)	7 (11)	3 (3)	0.29
Gender					0.13
Male	39 (41%)	21 (34%)	13 (59%)	5 (42%)	
Female	56 (59%)	40 (66%)	9 (41%)	7 (58%)	
Country					0.18
England	78 (82%)	53 (87%)	18 (82%)	7 (58%)	
Scotland	9 (9%)	5 (8%)	2 (9%)	2 (17%)	
Wales	7 (7%)	2 (3%)	2 (9%)	3 (25%)	
Northern Ireland	1 (1%)	1 (2%)	0 (0%)	0 (0%)	
Has a degree or equivalent qualification					0.08
Yes	51 (54%)	29 (48%)	12 (55%)	10 (83%)	
No	44 (46%)	32 (52%)	10 (45%)	2 (17%)	
Regular responsibility for children					0.48
Yes	26 (27%)	15 (25%)	6 (27%)	5 (42%)	
No	69 (73%)	46 (75%)	16 (73%)	7 (58%)	
Type of ALL					
Philadelphia chromosome positive			7 (32%)		
Philadelphia chromosome negative			4 (18%)		
Do not know/cannot remember			11 (50%)		
Type of AML					
High risk		31 (51%)			
Intermediate/standard risk		15 (25%)			
Low risk		3 (5%)			
Do not know/cannot remember		12 (20%)			
Remission and relapse history					0.06
Not yet achieved remission	9 (9%)	5 (8%)	4 (18%)	0 (0%)	
Never relapsed	66 (69%)	43 (70%)	12 (55%)	11 (92%)	
One relapse	18 (19%)	13 (21%)	4 (18%)	1 (8%)	
More than two relapses	2 (2%)	0 (0%)	2 (9%)	0 (0%)	

(Continued)

Table 2 (Continued).

	Total N = 95	AML N = 61	ALL N = 22	APL N = 12	p-value
Current treatment stage					0.08
None	55 (58%)	38 (62%)	6 (27%)	11 (92%)	
Induction therapy	2 (2%)	2 (3%)	0 (0%)	0 (0%)	
Consolidation therapy	7 (7%)	4 (7%)	2 (9%)	1 (8%)	
Maintenance therapy	10 (11%)	5 (8%)	5 (23%)	0 (0%)	
Awaiting BMT / SCT	1 (1%)	0 (0%)	1 (5%)	0 (0%)	
Recently received BMT / SCT	13 (14%)	9 (15%)	4 (18%)	0 (0%)	
Undertaking CAR-T / gene therapy	1 (1%)	0 (0%)	1 (5%)	0 (0%)	
Do not know/not sure	3 (3%)	2 (3%)	1 (5%)	0 (0%)	
Other	3 (3%)	1 (2%)	2 (9%)	0 (0%)	
Number of BMTs / SCTs					0.01
None	44 (46%)	23 (38%)	9 (41%)	12 (100%)	
One	49 (52%)	36 (59%)	13 (59%)	0 (0%)	
Two	1 (1%)	1 (2%)	0 (0%)	0 (0%)	
More than two	1 (1%)	1 (2%)	0 (0%)	0 (0%)	

Notes: Standard deviations in parentheses for continuous variables (proportions by column for categorical). P-values relate to chi2 tests for categorical variables and ANOVA for continuous variables.

Abbreviations: BMT, Bone Marrow Transplant; SCT, Stem Cell Transplant.

The mean age of respondents was 53 years old (range 18–81 years), over half were female (59%; $n = 56$), and the majority were based in England (82%; $n = 78$). Just over half of the respondents reported having degree or an equivalent qualification (54%; $n = 51$), and the majority reported that they did not have regular responsibility for children (73%; $n = 69$). AML was the most common type of leukemia (64%; $n = 61$), followed by ALL (23%; $n = 22$), and APL (13%; $n = 12$). The mean number of years since diagnosis across the sample was five, though the median was lower (three years) due to a strong negative skew (range 0–36 years). Most respondents had achieved remission and had not experienced a relapse (69%; $n = 66$) and a slim majority reported that they were not currently receiving any treatment (58%; $n = 55$). Around half of the sample had received one transplant in the past (52%; $n = 49$), with just under half reporting that they had never received a transplant (46%; $n = 44$).

There were some statistically significant ($p < 0.1$) differences in the characteristics of respondents with different types of leukemia. These were largely driven by the respondents with APL, as a higher proportion (compared to respondents with AML and ALL) reported having a degree or equivalent qualification, having never relapsed after achieving remission, and having never had a transplant. Another notable difference between the groups was that a higher percentage of respondents with ALL reported that they were actively receiving treatment or had recently received a transplant compared to respondents with AML or APL.

The results from the two-class latent class model can be found in Table 3. As the opt-out alternative was selected so infrequently (29 out of 1138 total choices; 2.5%), these opt-out choices were not included to simplify the analysis. Likewise, an alternative-specific constant was not included in the final specification as it was not statistically significant (as expected *a priori* due to the randomisation of the alternatives). In class 1, all attributes were statistically significant at the 1% level, except for outpatient injections (statistically significant at the 5% level), indicating that all attributes are important within this class. In contrast, in class 2, the only statistically significant attributes (all at the 1% level) were quality of life during treatment, chance of response, and quality of life during response. The class shares were 60% for

Table 3 Latent Class Model Results

	Class 1		Class 2	
Class share	0.603		0.397	
Attributes	Coefficient	95% CI	Coefficient	95% CI
Mode of administration (α)				
-Outpatient injections and tablets (β)	0.307**	[0.039, 0.576]	0.174	[-0.409, 0.756]
-Tablets only (β)	0.513***	[0.235, 0.791]	-0.025	[-0.568, 0.518]
Quality of life during treatment	0.018***	[0.012, 0.024]	0.037***	[0.022, 0.052]
Chance of response	0.043***	[0.030, 0.056]	0.244***	[0.175, 0.313]
Duration of response	0.100***	[0.051, 0.148]	0.142	[-0.032, 0.315]
Quality of life during response	0.025***	[0.019, 0.031]	0.033***	[0.018, 0.048]
Class membership	Coefficient	95% CI		
Constant	-0.967*	[-2.048, 0.115]		
Years since diagnosis	0.145**	[0.014, 0.276]		
AML	1.076*	[-0.015, 2.167]		
Model details				
Log-likelihood	-508			
Number of respondents	95			
Number of observations	2220			

Notes: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$. CI = Confidence Interval. (α) Dummy coded. The reference category is "Injections (requiring an inpatient hospital stay) followed by tablets (taken at home)". (β) Full labels are "Injections (at regular outpatient hospital appointments) and tablets (taken at home)" and "Tablets (taken at home)".

class 1 and 40% for class 2, indicating that a greater proportion of participants would be predicted to fall into class 1. The class membership coefficients indicate that those with ALL or APL and those more recently diagnosed are more likely to be in class 2. No other respondent characteristics were found to significantly predict class membership.

The RAI scores based on the latent class model can be found in [Figure 2](#). Whilst for both classes, chance of response was the most important attribute, it was far less important for class 1 compared to class 2 (45.4% compared to 77.1%). In class 1, quality of life during response and duration of response were the second and third most important attributes and had similar scores (17.9% and 17.0%, respectively), with quality of life during treatment the fourth most important (12.5%). In contrast, in class 2, the second to fourth most important attributes all had similar RAI scores (around 7%). The least important attribute in both classes was the mode of administration (7.3% in class 1 compared to 1.0% in class 2).

As the most important attribute in both classes was chance of response, marginal rates of substitution were estimated using this attribute as the numeraire. [Figure 3](#) provides a summary of the extent to which respondents would be willing to trade off some chance of response in order to achieve some favourable change in other treatment characteristics.

Respondents in class 1 would, on average, be willing to trade a 7.2% chance of response to receive a treatment as a combination of outpatient injections and tablets and be willing to trade a 12.0% chance of response to receive a treatment as tablets only, instead of having injections during an inpatient hospital stay (followed by tablets). In contrast, the estimates in class 2 were not statistically significant, indicating no willingness to trade-off any chance of response to receive a mode of administration that differs from having injections during an inpatient hospital stay (followed by tablets). Respondents in class 1 would, on average, be willing to trade a 4.1% chance of response for a 10% increase in quality of life during treatment and be willing to trade 5.9% chance of response for a 10% increase in

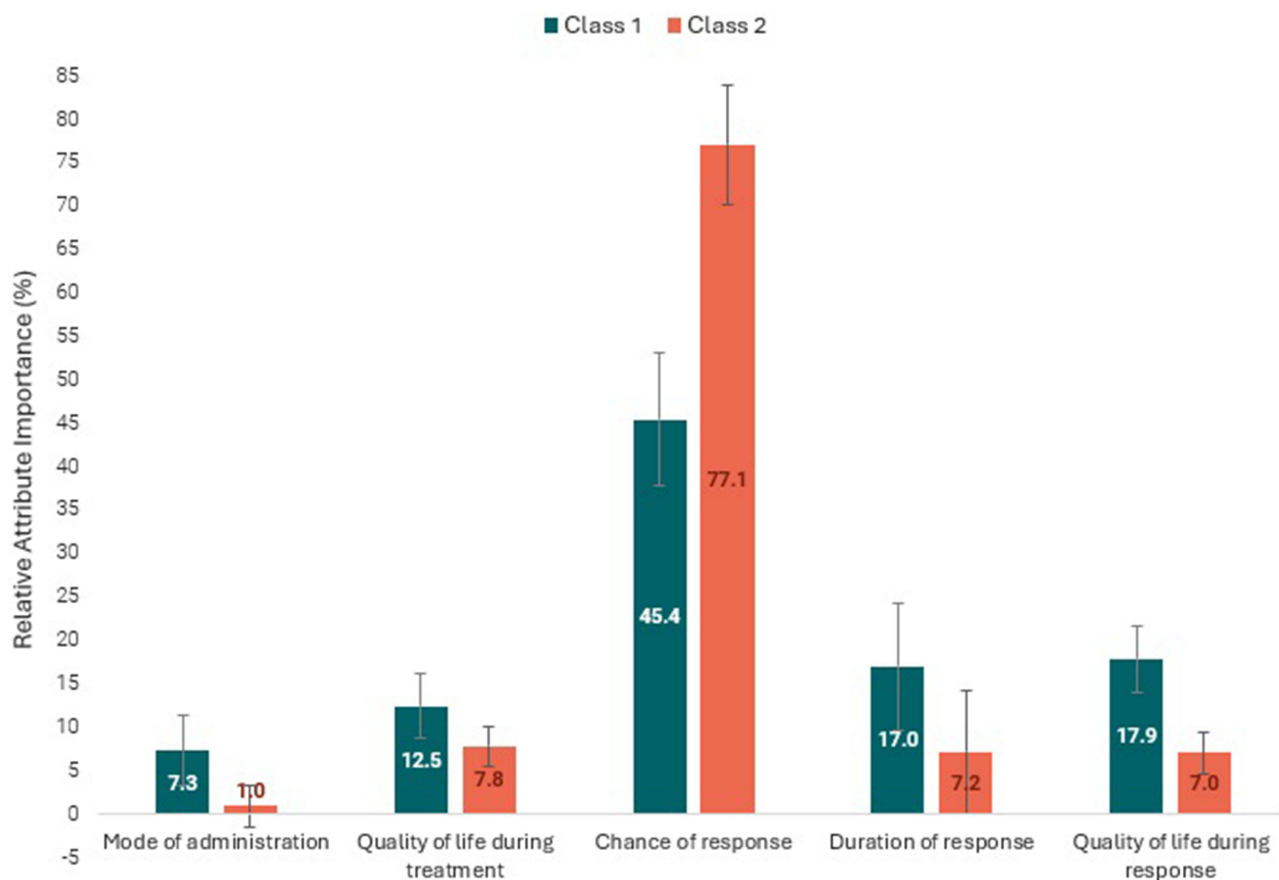


Figure 2 RAI scores, by class. Error bars indicate 95% confidence intervals.

quality of life during response. In contrast, respondents in class 2 would only be willing to trade a 1.5% and 1.4% chance of response for the same changes in quality of life, respectively. Respondents in class 1 would, on average, be willing to trade a 7.0% chance of response for a 3-month increase in duration of response, whereas respondents in class 2 would only be willing to trade a 1.7% chance of response for this increase (and this estimate is only statistically significant at the 10% level).

Aggregated results (estimated using a mixed logit model) and results by acute leukemia type (estimated using conditional logit models) can be found in [Tables S1](#) and [S2](#), respectively.

Discussion

Summary of Our Findings

In this study, we sought to understand patients' preferences for the treatment of relapsed/refractory acute leukemia. Based on the DCE results, the most important aspect of treatment within this setting is the chance of response. However, most respondents reported that they would be "unlikely" or "extremely unlikely" to reject treatment upon relapsing ($n = 72$; 76%) and there were very few instances where respondents selected the opt-out alternative in the DCE ($n = 29$; 2.5%). Therefore, whilst the chance of response is important to patients when deciding between treatments, it does not appear that a low(er) chance of response would result in patients choosing to forego treatment.

Our DCE results also illustrate that there is significant heterogeneity in patients' preferences. For one group, which was more likely to include those with AML and those diagnosed longer ago, all other treatment characteristics are important too, albeit to varying extents. For another group, which was more likely to include those with ALL or APL and those more recently diagnosed, chance of response dominates as the key characteristic of importance. In this group, only

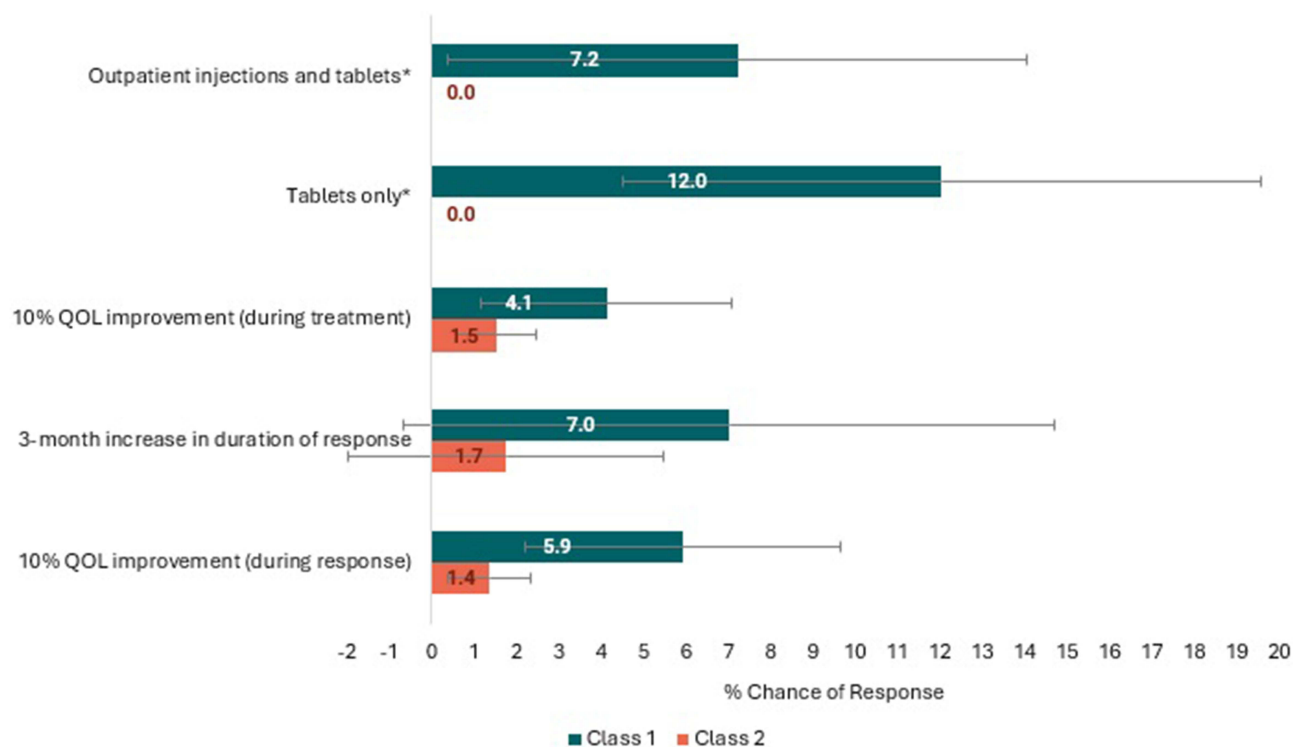


Figure 3 Marginal rates of substitution, by class. Error bars indicate 95% confidence intervals. QOL = Quality of Life. *Trade-off is relative to the reference category “Injections (requiring an inpatient hospital stay) followed by tablets (taken at home)”. Full labels are “Injections (at regular outpatient hospital appointments) and tablets (taken at home)” and “Tablets (taken at home)”. Estimates for class 2 were not statistically significant at the 10% level.

the quality of life attributes also have an influence on treatment choices, albeit to a far lesser extent than chance of response.

There are several potential explanations for these findings. Those that have more recently been diagnosed may recall more vividly their first-line treatment experience, which is often experienced as a traumatic “life or death” situation where the primary focus is on achieving remission. In contrast, those that were diagnosed longer ago may, on average, feel less concerned about their future risk of relapse (as more time has passed). This may partly explain the substantial difference in the weight these two groups gave to the chance of response when completing the task. It may also be the case that those diagnosed longer ago have a greater concern about other factors such as quality of life and mode of administration due to longer-term experience³⁹ with receiving maintenance treatment. Furthermore, the individual models (Table S2) suggest that a potential explanation for the differences by acute leukemia type could be that mode of administration is more important to those with AML compared to those with ALL or APL. However, the results by acute leukemia type should be taken with caution due to the low sample sizes.

To our knowledge, no other study has sought to identify patients’ preferences for relapsed/refractory treatment specifically across the different types of acute leukemia, reducing our ability to compare our results with other studies. However, Richardson et al²⁴ conducted a DCE in the US with people with AML which had similar attributes to ours. They ran a latent class model and identified two classes with different preferences where, similar to our results, one class primarily focused almost exclusively on overall efficacy (in terms of event-free survival and chance of complete remission), and the other class cared about the broad range of treatment characteristics (which also included time in hospital and both short- and long-term side effects). In their study, the primary factors that influenced class membership were age at diagnosis and gender, and time since diagnosis had less of an impact.

Outside of acute leukemia, time since diagnosis has been shown to impact on patients’ treatment preferences. Fifer et al⁴⁰ conducted a DCE in the UK with people with multiple myeloma, another type of blood cancer. They also conducted a two-class latent class model and, similar to our results, found that those more recently diagnosed were more likely to be in a class

where treatment outcomes were more important and other factors (such as mode/frequency of treatment, side effects, and costs) were less important compared to the other class.

In summary, our results suggest that treatment options with a greater chance of response would be highly valued in the relapsed/refractory setting. Whilst some treatment options such as CAR-T therapy are extremely effective,¹¹ such efficacious options are currently only available to a subset of the acute leukemia patient population. The development of future treatments that improve the chance of response in the relapsed/refractory setting therefore remains a priority. Importantly though, it is not a case of “efficacy at any cost”, as some patients are willing to trade off some chance of response to achieve better quality of life and more convenient mode of administration, especially among patients who were less recently diagnosed. Stakeholders involved in developing or assessing relapsed/refractory treatment options in acute leukemia should therefore be aware of the variation in preferences across the acute leukemia patient population, particularly in relation to time since diagnosis.

Strengths and Limitations

In this study, we developed a DCE following best practice guidance, which included conducting formative qualitative research using a novel method and conducting a range of cognitive “think aloud” pilot interviews with patients to refine our survey before launch. Our study was informed by patient and academic advisory groups at key stages, and with the assistance of ALAN and Leukemia Care we were able to achieve a good sample size given the relative rarity and severity of acute leukemia.

However, our study is not without its limitations. Our recruitment was conducted entirely through a patient advocacy group, and it may be the case that people involved in such groups differ in their characteristics and preferences compared to those that are less engaged. Our sample had a higher proportion of women and individuals with degrees (or equivalent) than the UK general population. There was also a lack of ethnic diversity in the sample, with 98% of the sample identifying with a white ethnic group ($n = 93$). Furthermore, the clinical status of respondents was varied in terms of subtype, remission and relapse history, as well as current treatment experience. All of this may impact the overall generalisability of our results in the broader acute leukemia population.

It is also worth noting that the relatively small sample sizes for the ALL and APL subgroups may have limited our ability to identify differences in the preferences of people with these subtypes of acute leukemia. That said, our latent class analysis was able to provide some insights in this regard.

Future Research

Whilst our study has provided insights into the broad treatment preferences of people with acute leukemia, the focus has been on the relapsed/refractory setting, and all respondents were from the UK. Further research into patients’ broad treatment preferences across different countries and treatment settings (eg, first-line) may also provide useful insights. Furthermore, whilst research into patient preference studies in relation to specific treatment options is increasingly taking place,^{25,26} as further treatment options are developed, further preference studies will inevitably be useful in informing regulatory and reimbursement decisions. That said, sample sizes may be a challenge for future preference studies as acute leukemia treatment becomes increasingly personalised. Therefore, alternative preference elicitation methods to the likes of DCE (which requires a relatively large number of respondents) may need to be considered in future.

Conclusions

Our results suggest that relapsed/refractory treatment preferences differ amongst the acute leukemia patient population. Many patients, particularly those less recently diagnosed and those with AML, care about a range of factors, such as quality of life (during both treatment and response), the duration of response and, to a lesser extent, the mode of administration. However, overall, the chance of response was by far the most important aspect of treatment to our survey respondents. The development of future treatment options that improve the chance of response in the relapsed/refractory setting should therefore be a priority.

Ethics Statement

Ethical approval for the study was granted by a Research Ethics Committee at City, University of London, United Kingdom (ETH2223-1008), and all participants provided consent before participating in the research activities. The study complied with the Declaration of Helsinki.

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Disclosure

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