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BMJ Open

Patients' experiences of early phase experimental medicine cancer trials

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-047813
Article Type:	Original research
Date Submitted by the Author:	11-Dec-2020
Complete List of Authors:	Sawyer, chelsea; The Christie NHS Foundation Trust, CPCR Preston, Laurie; The Christie NHS Foundation Trust, Christie Patient Centred Research Taylor, Sally; The Christie NHS Foundation Trust, Christie Patient Centred Research Davies, Michelle; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team, Carter, Louise; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Kreb, Matthew; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Cook, Natalie; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, ; The University of Manchester Division of Cancer Sciences Graham, Donna; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Thistlewaite, Fiona; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Yorke, Janelle ; The Christie NHS Foundation Trust, Christie Patient Centred Research (CPCR); University of Manchester , Division of Nursing, Midwifery and Social Work; School of Health Sciences
Keywords:	Adult oncology < ONCOLOGY, QUALITATIVE RESEARCH, Clinical trials < THERAPEUTICS

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Patients' experiences of early phase experimental medicine cancer trials

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Word count: 4450

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Abstract

Objectives: The study aimed to explore patients' experiences of Experimental Cancer Medicine (ECM) clinical trials.

Design: The study's design was qualitative. Two focus groups with patients were undertaken followed by semi-structured interviews, to explore patients' experiences of ECM clinical trials. Interviews and focus groups were audio recorded and transcribed verbatim. Data were analysed using thematic analysis.

Setting: A regional cancer centre (tertiary care) in North-West England.

Participants: Twelve patients (aged 52-89) who consented to participate in an early phase ECM trial participated in one of the two focus groups. An additional twenty-two patients (aged 42-83) who consented to participate in an early phase trial were interviewed.

Primary outcome measure: Patients experiences of an ECM trial.

Results: Four main themes were identified from the analysis. The main themes were around decision-making, information needs, experience of trial participation, and impact of trial participation.

Conclusion: The results from this study improve our understanding of patients experience on experimental cancer trials and can be used to inform clinical practice in this area.

Strengths and Limitations

- Participants demographic varied with regards to phase of trial, duration on trial, age range, and disease group to capture a range of experiences
- A limitation is the cross-sectional nature of the study, experiences and perspectives may change throughout the trial process.

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- The study was limited as participants were recruited from one comprehensive cancer centre, patients' experiences may vary across hospitals.

INTRODUCTION

Experimental cancer trials (or early phase clinical trials) play an important role in the progression and advancement of cancer treatments. It is estimated in the United Kingdom (UK) that one in five cancer patients participate in clinical trials.[1] Early phase clinical trials (defined as Phase I and non-randomised phase II) are designed to assess the pharmacodynamics, pharmacokinetics and safety of novel drugs.[2] The drug does is gradually increased Phase I trials, to explore safety and best dose. In phase II trials the efficacy of the drug is evaluated, side effects and safety are also investigated. Early phase clinical research primarily focuses on the physical outcomes of experimental therapies including appropriate drug dosing, treatment toxicities, survival, and response rate.[2]. Within the protocol and trial design limited attention is afforded to patient experience, consequently, little is understood about the personal impact of trial participation.[3]

Understanding the patient experience is of particular importance in relation to early phase trials, where significant adverse events associated with treatment toxicity may outweigh any possible therapeutic benefit.[4] Undesirable side effects are an important factor in shaping patients' experiences of trial involvement, influencing their psychological wellbeing and sense of hope, and in some instances increased participants' fear of death.[5] Furthermore, patients may not fully understand the burden and demands of participation in clinical trials, and the impact trial participation could have on their Quality of Life (QoL) and that of their loved ones.[3]

Despite the various physical, emotional and practical challenges, patients have generally reported positive experiences of trial participation and feel an increased sense of 'control' over their illness.[5] Moore also suggested that trial participation reflects a coping

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strategy against hopelessness.[6] When standard treatment is ineffective, clinical trials are perceived by some to offer a 'second chance' at finding a cure.[3] Early phase trials can be perceived by others to be a "last ditch effort" for patients who are otherwise considered to have exhausted all other treatment options.[4] Cox also found that participants derived comfort from being closely monitored by clinicians due to the belief that they were in 'expert' hands, and in providing a sense of purpose through helping others.[3] However, patients often misunderstand trial information, their understanding and the meanings that patients ascribe to their participation will determine how they make sense of their experiences throughout the trial process.[7]

Patient experience is considered to be an integral component of excellent healthcare.[8] As outlined in the NHS Outcomes Framework, a deeper understanding of patient perceptions of trial involvement will drive quality improvement and aid learning.[8] Yet there is limited understanding into patients' experiences of participating in early phase clinical trials. Therefore, this study aimed to explore the experience of patients who consented to participate in a Phase I or II experimental cancer medicine trial.

METHOD:

Study Design

In this qualitative study, semi-structured interviews and focus groups were used to explore patients' experiences of Experimental Cancer Medicine (ECM) trials. Participants were recruited from a regional cancer centre in North-west England. The inclusion criteria for the study were (a) any cancer type, and (b) anyone who has been screened for a observational trial or a phase I-II experimental cancer medicine trial. Participants were excluded if they were unable to provide informed consent, or comprehend written English.

Potential participants were approached by the research team, who provided written study information and answered any questions. Informed signed consent was obtained.

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Face to face interviews were conducted at either the patient's home or in a quiet hospital room, depending on the patient's preference.

Two focus groups were conducted face to face in a quiet hospital room. The interviews and focus groups were audio recorded and lasted from 14 to 62 minutes and 48 to 108 minutes, respectively. Ethical approval was gained from the south central-Oxford b Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.

Sample

A total of 34 patients participated in an interview or a focus group. Participants' demographics are presented in Table 1. Twenty-two patients participated in a semi-structured interview and the cancer disease groups included breast, lung, lymphoma, colon, and stomach. Twelve participants in total participated in one of the two focus groups and the cancer disease groups included lung, lymphoma, leukaemia, renal, and larynx (head and neck).

Insert Table 1. here Participants demographic information

Table 1. Participants' demographic information

	Interviews (*n* = 22)	Focus groups (*n* =12)
Age range (years (Median))	42 – 83 (65.5)	52-89 (68.5)
Gender (female %)	59%	8%
Ethnicity %		
White British	95%	100%
Chinese	5%	
Type of trial n (%)		
Not eligible for the trial (Screen fails)	2 (9%)	-
Observational	2 (9%)	-

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Phase I	9 (41%)	7(67%)
Phase II	9 (41%)	5 (33%)

Data analysis

The interviews were analysed using an inductive thematic approach.[9] An initial transcript was read by two authors (J.Y, C.S) to explore patterns/themes in the data. Two reviewers then coded an additional three transcripts and compared these to assess for inter-rater reliability (86%). Remaining transcripts were subsequently coded by one researcher (CS). Themes and interpretations of the data were discussed in regular meetings (J.Y, C.S). Data were presented as four overarching themes: (a) Decision-making, (b) Information needs, (c) Experience of trial participation, and (d) Impact of trial participation. Quotes from the interviews are presented as participant's ID, gender (M=male, F=female) and age (in years). Quotes from the focus groups are presented as FG and number (1 or 2).

Patient and Public Involvement:

Patients reviewed and provided feedback on all study documents including participant information sheets, informed consent sheet, and interview schedule. Once the interviews were analysed the main themes were discussed with the study team and patient representatives. The final study results will be disseminated via a letter with summary of the study to participants who stated they would like to receive the summary.

RESULTS

Decision-making

Patient preference regarding involvement in decision-making varied. Some patients highlighted the importance of including family and friends in their decisions, whereas other

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patients felt the decision as to whether to participate in a trial was only theirs to make. Due to the difficulties understanding the information, the uncertainties around trials, and patient perception that the doctors are the experts, some patients relied on the doctors to make the best decision for them.

"It was mine [decision]. It's got to be, it's my life."(25M83)

"I think the consultants made the decision about what was most suitable."(28F72)

A few patients perceived the clinical trial as their only option and for those who were ineligible for the trial, this view lead to feelings of despair and uncertainty about their options. Conversely the majority of the patients felt the clinical trial provided them with another treatment option. This was particularly important for patients who did not want the alternative treatment options.

"I had no other choice, so at the end of the day, that's the one."(25M83)

The clinical trial also provided the majority of patients with hope. For some it was a potential chance for a cure, stopping the progression of the cancer, and/or extending their life. While others hoped their participation would help others with cancer in the future.

"There's that hope there that the…a chance of a cure."(19M56)

Information needs

Patients wanted enough information about their choices to make the best decision regarding their treatment. Patients also highlighted the need for more simplified information, as the information they received regarding trials was scientific and on occasions difficult to understand.

"doctors know all the technical terms, but we don't, most of us; and it has to be said in plain English"(22F52)

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Patients were divided on whether they had received enough information about the possible side effects of the trial prior to participation, with a number of patients reporting that they were not fully informed. Patients recognised however that it might not always be possible to provide this information, as the purpose of clinical trial are to identify side effects produced by the trial treatment. One patient felt the risk of permanent side effects had not been fully explained to them, and prior knowledge of this risk, would have affected their decision to participate in the trial.

"I don't remember anybody sitting down and saying, before you go on this, your thyroid could do this, that and the other, and it will be permanent"(23F68)

"Well I think the list of possible side effects is they just think of everything they can think of that might go wrong and list them all down" (FG2)

During the trial, patients wanted updated information regarding i) their response to the treatment, ii) alternative options to the trial, iii) the success of the overall trial to date, and iv) the experiences of other patients on the trial. This information helped them to re-evaluate their trial involvement and make decisions about future participation.

"I want him to say to me, now look here, if this doesn't work it's chemo."(21F70)

A few patients who felt they had been given false hope and had been misled about the personal benefit they would gain from the trial. These patients believed this false hope reduced their ability to cope with updates regarding no or negative response to the trial. These patients felt information about possible outcomes of the trial should not focus on potential benefits but should also highlight the risks and possibilities the trial may not work, even if the trial has previously had some positive results.

"if they hadn't built my expectation, then the crash wouldn't have been as hard"(03M42)

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Patients were informed on whom to contact if they required medical support. However, many were unaware of the psychological support available to them and could not recall doctors discussing psychological support options. Some patients who knew support was available highlighted that the psychological support was not always accessible to patients and/or their family due to length of treatments and distance travelling to the hospital. The majority of patients also did not know if there was any psychological/financial/practical support available for family members.

"you do feel that there's a void like, you know, where do I get that information [about support]."*(FG2)*

Experience of trial participation

Many patients perceived themselves as a guinea pig with regards to side effects. Despite this perception, the majority of patients reported receiving personalised care and some participants discussed how the trial team were able to rearrange their appointments to fit in around their priorities. However there were a few patients who felt they were treated impersonally.

"the clinical trials team were I felt tailoring their treatment of me."(24F56)

"it didn't feel personal; it felt as though I was being treated as a number that was insignificant."(22F52)

One of the main concerns for patients was disclosing side effects from the clinical trial, for fear of being taken off the trial, especially among those who felt the trial was their only treatment option. Some patients who did disclose side effects even reported "down playing" side effects and/or regretting disclosing side effects due to being taken off the trial.

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"is the most frightening thing because you say, at that point in time when you come off that point when you've been given, this is your one hope to live and somebody says, I'm just going to take it away from you, and that's the end of the matter." (FG2)

One patient who was taken off the trial admitted they would be reluctant to disclose side effects if they participated in future trials. Other patients discussed the internal conflict of the fear of being taken off the trial and the risk to themselves if they did not disclose side effects. A few patients highlighted the fact that by not disclosing side effects they may be compromising the trial and patients own safety.

"and I made the mistake of telling them about some of the side effects" (FG2)

"if you don't tell them about it, then you're compromising not only the trial but you're compromising yourself more importantly."(FG2)

Patients felt they needed more information from the research team about what would happen if they experienced side effects. They felt patients needed to be aware that experiencing side effects does not always result in withdrawal from the trial, and instead the dosage may be reduced.

"if they[trial team] said to you that if you were to disclose the side-effects you're having, that they would be more likely to change your treatment levels or do something about it, other than say on or off because it's the fear of the on or off is the most frightening thing".(FG2)

Impact of trial participation

Trial participation affected many aspects of a participant's life including their QoL, their free time, their finances, and their family. Patients highlighted the need to fit their life around the trials schedule (due to the frequency and long duration of trial days, and travelling to the hospital). Patients frequently stated once the trial had finished they could *get their "life back."*

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"It's an impact on your life having to come in every two weeks, especially the thing I was on initially was an all-day effort" (FG2)

The impact on QoL was mixed. Some patients believed their QoL had improved, for example they were once again able to perform activities that they had been unable to due to ill health. In contrast other patients were unable to partake in regular activities or trips away, due to side effects or their frequent hospital visits, with some of these visits requiring inpatient admission.

"I was in and out like a yo yo And I didn't realise it was the trial"(14M66)

"Our life has changed absolutely beyond recognition. I had a good job and we were very active, cycled everywhere and went diving on holiday and all of those things which we can't do now"(24F56)

Patients discussed the burden of clinical trials on their time, due to frequency and duration of hospital visits. Some patients reported requiring the next day to recover and rest, so perceived they had "lost" another day due to the trial. However, patients reported some benefits to their frequent hospital visits. This included seeing experienced doctors and additional monitoring, care, and support they perceived they would not receive with standard treatment. Patients reported a lot of waiting around, which was tiring but understandable. Some patients were frustrated when they were not informed of delays to their treatment.

"the frequency of the visits is good and bad, as I say It's travelling every week but having that line of contact and support weekly is great." (24F56)

An unanticipated impact of the trial was on patients and their significant others holidays and trips away. This was due to the trials schedule preventing them from going away for their preferred duration. Patients also perceived their participation in the trial affected patients' ability to get travel insurance. There were also concerns around what would happen if the patient became ill during their travels and if the treatment they received

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from other hospitals could react with trial treatment or affect trial participation. Limitation to travel was especially difficult for patients who were unable to see their family who lived abroad.

Patients felt their participation on a clinical trial was a shared experience with their families and discussed the psychological impact of trial participation on their family and friends. Some patients felt their spouses were "trapped" or they were a "burden" to their family. While others mentioned their family/friends had to change their usual activities due to their participation in the trial. Patients highlighted the need for support for their family/friends. Many patients felt it was crucial that clinical trial teams ask family/friends about the impact of the trials on them as well.

"*It's a really valid question to ask around carers and family members and how are they coping"(26F48)*

"it's difficult for my daughter because she had her studies and she came with me every time"(29M55)

Some patients described the financial burden of participating in a trial, due to travel costs, as well as food and drinks needed during visits. These patients were not aware of any financial aids available.

"It costs you a lot of money"(07F61)

Patients also mentioned during the screening process they experience anxiety and depression around not knowing if they were eligible for the trial. Patients also mentioned they feared their trial space may go to another patient whilst waiting for their results, as they were aware the trials had limited spaces. One patient even said they felt rushed to make a decision.

"Depressed. it got me down, the waiting"(28F72)

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"So I'm on the waiting list. They may pick somebody else. I don't know." (25M83)

DISCUSSION

The study explored the experience of patients who were screened and/or recruited onto an ECM clinical trial. Overall the majority of patients had a positive experience and perceived the care they received as patient-centred. To aid decision-making regarding initial and continued participation patients identified several areas which could be improved (a) the simplification of trial information (b) more information on side effects, (c) regular updates on their response to the treatment, and (d) to be informed of alternative options. Patients also needed more information about support available for themselves and their family members. Patients admitted to being reluctant to inform clinical trial teams about side effects they were experiencing.

Patients found the information about the trials too scientific and difficult to understand, which is consistent with previous studies.[7, 10-11] Patients also wanted more information about the risk of side effects but also mentioned how daunting the long list of side effects could be. However, patients seemed to focus on the personal benefit they hoped they would get from the trial rather than the potential side effects. Previous studies have shown patients often have unrealistic expectations about the benefit they will receive and their reduced susceptibly to side effects when compared with other patients.[12-17] In order to make the information easier to read and ensure patients fully understand what they are consenting to and the potential risks, Donovan has recommended interviews with patients reviewing study documentation to identify any aspects that are unclear or could be misinterpreted.[18]

Misinterpretation of the trial information provided could lead to 'false hope' (the patient hopes the treatment results in a cure, improvement of health, or prolongation of life).[19]. False hope may have also been caused by patients overestimating the personal benefit of clinical trials (therapeutic misconceptions) or by the clinical trial team emphasising the

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benefits of being on a trial (regular appointments, great care, extra attention to their health, and potential benefit for future patients).[12, 17, 19] These patients with 'false hope' perceived their ability to cope with bad news had been reduced and feelings of frustration and disappointment were amplified and more destructive.[19] This also may call into question whether the patient gave fully informed consent. Early phase dose escalation trials are not designed to provide personal medical benefit to patients of the trial,[14] yet this is often a reason for participation, therefore the unlikelihood of personal benefit may need to be emphasised more clearly to patient.[13-14,20-25] From the current evidence,[14, 21-22] it seems that the hope to obtain medical benefit is not indicative of compromised informed consent. However, when introducing patients to trials and providing them with possible treatment options there is a need for equipoise (the assumption that there is not one 'better' treatment option).[18, 26-27] Any inkling of preferential treatment combined with the patient's belief that doctors and nurses act in the patient's best interest, could lead to patients feeling they have been given false hope.[3,18]

A few patients reported feeling rushed to make a decision; these patients had anxieties that if they did not decide quickly they may lose the trial to another patient. It is crucial that patients are given the time and information they require, to make a fully informed decision about trial participation. The patient's anxieties may have been caused by the patient's therapeutic misconceptions or unrealistic expectations that the trial will benefit them combined with the knowledge that early phase trials recruit small numbers of patients across multiple sites.[12, 22] The clinical trial teams may need to consider these factors when discussing trial participation. In addition the wording used to inform patients they are "eligible" may also affect patient's decision-making regarding trial participant. Previous studies have found patients reported feeling "lucky" or "honoured" they were eligible for a trial, as it gave them another chance for a cure.[26, 28] Therefore it was important to also capture their experiences of being screened and failing to meet the eligibility criteria for a clinical trials. [3, 4] Those who were ineligible felt disappointed and as if they were out of

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options. Brown et al. found patients suggested instead of “eligible” the phrase “the trial is suitable for you’’ could be used, as the phrase was perceived to objectify the study and highlight there may be other treatment options which are also suitable for the patient. In addition the use of “unsuitable” may minimise the disappointment felt by those ineligible for the study.[26]

To aid decision making regarding continued participation in early phase clinical trials, patients desired regular updates about their response to trial treatment. Patients also desired information about other patients’ experiences of side effects while on the trial and response to the trial and more detailed feedback about the trial progress (i.e. recruitment and retention). Previous studies also found patients desired feedback and regular updates on the trials results and patients frequently share information with each other about side effects and their experience on the trial.[24, 29-30] Providing information about other patients’ experiences may be feasible depending on the information received from the trial sponsor. However, it is important to ensure the information is presented in a way that does not lead to false hope emphasising that there are no guaranteed benefits or side effects, and that patients have different reactions to treatment.

For the majority of early phase trials the main aim is to investigate the safe dosage range and side effects experienced by patients.[3] Therefore to ensure patients safety and validity of the trial, it is crucial patients are honest about the side effects and severity of side effects they are experiencing.[12] Yet many patients admitted holding back information about side effects due to fear of being taken off the trial.

The disclosure of side effects is likely influenced by the patients beliefs.[12, 28] Previous studies have found trial patients believed that the higher the dose the more effective the trial treatment is and that side effects were caused by effective treatment.[31-32]. In order to reduce fear and address any misconceptions detailed information regarding dose level and effectiveness, and the possible outcomes if they were to disclose side effect,

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such as dose reduction) could be incorporated into a question prompt list (is a list comprised of standard questions, which prompt discussion between patient and doctor).[13, 34] However, further research is required to see if providing this information would reduce under-reporting of side effects.

Another possible option to improve accuracy of reporting side effects is the integration of electronic Patient Reported Outcomes (ePROs) in clinical trials. Patients often delay reporting side effect which can lead to their effect being minimised [16, 33-34]. The integration of ePROs enables regular monitoring of patients side effects and can improve the accuracy and timing of reporting side effects.[36-37] EPROs aid real time data collection, which can be used to notify their clinical trial team of adverse events, allowing for earlier clinical decisions. In addition relevant medical advice, tailored to the patients response, can be provided.[38] Therefore, enhancing the patients quality of care and communication with their clinical trial team.[39]

Participation in clinical trials led to a reduced QoL for some patients. However, some of these patients were not aware their poor health was due to treatment toxicity from the trial and attributed it to their cancer instead. Some of these patients may have limited ife expectancy [3] and the quality of that time left may be more important than staying on the trial. Therefore, clinical trial teams should have on-going discussions throughout the trial about the patient's trial response, the risks and benefit of trial continuation, and other treatment options including palliative care. These discussion may enable patients to make fully informed choices and find a balance between trial participation and QoL.[3, 40]

As well as impacting the patient's QoL, research has shown trial patients can experience undesirable side effects, which can have a negative impact on patient's psychological wellbeing.[5] Yet the majority of patients felt they did not need emotional/psychological support. Despite this perception, patients experienced psychological distress (anxiety and/or depression) at various points throughout the trial (initial screening to

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determine if patients were eligible or awaiting test results). Previous research has also shown patients impacted either physically or psychologically may benefit from specialist palliative care.[41] However, due to the conflicting beliefs (that palliative care is for end of life whereas the trial provides hope for another treatment option) patients were less likely to access specialist palliative care.[41] The clinical trial teams may need to provide more information and education about the supports available to patients and the potential benefit of specialist palliative care alongside trial treatment. [41]

Trial participation can require both the patient and their families' time, physical and emotional energy, and some parts of their lives to be put on hold.[40] Due to this patients felt that it was important that their family had psychological, financial, and/ or practical support. Family and friends acting in a caregiver role (this includes management of medications and/ or appointment schedules, providing emotional support and/ or physical care, and managing finances) commonly experience burden and depression.[42]This perception of caregivers life being on hold was also found in patients with advanced cancer, but was only perceived by patients when the caregiver was their child.[43] In addition caregivers of trial patients experience greater distress and anxiety than population norms of caregivers of cancer patients.[44] If anxiety and depression are untreated it can lead to both poor physical and mental health, as well as reduced QoL for carers and potentially patients as well.[42] Despite this, very few patients knew if there was any support available to their family and friends, other than the medical support provided by the clinical trials team. The clinical trial team should provide information about various support service available to both the patient and their family throughout the trial. However, there is minimal literature on the most effective support for carers of cancer patients and further research is required to identify the support needs of carers.[42]

Limitations

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One of the studies limitations is the cross-sectional nature of the study which may limit the data about their experiences and perspectives throughout the trial process. Future studies could use a longitudinal design targeting people at the various stages (initial introduction to the trial, screening, consenting, experience of first treatment, on-going experience on the trial, and, withdrawing from the trial). Secondly the study was limited in the samples ethnic diversity and therefore non-representative of the area where the data was collected. Finally the study recruited participants from a single site comprehensive cancer centre, patients' experiences may vary across hospitals.

Conclusion

Overall the study has improved our understanding of patients' experiences of being screened and/or recruited onto a clinical trial. Our findings found patients required the simplification of trial information and required more information about side effects, support, their response to trial treatment and trial progress. Due to trial burden and impact on patients QoL on-going discussions are required to help patients find the balance between QoL and trial participation.

Contributors: J.Y and S.T developed the study design. J.Y has supervised the study. C.S and JY analysed the materials. CS and LP wrote the manuscript. J.Y, S.T, L.C, N.C, M.K, D.G, F.T, and M.D, have given substantial input throughout the development and writing of the paper. J.T (patient representative) was involved with the study design and discussion of main themes.

Funding: The study was funded by Manchester Experimental Cancer Medicine Centres (ECMC) and The Christie CRF Charity, there is no grant number for this award. The study was supported by the NIHR Manchester Biomedical Research Centre.

Conflicts of Interest: The authors declare that they have no conflict of interest.

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Ethics approval: Ethical approval was gained from the appropriate Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.

Data sharing statement: The interview transcripts are available to show proof of the paper. However, they would only be available for legal purposes. They are confidential and can only be given access to in case of legal Requirements

Acknowledgements: Patients, Carer's, the Christie Experimental Cancer Medicine Team. We would also like to thank Elaine Blowers, Rana Lee, Grant Punnett, and Sarah Bellhouse for their help with the study. We would also like to thank J.T for all their help with the study.

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BMJ Open

Oncology patients' experiences in experimental medicine cancer trials: a qualitative study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-047813.R1
Article Type:	Original research
Date Submitted by the Author:	24-Jun-2021
Complete List of Authors:	Sawyer, chelsea; The Christie NHS Foundation Trust, CPCR Preston, Laurie; The Christie NHS Foundation Trust, Christie Patient Centred Research Taylor, Sally; The Christie NHS Foundation Trust Christie Patient Centred Research, Christie Patient Centred Research Davies, Michelle; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team, Carter, Louise; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Krebs, Matthew; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, Manchester; The University of Manchester Faculty of Biology Medicine and Health, Division of Cancer Sciences Cook, Natalie; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, ; The University of Manchester Division of Cancer Sciences Graham, Donna; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Thistlewaite, Fiona; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Yorke, Janelle ; The Christie NHS Foundation Trust Christie Patient Centred Research, Christie Patient Centred Research (CPCR); The University of Manchester, Division of Nursing, Midwifery and Social Work; School of Health Sciences
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Qualitative research
Keywords:	Adult oncology < ONCOLOGY, QUALITATIVE RESEARCH, Clinical trials < THERAPEUTICS

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Oncology patients' experiences in experimental medicine cancer trials: a qualitative study

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Word count: 3929

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Abstract

Objectives: The study aimed to explore patients' experiences of early phase Experimental Cancer Medicine (ECM) clinical trials.

Design: The study's design was qualitative. Two focus groups with patients were undertaken followed by semi-structured interviews, to explore patients' experiences of ECM clinical trials. Interviews and focus groups were audio-recorded and transcribed verbatim. Data were analysed using thematic analysis.

Setting: A regional cancer centre (tertiary care) in North-West England.

Participants: Twelve patients (aged 52-89) participated in one of the two focus groups and twenty-two patients (aged 42-83) participated in interviews.

Primary outcome measure: Patients' experiences of an ECM trial.

Results: Four main themes were identified from the analysis: decision-making, information needs, the experience of trial participation, and impact of trial participation. Subthemes are presented in the manuscript.

Conclusion: To make fully informed decisions about trial participation, patients required the simplification of trial information and wanted more information about side effects, their response to trial treatment, and the overall trial progress throughout the trial. Patients highlighted the need for improvement for the support provided to their family and friends.

Strengths and Limitations

- The study explored the perspectives of a diverse group of patients approached to participate in early phase clinical trials, allowing the study to capture an abundance of experiences. Aspects of diversity included age range, duration on trial, disease

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group, and phase of the trial. Patients who had been ineligible or withdrawn from the trial were also included.

- The study generated comprehensive and detailed insights as interviews were conducted to build on experiences highlighted in focus groups, and interviews were conducted until data saturation.
- A limitation is the cross-sectional nature of the study, experiences and perspectives may change throughout the trial process.
- Participants were recruited from one comprehensive cancer centre, patients' experiences may vary across hospitals.

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INTRODUCTION

Experimental cancer trials (or early phase clinical trials) play an important role in progressing and advancing cancer treatments. It is estimated in the United Kingdom (UK) one in five cancer patients participate in clinical trials.[1] Early phase clinical trials (defined as Phase I and non-randomised phase II) are designed to assess the safety of novel drugs, pharmacodynamics, and pharmacokinetics.[2] The drug doses is gradually increased Phase I trials, to explore safety and the best dose. In phase II trials the efficacy of the drug is evaluated, side effects and safety are also investigated. Early phase clinical research primarily focuses on physical outcomes of experimental therapies, including appropriate drug dosing, treatment toxicities, survival, and response rate.[2] Within the protocol and trial design, limited attention is afforded to patient experience, consequently, little is understood about the personal impact of trial participation.[3]

Understanding patient experience is of particular importance concerning early phase trials, where significant adverse events associated with treatment toxicity may outweigh possible therapeutic benefit.[4] Undesirable side effects are an important factor in shaping patients' experiences of trial involvement, influencing their psychological wellbeing and sense of hope, and in some instances increased participants' fear of death.[5] Furthermore, patients may not fully understand the burden and demands of participation in clinical trials, and the impact trial participation could have on their and their loved one's quality of life.[3]

Despite the various physical, emotional and practical challenges, patients generally report positive experiences of trial participation and feel an increased sense of "control" over their illness.[5] Moore suggested trial participation reflects a coping strategy against hopelessness.[6] When standard treatment is ineffective, clinical trials are perceived by some to offer a 'second chance' at finding a cure.[3] Early phase trials can be perceived by others to be a "last-ditch effort" for patients who are otherwise considered to have exhausted all other treatment options.[4] Cox also found participants derived comfort from being closely monitored

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by clinicians due to the belief they were in 'expert' hands, and in providing a sense of purpose through helping others.[3] However, patients often misunderstand trial information, their understanding and the meanings patients ascribe to their participation will determine how they make sense of their experiences throughout the trial process.[7]

Patient experience is considered to be an integral component of excellent healthcare.[8] As outlined in the NHS Outcomes Framework, a deeper understanding of patient perceptions of trial involvement will drive quality improvement and aid learning.[8] Yet there is limited understanding of patients' experiences of participating in early phase clinical trials. Due to the aims of early phase trials and the uncertainties around drug side effects and safety, the present study aimed to explore the experiences of participants in early phase ECM clinical trials.

METHOD:

Study Design

In this qualitative study, focus groups were conducted first to explore patients' experiences of ECM trials and capture main themes/experiences, which were explored in more depth in semi-structured interviews.[9] The same topic guide was used for focus groups and interviews (Appendix 1). Questions captured patients' experiences of trial introduction and participation and their decision-making process regarding participating in the trial they were offered.

Sample/data collection

Participants were recruited from a regional cancer centre in North-west England. The inclusion criteria for the study were (a) any cancer type, and (b) anyone who has been screened for an observational trial or a phase I-II ECM trial. Participants were excluded if they were unable to provide informed consent, or comprehend written English.

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The clinical team identified potential participants, who were approached by the research team, who explained the study and provided written information. Participants were given the opportunity to ask any questions about study participation or the information provided. Written informed signed consent was obtained. Twenty-one face-to-face interviews were conducted in a quiet hospital room and one face-to-face interview was conducted at the patient's home, determined by the patient's preference.

Both focus groups were conducted face-to-face in a quiet hospital room. The interviews and focus groups were audio-recorded and lasted from 14 to 62 minutes and 48 to 108 minutes, respectively. Ethical approval was gained from South central-Oxford b Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.

Figure 1. Present the study's recruitment process. Participant demographics are presented in Table 1.

Insert Figure 1. here Study flow diagram

Insert Table 1. here Participants' demographic information

Table 1. Participants' demographic information

	Interviews (*n* = 22)	Focus groups (*n* =12)
Age range (years (Median))	42 – 83 (65.5)	52-79 (68.5)
Gender (female %)	59%	8%
Ethnicity %		
White British	95%	100%
Chinese	5%	
Marital status (%)		
Single	4.55%	16.67%
Married/domestic partner	90.91%	66.67%
Widowed	4.55%	8.33%

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Divorced	-	8.33%
Employment status (%)		
Self-employed	-	8.33%
Retired	75.00%	83.33%
Unable to work	18.75%	8.33%
Homemaker	6.25%	-
Performance status (%)		
0	52.94%	45.45%
1	47.06%	54.55%
Type of trial n (%)		
Patients who are considered for the trial and then deemed ineligible (are often referred to as 'screen fail')	2 (9%)	-
Observational	2 (9%)	-
Phase I	9 (41%)	7(67%)
Phase II	9 (41%)	5 (33%)
Time on trial (<1 year, %)	54.55%	50%
Disease group		
Breast	31.82%	-
Colorectal	13.64%	16.67%
Head & Neck	-	8.33%
Haematological	9.09%	-
Lung	22.73%	16.67%
Leukemia		8.33%
Lymphoma	18.18%	41.67%
Penile	4.55%	-
Renal	-	8.33%

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Data analysis

The interviews and focus groups were analysed by hand using an inductive thematic approach.[10] The six-phase guidelines of Braun and Clarke were used to analyse the data, the first step was familiarisation with the data.[10] Two authors (J.Y, C.S) explored themes in the data from an initial transcript and produced a document outlining key themes and findings. Two reviewers then coded an additional three transcripts and compared these to determine inter-rater reliability (86%). One researcher (CS) subsequently coded the remaining transcripts. Themes and interpretations of the data were discussed in regular meetings (J.Y, C.S).

Patient and Public Involvement:

The patient representative is a patient with secondary breast cancer, who has participated in an early phase clinical trial. They reviewed and provided feedback on all study documents including participant information sheets, informed consent form, and interview schedule. Once the interviews were analysed the main themes were discussed with the study team and patient representative, who all provided feedback. A letter providing a summary of the study's results will be sent to all participants who stated they would like to receive the summary.

Reflexivity:

Interviews were conducted sensitively by five researchers (J.Y, C.S, R.L, S.B, D.C) who were not part of the patients' clinical team and all have experience in interviewing people with cancer or regarding sensitive topics (self-harm). The analysis was discussed with the research team (J.Y, C.S, L.C, M.D). All members of the research team have relevant research or clinical experience. Researchers conducted balanced interviews and focus groups, and reminded patients the research team was not involved in the clinical trial.

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RESULTS

We identified four main themes: decision-making, information needs, the experience of trial participation, and impact of trial participation. The subthemes are described below with supporting quotations provided in table 2.

Insert table 2 here

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151 **Table 2 Presents the themes and their sub-themes with supporting quotations.**

1. Decision-making	
1.1 Decision maker	*"It was mine [decision]. It's got to be, it's my life."(25M83)* *"I think the consultants made the decision about what was most suitable."(28F72)* *"The whole family read it, all my children, my husband. We discussed it, come back and said yes." (07F61)*
1.2 No other option	*"I had no other choice, so at the end of the day, that's the one."(25M83)*
1.3 Hope	*"There's that hope there that the…a chance of a cure."(19M56)*
2. Information needs	
2.1 Volume & simplicity of information	*"doctors know all the technical terms, but we don't, most of us; and it has to be said in plain English"(22F52)*
2.2 Side effects	"I don't remember anybody saying, before you go on this, your thyroid could do this, and it will be permanent"(23F68) "Well I think the list of possible side effects is they just think of everything they can think of that might go wrong and list them all down" (FG2)
2.3 Updates throughout treatment	*"I want him to say to me, now look here, if this doesn't work it's chemo."(21F70)*
2.4 Provision of False hope	"if they hadn't built my expectation, then the crash wouldn't have been as hard" (03M42)
2.5 Support available	"you do feel that there's a void like, you know, where do I get that information [about support]."*(FG2)*
3. Experience of trial	
3.1 Patient centred	"the clinical trials team were I felt tailoring their treatment of me."(24F56) "it didn't feel personal; it felt as though I was being treated as a number that was insignificant."(22F52)
3.2 Disclosing side effects	"is the most frightening thing, at that point in time when you come off that point when you've been given, this is your one hope to live and somebody says, I'm just going to take it away from you, and that's the end of the matter." (FG2) "and I made the mistake of telling them about some of the side effects" (FG2) "if you don't tell them [side effects], then you're compromising not only the trial but you're compromising yourself more importantly."(FG2) "if they [trial team] said to you that if you were to disclose the side-effects you're having, that they would be more likely to change your treatment levels or do something about it, other than say on or off because it's the fear of the on or off is the most frightening thing".(FG2)
4. Impact of trial participation	
4.1 Quality of Life (QoL)	"It's an impact on your life having to come in every two weeks, especially the thing I was on initially was an all-day effort" (FG2) "I was in and out like a yo yo And I didn't realise it was the trial"(14M66) "Our life has changed absolutely beyond recognition. I had a good job and we were very active, cycled everywhere and went diving on holiday and all of those things which we can't do now"(24F56)

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4.2 Time	"the frequency of the visits is good and bad, as I say It's travelling every week but having that line of contact and support weekly is great." (24F56)
4.3. Family	"It's a really valid question to ask around carers and family members and how are they coping"(26F48) "it's difficult for my daughter because she had her studies and she came with me every time"(29M55)
4.4 Financial	"It costs you a lot of money"(07F61)
4.5 Psychological impact	"Depressed. it got me down, the waiting"(28F72) "So I'm on the waiting list. They may pick somebody else. I don't know." (25M83)

Quotes from the interviews are presented as participant's ID, gender (M=male, F=female), and age (in years). Quotes from the focus groups are presented as FG and number (1 or 2).

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Decision-making

Decision-makers

Patient preference regarding involvement in decision-making varied. Some patients highlighted the importance of including family and friends in their decisions, whereas others felt it was only their decision to make. Due to difficulties understanding the information, uncertainties around trials, and patients' perception of doctor's expertise, some patients relied on the doctors to make the best decision for them.

No other option

A few patients perceived clinical trials as their only option and for those who were ineligible for the trial, this view led to feelings of despair and uncertainty about their options. Conversely, the majority of patients felt clinical trials provided them with another treatment option. This was particularly important for patients who did not want the alternative treatment options.

Hope

Clinical trials provided the majority of patients with hope. For some it was a potential chance for a cure, stopping the progression of their cancer, and/or extending their life. While others hoped their participation would help others with cancer in the future.

Information needs

Wealth/volume and simplicity of information

Patients wanted enough information about their choices to make the best decision regarding their treatment. Patients highlighted the need for more simplified information, as the information they received regarding trials was scientific and sometimes difficult to understand.

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Side effects

Patients were divided on whether they had received enough information about possible side effects of the trial before participation, with some patients reporting they were not fully informed. Patients recognised it might not always be possible to provide this information, as the purpose of clinical trials is to identify side effects. One patient felt the risk of permanent side effects had not been fully explained to them, and prior knowledge of this risk would have affected their decision to participate.

Updates throughout treatment

During the trial, patients wanted updated information regarding i) their response to the treatment, ii) alternative options to the trial, iii) the success of the overall trial to date, and iv) the experiences of other patients on the trial. This information helped them to re-evaluate their trial involvement and make decisions about future participation.

Provision of False hope

A few patients felt they received false hope and were misled about potential personal benefit from trial participation. These patients believed this false hope reduced their ability to cope with updates regarding no or negative response to the trial. These patients felt information about possible outcomes of the trial should not focus on potential benefits but highlight the risks and possibilities the trial may not work, even if the trial has previously had some positive results.

Patients who were ineligible for the trial (screen fail) recalled how upsetting it was to be told they were ineligible. One patient even stated it felt like a "death sentence".

Support available

Patients were informed of whom to contact if they required medical support. However, many were unaware of the psychological support available and could not recall doctors

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discussing psychological support options. Some patients who knew support was available highlighted the psychological support was not always accessible to patients and/or their families due to the length of treatments and distance travelling to the hospital. The majority of patients did not know if there was any psychological/financial/practical support available for family members.

Experience of trial participation

Patient-centred

Many patients perceived themselves as a guinea pig concerning side effects. Despite this perception, the majority of patients reported receiving personalised care and some discussed the flexibility to fit appointments around their priorities. However, a few patients felt their treatment was impersonal.

Disclosing side effects

The main concern for patients was disclosing side effects from the clinical trial, for fear of being taken off the trial, especially among those who felt the trial was their only treatment option. Some patients who disclosed side effects even reported “downplaying” side effects and/or regretting disclosing side effects due to being taken off the trial.

One patient who was taken off the trial admitted they would be reluctant to disclose side effects in future trials. Other patients discussed the internal conflict between the fear of being taken off the trial and the risk to themselves if they did not disclose side effects. Some patients were aware by not disclosing side effects they are compromising the trial and the patient's safety.

Patients felt they needed more information from the research team about what would happen if they experienced side effects. They felt patients needed to be aware experiencing

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side effects does not always result in withdrawal from the trial, and instead, the dosage may be reduced.

Impact of trial participation

Quality of Life

Trial participation affected many aspects of a participant's life including QoL, free time, finances, and their family. Patients highlighted the need to fit their life around the trial schedule (due to the frequency and long duration of trial days, and travelling to the hospital). Patients frequently stated once the trial had finished they could *get their "life back."*

The impact on QoL was mixed. Some patients believed their QoL had improved, for example, they were once again able to perform activities they had been unable to due to ill health. In contrast, other patients were unable to partake in regular activities or trips away, due to side effects or their frequent hospital visits, which on occassion required inpatient admission.

Time

Patients discussed the burden of clinical trials on their time, due to the frequency and duration of hospital visits. Some patients reported requiring the next day to recover and rest, perceiving they had "lost" another day due to the trial. However, some benefits to frequent hospital visits were reported. This included seeing experienced doctors and additional monitoring, care, and support they perceived they would not receive with standard treatment. Patients reported a lot of waiting around, which was tiring but understandable. Some patients were frustrated when they were not informed of delays to their treatment.

An unanticipated impact of the trial was on patients and their significant others' holidays and trips away. This was due to the trial schedule preventing them from going away for their preferred duration. Patients perceived their participation in the trial affected patients'

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ability to get travel insurance. There were concerns around what would happen if the patient became ill during their travels and if the treatment they received from other hospitals could react with trial treatment or affect trial participation. Limitation to travel was especially difficult for patients who were unable to see their family who lived abroad.

Family

Patients felt their participation in a clinical trial was a shared experience with their families and discussed the psychological impact of trial participation on their family and friends. Some patients felt their spouses were "trapped" or they were a "burden" to their family. While others mentioned their family/friends had to change their usual activities due to their participation in the trial. Patients highlighted the need for support for their family/friends. Many patients felt it was crucial that clinical trial teams ask family/friends about the impact of the trials on them as well.

Financial

Some patients described the financial burden of participating in trials, due to travel costs, as well as food and drinks needed during visits. These patients were not aware of any financial aids available.

Psychological impact

Patients mentioned experiencing anxiety and depression, during the screening process, due to uncertainties around their trial eligibility. Patients feared "their" trial space could be allocated to another whilst awaiting their results, due to their knowledge of limited trial spaces. One patient even felt "rushed" to make a decision.

DISCUSSION

Overall, the majority of patients had a positive experience and received patient-centred care. To aid decision-making regarding initial and continued participation, patients identified

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several areas of improvement (a) the simplification of trial information (b) more information on side effects, (c) regular updates on their response to the treatment, and (d) to be informed of alternative options. Patients needed more information about support available for themselves and their family members. Patients admitted to being reluctant to inform clinical trial teams about side effects experienced.

Patients found the trial information too scientific and difficult to understand, which is consistent with previous studies.[7 11 12] Patients wanted more information about the risk of side effects but mentioned the long list of side effects could be daunting. However, patients often focused on the anticipated personal benefit they would get from the trial rather than potential side effects. Previous studies reported patients often have unrealistic expectations about their potential benefit and reduced susceptibility to side effects when compared with other patients.[6 13-17] To improve comprehension of information, ensure patients provide fully informed consent, and understand the potential risks, Donovan recommends interviewing patients while reviewing study documentation to identify any aspects that are unclear or could be misinterpreted.[18]

Misinterpretation of the trial information provided could have led to 'false hope' (the patient hopes the treatment results in a cure, improvement of health, or prolongation of life).[19] For example, patients overestimation of personal benefit (therapeutic misconceptions) or if the clinical team emphasised the benefits of being on trials (regular appointments, great care, extra attention to their health, and potential benefit for future patients).[13 17 19] False hope was perceived to reduce the patient's ability to cope with bad news, and lead to feelings of frustration and disappointment being amplified and more destructive.[19] This calls into question whether the patient gave fully informed consent. Early phase dose-escalation trials may not lead to personal medical benefit to patients of the trial, yet this is often a reason for participation.[15] The unlikelihood of personal benefit needs to be emphasised more clearly to the patients.[14 15 20-25] From the current evidence, it seems the hope to obtain

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medical benefit is not indicative of compromised informed consent.[15 21 22] However, when introducing patients to trials and providing them with possible treatment options there is a need for equipoise (the assumption there is not one 'better' treatment option).[18 26 27] Any inkling of preferential treatment combined with the patient's belief that doctors and nurses act in the patient's best interest, could lead to patients feeling they have been given false hope.[3 18]

A few patients reported feeling rushed to make a decision; these patients had anxieties that if they did not decide quickly they may lose the trial to another patient. It is crucial patients are given the time and information they require, to make a fully informed decision about trial participation. The patient's anxieties may be due to their therapeutic misconceptions or unrealistic expectations about the benefit, combined with their knowledge of small recruitment numbers across multiple sites.[13 22] Clinical trial teams should consider these factors when discussing trial participation. In addition, the wording used to inform patients they are "eligible" could affect patient's decision-making regarding trial participation. Patients frequently report feeling "lucky" or "honoured" they were eligible for the trial, as it gave them another chance for a cure.[26 28] Therefore it was important to capture patients' experiences who were ineligible for clinical trials.[3 4] Those who were ineligible felt disappointed and were out of treatment options. Brown et al. found patients suggested the phrase "the trial is suitable for you'' could be used instead of "eligible", as the phrase was perceived to objectify the study and highlight the possibility of other treatment options. In addition the use of "unsuitable" may minimise the disappointment felt by those ineligible for the study.[26]

To aid decision-making regarding continued participation in early phase clinical trials, patients desired regular updates about their response to trial treatment. Patients desired information about other patients' experiences of side effects while on the trial and response to the trial and more detailed feedback about the trial progress (i.e. recruitment and

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retention). This is in line with previous studies, which also found patients frequently shared information with each other about side effects and their experience on the trial.[24 29 30] Providing information about other patients' experiences will depend on the information received from the trial sponsor. However, it is crucial information is presented in a way that does not lead to false hope emphasising there are no guaranteed benefits or side effects, and patients have different reactions to treatment.

The main aim of the majority of early phase trials is to investigate the safe dosage range and side effects experienced by patients.[3] Therefore to ensure patients' safety and validity of the trial, it is crucial patients are honest about the side effects and severity of side effects they are experiencing.[13] Yet many patients admitted holding back information about side effects due to fear of being taken off the trial.

The disclosure of side effects is likely influenced by patients' beliefs.[13 28] Previous studies found trial patients believed higher doses were more effective and side effects were caused by effective treatment.[31 32] To reduce fear and address any misconceptions (regarding dose level and effectiveness, and withdrawal of trial if they disclose the trial), these misconceptions could be incorporated into a question prompt list (a list comprised of standard questions to prompt discussion between patient and doctor) highlighting dose reduction as an option if side effects are disclosed.[14 33] However, further research is required to see if providing this information would reduce the under-reporting of side effects.

Another possible option to improve the accuracy of reporting side effects is the integration of electronic Patient Reported Outcomes (ePROs) in clinical trials. Patients often delay reporting side-effect leading to their effect being minimised.[16 33 34] The integration of ePROs enables regular monitoring of patients' side effects and can improve the accuracy and timing of reporting side effects.[35 36] EPROs aid real-time data collection, which can be used to notify their clinical trial team of adverse events, allowing for earlier clinical decisions,

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and provide relevant medical advice, tailored to patients' responses.[37] Therefore, enhancing the patients' quality of care and communication with their clinical team.[35]

Participation in clinical trials led to a reduced quality of life for some patients and not all were aware their poor health was due to treatment toxicity and attributed it to their cancer instead. Some of these patients may have a limited life expectancy and their quality of time left may be more important than staying on the trial.[3] Therefore, clinical trial teams should have ongoing discussions throughout the trial about the patient's trial response, risks and benefits of trial continuation, and other treatment options including palliative care. These discussions will enable patients to make fully informed choices and find a balance between trial participation and quality of life.[3 38]

As well as impacting patient's quality of life, patients can experience undesirable side effects, which can have a negative impact on patient's psychological wellbeing.[5] Yet the majority of patients felt they did not need emotional/psychological support. Despite this perception, patients experienced psychological distress (anxiety and/or depression) at various points throughout the trial (initial screening to determine if patients were eligible or awaiting test results). Patients, who are physically or psychologically impacted, may benefit from specialist palliative care.[39] However, due to the conflicting beliefs (palliative care is for end of life whereas the trial provides hope for another treatment option) patients were less likely to access specialist palliative care.[39] The clinical trial teams may need to provide more information and education about the supports available to patients and the potential benefit of specialist palliative care alongside trial treatment.[39]

Trial participation can require both the patient and their families' time, physical and emotional energy, and some parts of their lives to be put on hold.[40] Therefore, patients felt it was important their family had psychological, financial, and/or practical support. Family/friends acting in a caregiver role (including managing medications, appointment schedules, finances, and/or providing emotional support and/or physical care) commonly

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experience burden and depression.[41] Patients with advanced cancer also perceived their caregivers' lives were on hold when the caregiver was their child.[41] Additionally, caregivers of trial patients experience greater distress and anxiety when compared with the population norms of caregivers of cancer patients.[42] Untreated anxiety and depression can lead to poor physical and mental health, as well as reduced quality of life for carers and potentially patients as well.[41] Despite this, very few patients knew if there was any support available to their family and friends, other than the medical support provided by the clinical trials team. The clinical trial team should provide information about various support services available to patients and their families throughout the trial. However, there is minimal literature on the most effective support for carers of cancer patients and further research is required to identify the support needs of carers.[41 42]

Limitations

One limitation is the cross-sectional nature of the study, as experiences and perspectives may vary throughout the trial. Future studies should use a longitudinal design targeting people at various stages throughout the trial. A second limitation is the study's sample. All participants are from a single comprehensive cancer centre, patients' experiences may vary across hospitals and clinical trial units. However, the study has a large sample size and heterogeneous population in terms of cancer diagnosis, duration of trial participation, and stage of the clinical trial (only two patients interviewed were "screen fails", but it was still important to capture their experiences). The ethnic diversity of the sample was limited and therefore not representative of the area where the data was collected. However, recruitment levels for clinical trials are lower for ethnic minority groups. The majority of trial patients are white British, therefore the sample used was representative of people who usually participate in clinical trials.[43 44]

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Conclusion

Patients require the simplification of trial information and want more information regarding side effects, available support, their response to trial treatment, and overall trial progress throughout the trial, to make fully informed decisions about ongoing trial participation. Due to the trial burden, ongoing discussions are required to help patients find the balance between quality of life and trial participation. Patients were unaware of the support available for their family and wanted more support for their family.

Contributors: J.Y and S.T developed the study design. J.Y has supervised the study. C.S and JY analysed the materials. CS and LP wrote the manuscript. J.Y, S.T, L.C, N.C, M.K, D.G, F.T, and M.D, have given substantial input throughout the development and writing of the paper. J.T (patient representative) was involved with the study design and discussion of main themes.

Funding: The study was funded by Manchester Experimental Cancer Medicine Centres (ECMC) and The Christie CRF Charity, the grant number for this award is A01008. The study was supported by the NIHR Manchester Biomedical Research Centre.

Conflicts of Interest: The authors declare that they have no conflict of interest.

Ethics approval: Ethical approval was gained from the appropriate Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.

Data sharing statement: The interview transcripts are available to show proof of the paper. However, they would only be available for legal purposes. They are confidential and can only be given access to in case of legal Requirements

Acknowledgements: Patients, Carer's, the Christie Experimental Cancer Medicine Team. We would also like to thank Elaine Blowers, Rana Lee, Grant Punnett, and Sarah Bellhouse for their help with the study. We would also like to thank J.T for all their help with the study.

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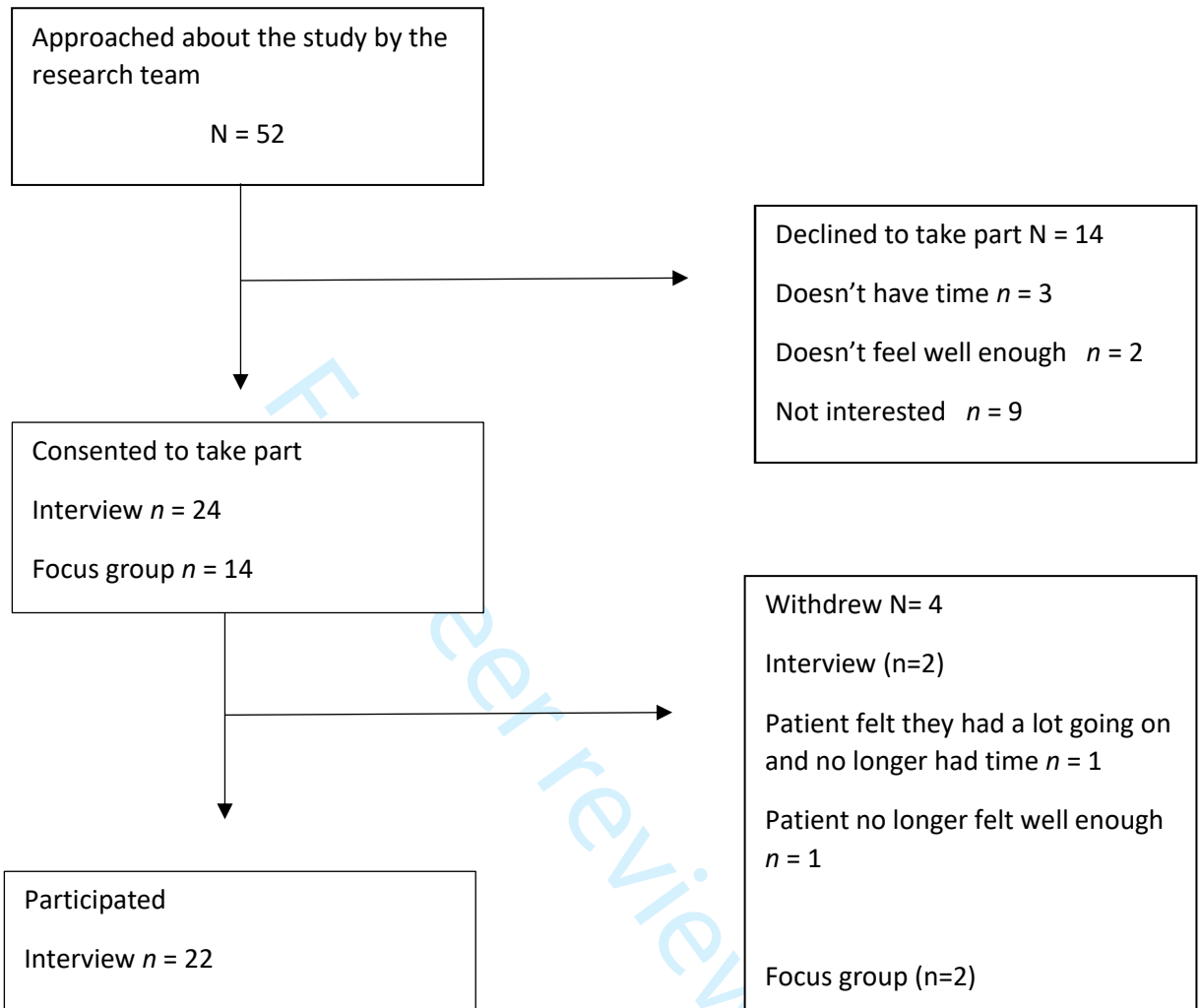
Figure 1. Study flow diagram



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Questions

Pre Trial

1. At diagnosis, how were you informed about your illness?
   - Was there anything that could have been done differently?
2. What was your understanding of the treatment?
   - Was there a discussion about different options for treatment?
   - Was there a discussion about if the treatment didn't work, how was that approached?
3. How were you involved in decisions about your treatment?
4. How did you feel after your first meeting with the doctors at the Christie?
   - Was this for a trial or standard of care?
   - Were you seen by different teams for trial and non-trial visits?
   - If so how were the visits different?
5. How was the subject of a clinical trial approached?
   - At what point was this done?
   - Was the timing appropriate for you?
6. Was there a discussion about side effects and management?
   - How was this approached?
   - What advice and information was given?
   - Did this change your decision making and how?
7. Was there a discussion about supportive care?
   - When did this take place?
   - What was discussed?
   - How did this make you feel?
   - Would you like this to have been approached differently or at a different time?
   - How did this information impact your decision making going onto a trial?
8. Were your family and friends involved if you wanted them to be?
9. Was there anything you would have like to be prioritised more?

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10. When you were told that a trial was the next option, how were you supported?
    - How was the care pathway explained to you?
    - Was it consistent across all members of staff?
    - Was the pathway updated to suit your needs? Can you give an example?
    - What could have been done differently?
11. What was your impression of communication between your clinical team?
    - Was everyone you spoke to aware of your care path?
12. Was everything explained to you in a way that you understood, how was this done?
13. Were you given time to ask questions?
    - How did you feel about asking questions?
14. Did you know who to contact if you had questions or needed support?
    - How were you told about this?
    - Who were you told to contact?
    - What information were you given about when and why to contact?
15. Going onto a clinical trial, what were your expectations?
    - What did you expect from the treatment?
    - What did you expect from your doctors and nurses?
    - Were these expectations met?
16. Did the care you receive feel personal?
    - What was/could have been done to make it feel personal?
17. Was there anything that detracted from your care?
18. How were the visits organised?
    - Did they run on time?
    - What were some problems you encountered?
    - Were you waiting for long periods of time?
    - If so were you kept informed?
    - Do you think this would have been different if you weren't on a trial and how?

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19. In a questionnaire – what questions would allow you to get your experience across?
    - What would you like to be/have been asked?
20. What would you like to see change?
21. Based on your experience, would you go onto another trial in the future and why?
22. *Do you worry about your carers?*

    What support do you think they need?

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BMJ Open

Oncology patients' experiences in experimental medicine cancer trials: a qualitative study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-047813.R2
Article Type:	Original research
Date Submitted by the Author:	10-Aug-2021
Complete List of Authors:	Sawyer, chelsea; The Christie NHS Foundation Trust, CPCR Preston, Laurie; The Christie NHS Foundation Trust, Christie Patient Centred Research Taylor, Sally; The Christie NHS Foundation Trust Christie Patient Centred Research, Christie Patient Centred Research Davies, Michelle; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team, Carter, Louise; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Krebs, Matthew; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, Manchester; The University of Manchester Faculty of Biology Medicine and Health, Division of Cancer Sciences Cook, Natalie; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, ; The University of Manchester Division of Cancer Sciences Graham, Donna; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Thistlewaite, Fiona; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Yorke, Janelle ; The Christie NHS Foundation Trust Christie Patient Centred Research, Christie Patient Centred Research (CPCR); The University of Manchester, Division of Nursing, Midwifery and Social Work; School of Health Sciences
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Qualitative research
Keywords:	Adult oncology < ONCOLOGY, QUALITATIVE RESEARCH, Clinical trials < THERAPEUTICS

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Oncology patients' experiences in experimental medicine cancer trials: a qualitative study

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Word count: 3999

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Abstract

Objectives: The study aimed to explore patients' experiences of early phase Experimental Cancer Medicine (ECM) clinical trials.

Design: The study's design was qualitative. Two focus groups with patients were undertaken followed by semi-structured interviews, to explore patients' experiences of ECM clinical trials. Interviews and focus groups were audio-recorded and transcribed verbatim. Data were analysed using thematic analysis.

Setting: A regional cancer centre (tertiary care) in North-West England.

Participants: Twelve patients (aged 52-89) participated in one of the two focus groups and twenty-two patients (aged 42-83) participated in interviews.

Primary outcome measure: Patients' experiences of an ECM trial.

Results: Four main themes were identified from the analysis: decision-making, information needs, the experience of trial participation, and impact of trial participation. Subthemes are presented in the manuscript.

Conclusion: To make fully informed decisions about trial participation, patients required the simplification of trial information and wanted more information about side effects, their response to trial treatment, and the overall trial progress throughout the trial. Patients highlighted the need for improvement for the support provided to their family and friends.

Strengths and Limitations

- The study explored the perspectives of a diverse group of patients approached to participate in early phase clinical trials, allowing the study to capture an abundance of experiences. Aspects of diversity included age range, duration on trial, disease

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group, and phase of the trial. Patients who had been ineligible or withdrawn from the trial were also included.

- The study generated comprehensive and detailed insights as interviews were conducted to build on experiences highlighted in focus groups, and interviews were conducted until data saturation.
- A limitation is the cross-sectional nature of the study, experiences and perspectives may change throughout the trial process.
- Participants were recruited from one comprehensive cancer centre, patients' experiences may vary across hospitals.

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INTRODUCTION

Experimental cancer trials (or early phase clinical trials) play an important role in progressing and advancing cancer treatments. It is estimated in the United Kingdom one in five cancer patients participate in clinical trials.[1] Early phase clinical trials (Phase I and non-randomised phase II) are designed to assess the safety of novel drugs, pharmacodynamics, and pharmacokinetics.[2] Drug doses are gradually increased Phase I trials, to explore safety and optimum dose. In phase II trials, drug efficacy, side effects, and safety are also investigated. Early phase clinical research primarily focuses on physical outcomes, including appropriate drug dosing, treatment toxicities, survival, and response rate.[2] Limited attention is afforded to patient experience, consequently, little is understood about the personal impact of trial participation.[3]

Understanding patient experience is particularly important in early phase trials, where significant adverse events associated with treatment toxicity may outweigh possible therapeutic benefit.[4] Undesirable side effects are an important factor in shaping patients' experiences of trial involvement, influencing their psychological wellbeing, sense of hope, and potentially increasing fear of death.[5] Furthermore, patients may not fully understand the burden and demands of participation in clinical trials, and the impact trial participation could have on their and their loved one's quality of life.[3]

Despite the various physical, emotional and practical challenges, patients generally report positive experiences of trial participation and feel an increased sense of "control" over their illness.[5] Moore suggested trial participation reflects a coping strategy against hopelessness.[6] When standard treatment is ineffective, clinical trials are perceived by some to offer a 'second chance' at finding a cure.[3] Early phase trials can be perceived by others to be a "last-ditch effort" for patients who are otherwise considered to have exhausted all other treatment options.[4] Cox also found participants derived comfort from being closely monitored by clinicians due to the belief they were in 'expert' hands, and in providing a sense of

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purpose through helping others.[3] However, patients often misunderstand trial information, their understanding and the meanings patients ascribe to their participation will determine how they make sense of their experiences throughout the trial process.[7]

Patient experience is considered to be an integral component of excellent healthcare.[8] As outlined in the NHS Outcomes Framework, a deeper understanding of patient perceptions of trial involvement will drive quality improvement and aid learning.[8] Yet there is limited understanding of patients' experiences of participating in early phase clinical trials. Due to the aims of early phase trials and the uncertainties around drug side effects and safety, the present study aimed to explore the experiences of participants in ECM clinical trials.

METHOD:

Study Design

In this qualitative study, focus groups and semi-structured interviews were used. Focus groups were conducted first to explore patients' experiences of ECM trials allowing patients to discuss similarities and differences in their experiences. The main themes/experiences from the focus groups were explored in more depth in semi-structured interviews.[9] The same topic guide was used for focus groups and interviews (Appendix 1). Questions captured patients' experiences of trial introduction and participation and their decision-making process regarding participating in the trial they were offered. For those on observational trial studies, the interviews focused on their experiences of trial introduction and decision-making process.

Sample/data collection

Participants were recruited from a regional cancer centre in North-west England. The inclusion criteria for the study were (a) any cancer type, and (b) anyone who has been screened for an observational or phase I-II ECM trial. Participants were excluded if they were unable to provide informed consent, or comprehend written English.

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After identification by the clinical team, potential participants were approached by the research team, who explained the study and provided written information. Participants were given the opportunity to ask questions about study participation or the information provided. Written informed signed consent was obtained. Twenty-one face-to-face interviews were conducted in a quiet hospital room and one face-to-face interview was conducted at the patient's home, determined by the patient's preference.

Both focus groups were conducted face-to-face in a quiet hospital room. The interviews and focus groups were audio-recorded and lasted from 14 to 62 minutes and 48 to 108 minutes, respectively. Ethical approval was gained from South central-Oxford b Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.

Figure 1. Present the study's recruitment process. Participant demographics are presented in Table 1.

Insert Figure 1. here Study flow diagram

Insert Table 1. here Participants' demographic information

Table 1. Participants' demographic information

	Interviews (*n* = 22)	Focus groups (*n* =12)
Age range (years (Median))	42 – 83 (65.5)	52-79 (68.5)
Gender (female %)	59%	8%
Ethnicity %		
White British	95%	100%
Chinese	5%	
Marital status (%)		
Single	4.55%	16.67%
Married/domestic partner	90.91%	66.67%
Widowed	4.55%	8.33%

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Divorced	-	8.33%
Employment status (%)		
Self-employed	-	8.33%
Retired	75.00%	83.33%
Unable to work	18.75%	8.33%
Homemaker	6.25%	-
Performance status (%)		
0	52.94%	45.45%
1	47.06%	54.55%
Type of trial n (%)		
Patients who are considered for the trial and then deemed ineligible (are often referred to as 'screen fail')	2 (9%)	-
Observational	2 (9%)	-
Phase I	9 (41%)	7(67%)
Phase II	9 (41%)	5 (33%)
Time on trial (<1 year, %)	54.55%	50%
Disease group		
Breast	31.82%	-
Colorectal	13.64%	16.67%
Head & Neck	-	8.33%
Haematological	9.09%	-
Lung	22.73%	16.67%
Leukemia		8.33%
Lymphoma	18.18%	41.67%
Penile	4.55%	-
Renal	-	8.33%

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Data analysis

Interviews and focus groups were analysed by hand using an inductive thematic approach.[10] The six-phase guidelines of Braun and Clarke were used.[10] After familiarisation with the data, two authors (J.Y, C.S) coded an initial transcript and produced a coding document. After creating the coding document, themes were developed and discussed. Any disagreements regarding codes and themes were discussed between the authors until a consensus was agreed. The codes and themes were then refined to improve clarity. Two reviewers then coded an additional three transcripts and compared these to determine inter-rater reliability (86%). One researcher (CS) subsequently coded the remaining transcripts. Themes and interpretations of the data were discussed in regular meetings (J.Y, C.S).

Patient and Public Involvement:

The patient representative is a patient with secondary breast cancer, who has participated in an early phase clinical trial. They reviewed study documents (participant information sheets, informed consent form, interview schedule) and provided feedback. After analysis, the main themes were discussed with the study team and patient representative, who all provided feedback. A summary of study results will be sent to all participants who requested it.

Reflexivity:

Interviews were conducted sensitively by five researchers (J.Y, C.S, R.L, S.B, D.C) who were not part of the patients' clinical team and all have experience in interviewing people with cancer or regarding sensitive topics (self-harm). The data analysis was primarily conducted by one researcher (C.S) who took an inductive approach and was unfamiliar with the relevant literature at that time. They had no previous experience working in clinical trials, or any personal experiences with clinical trials. This allowed the researcher to analyse the data without looking for preconceived themes or experiences. The analysis was then

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discussed with the research team (J.Y, C.S, L.C, M.D), to minimise any biases which may have occurred. All members of the research team have relevant research or clinical experience. Researchers conducted balanced interviews and focus groups, and reminded patients the research team was not involved in the clinical trial.

RESULTS

We identified four main themes: decision-making, information needs, experience of trial participation, impact of trial participation. The subthemes are described below with supporting quotations provided in Table 2. All themes were mentioned in both the interviews and focus groups. However, false hope was more prominent in the interviews. All patients mentioned fear around disclosing side effects, patients in the focus group emphasised the impact of not disclosing side effects and discussed how to try and encourage patients to disclose side effects.

Insert table 2 here

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Table 2 Presents the themes and their sub-themes with supporting quotations.

1. Decision-making	
1.1 Decision maker	*"It was mine [decision]. It's got to be, it's my life."(25M83)* *"I think the consultants made the decision about what was most suitable"(28F72)* *"The whole family read it, all my children, my husband. We discussed it, come back and said yes." (07F61)*
1.2 No other option	*"I had no other choice, so at the end of the day, that's the one."(25M83)*
1.3 Hope	*"There's that hope there that the…a chance of a cure."(19M56)*
2. Information needs	
2.1 Volume & simplicity of information	*"doctors know all the technical terms, but we don't, most of us; and it has to be said in plain English"(22F52)*
2.2 Side effects	"I don't remember anybody saying, before you go on this, your thyroid could do this, and it will be permanent"(23F68) "Well I think the list of possible side effects is they just think of everything they can think of that might go wrong and list them all down" (FG2)
2.3 Updates throughout treatment	*"I want him to say to me, now look here, if this doesn't work it's chemo." (21F70)*
2.4 Provision of False hope	"if they hadn't built my expectation, then the crash wouldn't have been as hard" (03M42)
2.5 Support available	"you do feel that there's a void like, you know, where do I get that information [about support]."*(FG2)*
3. Experience of trial	
3.1 Patient centred	"the clinical trials team were I felt tailoring their treatment of me."(24F56) "it didn't feel personal; it felt as though I was being treated as a number that was insignificant."(22F52)
3.2 Disclosing side effects	"is the most frightening thing, at that point in time when you come off that point when you've been given, this is your one hope to live and somebody says, I'm just going to take it away from you, and that's the end of the matter." (FG2) "and I made the mistake of telling them about some of the side effects" (FG2) "if you don't tell them [side effects], then you're compromising not only the trial but you're compromising yourself more importantly."(FG2) "if they [trial team] said to you that if you were to disclose the side-effects you're having, that they would be more likely to change your treatment levels or do something about it, other than say on or off because it's the fear of the on or off is the most frightening thing".(FG2)

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4. Impact of trial participation	
4.1 Quality of Life (QoL)	"It's an impact on your life having to come in every two weeks, especially the thing I was on initially was an all-day effort" (FG2)
	"I was in and out like a yo yo And I didn't realise it was the trial"(14M66)
	"Our life has changed absolutely beyond recognition. I had a good job and we were very active, cycled everywhere and went diving on holiday and all of those things which we can't do now"(24F56)
4.2 Time	"the frequency of the visits is good and bad, as I say It's travelling every week but having that line of contact and support weekly is great." (24F56)
4.3. Family	"It's a really valid question to ask around carers and family members and how are they coping"(26F48)
	"it's difficult for my daughter because she had her studies and she came with me every time"(29M55)
4.4 Financial	"It costs you a lot of money"(07F61)
4.5 Psychological impact	"Depressed. it got me down, the waiting"(28F72)
	"So I'm on the waiting list. They may pick somebody else. I don't know."(25M83)

Quotes from the interviews are presented as participant's ID, gender (M=male, F=female), and age (in years). Quotes from the focus groups are presented as FG and number (1 or 2).

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Decision-making

Decision-makers

Patient preference regarding involvement in decision-making varied. Some patients highlighted the importance of including family and friends in their decisions, whereas others felt it was only their decision to make. Due to difficulties understanding the information, uncertainties around trials, and patients' perception of doctor's expertise, some patients relied on the doctors to make the best decision for them.

No other option

A few patients perceived clinical trials as their only option and for those who were ineligible for the trial, this view led to feelings of despair and uncertainty about their options. Conversely, the majority of patients felt clinical trials provided them with another treatment option. This was particularly important for patients who did not want the alternative treatment options.

Hope

Clinical trials provided the majority of patients with hope. For some it was a potential chance for a cure, stopping the progression of their cancer, and/or extending their life. While others hoped their participation would help others with cancer in the future.

Information needs

Wealth/volume and simplicity of information

Patients wanted enough information about their choices to make the best decision regarding treatment. Patients highlighted the need for more simplified trial information, as the information they received was scientific and sometimes difficult to understand.

Side effects

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Patients were divided on whether they had received enough information about possible side effects of the trial before participation, with some patients reporting they were not fully informed. Patients recognised it might possible difficult to provide this information, as the purpose of clinical trials is to identify side effects. One patient felt the risk of permanent side effects had not been fully explained, and prior knowledge of this risk would have affected their decision to participate.

Updates throughout treatment

During the trial, patients wanted updated information regarding i) their response to treatment, ii) alternative treatment options, iii) the success of the overall trial to date, and iv) the experiences of other patients on the trial. This information helped them to re-evaluate their trial involvement and make decisions about future participation.

Provision of False hope

A few patients felt they received false hope and were misled about potential personal benefit from trial participation. These patients believed this false hope reduced their ability to cope with a negative response to treatment. These patients felt information about possible outcomes of the trial should highlight the risks and the possibility the trial may not work, rather than focusing on potential benefits.

Patients who were ineligible for the trial (screen fail) recalled how upsetting it was to be told they were ineligible. One patient even stated it felt like a “death sentence”.

Support available

Patients were informed of whom to contact if they required medical support. However, many were unaware of the psychological support available and could not recall doctors discussing psychological support options. Some patients who were aware of psychological support, highlighted difficulties access the support due to the length of treatments and

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distance travelling to the hospital. The majority of patients did not know if there was any psychological/financial/practical support available for family members.

Experience of trial participation

Patient-centred

Many patients perceived themselves as a guinea pig concerning side effects and some felt their treatment was impersonal. The majority of patients however, reported receiving personalised care and some discussed the flexibility to fit appointments around their priorities.

Disclosing side effects

Patients, especially those who saw the trial as their only treatment option, were concerned about disclosing side effects in case it impacted trial participation. Some patients who disclosed side effects even reported “downplaying” side effects and/or regretting disclosing side effects due to withdrawal from the trial.

This theme was discussed in great detail in the second focus group, with one patient who was taken off the trial admitted they would be reluctant to disclose side effects in future trials. Other patients discussed the internal conflict between the fear of withdrawal from the trial and the risk to themselves if they did not disclose side effects. Some patients were aware by not disclosing side effects they are compromising the trial and the patient's safety.

Patients in the focus group felt they needed more information from the clinical team about what would happen if they experienced side effects. Particularly emphasising that experiencing side effects does not always result in withdrawal from the trial, instead, the dosage may be reduced.

Impact of trial participation

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Quality of Life

Trial participation affected many aspects of a participant's life including QoL, free time, finances, and their family. Patients highlighted the need to fit their life around the trial schedule (due to the frequency and long duration of trial days, and travelling to the hospital). Patients frequently stated once the trial had finished they could *get their "life back."*

The impact on QoL was mixed. Some patients believed their QoL had improved, for example, they were able to perform activities they had been unable to due to ill health. In contrast, other patients were unable to partake in regular activities or trips away, due to side effects or frequent hospital visits, which on occasion required inpatient admission.

Time

Patients discussed the burden of clinical trials on their time, due to the frequency and duration of hospital visits. Some patients reported requiring the next day to recover and rest, perceiving they had "lost" another day due to the trial. However, some benefits to frequent hospital visits were reported including seeing experienced doctors and additional monitoring, care, and support they perceived they would not receive with standard treatment. Patients reported a lot of waiting around, which was tiring but understandable. Some patients were frustrated when they were not informed of delays to their treatment.

An unanticipated impact of the trial was on holidays and trips away. Trial schedules often prevented patients from going away for their preferred duration. Travel insurance was also often difficult to obtain. There were concerns around what would happen if the patient became ill on holiday and if the treatment they received from other hospitals could react with trial treatment or affect trial participation. Limitation to travel was especially difficult for patients who were unable to see their family who lived abroad.

Family

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Patients felt their participation in a clinical trial was a shared experience with their families and discussed the psychological impact of trial participation on their family and friends. Some patients felt their spouses were “trapped” or they were a “burden” to their family. While others mentioned their family/friends had to change their usual activities due to their participation in the trial. Patients highlighted the need for support for their family/friends. Many patients felt it was crucial that clinical trial teams ask family/friends about the impact of the trials on them as well.

Financial

Some patients described the financial burden of participating in trials, due to travel costs, as well as food and drinks needed during visits. These patients were not aware of any financial aids available.

Psychological impact

Patients mentioned experiencing anxiety and depression, during the screening process, due to uncertainties around their trial eligibility. Patients feared “their” trial space could be allocated to another whilst awaiting their results, due to their knowledge of limited trial spaces. One patient even felt “rushed” to make a decision.

DISCUSSION

Overall, the majority of patients had a positive experience and received patient-centred care. To aid decision-making regarding initial and continued participation, patients identified several areas of improvement (a) simplification of trial information (b) more information on side effects, (c) regular updates on response to treatment, and (d) information about alternative options. Patients needed more information about support available for themselves and their family members. Patients admitted to being reluctant to inform clinical trial teams about side effects experienced.

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Patients found trial information too scientific and difficult to understand, which is consistent with previous studies.[7 11 12] Patients wanted more information about the risk of side effects but mentioned the long list of side effects could be daunting. However, patients often focused on the anticipated personal benefit they would get from the trial rather than potential side effects. Previous studies reported patients often have unrealistic expectations about their potential benefit and reduced susceptibility to side effects when compared with other patients.[6 13-17] To improve comprehension of information, ensure patients provide fully informed consent, and understand the potential risks. Donovan recommends interviewing patients while reviewing study documentation to identify any aspects that are unclear or could be misinterpreted.[18]

Misinterpretation of trial information could have led to 'false hope' (the patient hopes the treatment results in a cure, improvement of health, or prolongation of life).[19] For example, patients overestimating personal benefit (therapeutic misconceptions) or if the clinical team emphasised the benefits of being on trials (regular appointments, great care, extra attention to their health, and potential benefit for future patients).[13 17 19] False hope was perceived to reduce the patient's ability to cope with bad news, and lead to feelings of frustration and disappointment being amplified and more destructive.[19] This calls into question whether the patient gave fully informed consent. Early phase dose-escalation trials may not lead to personal medical benefit to patients of the trial, yet this is often a reason for participation.[15] The unlikelihood of personal benefit needs to be emphasised more clearly to the patients.[14 15 20-25] From the current evidence, it seems the hope to obtain medical benefit is not indicative of compromised informed consent.[15 21 22] However, when introducing patients to trials and providing them with possible treatment options there is a need for equipoise (the assumption there is not one 'better' treatment option).[18 26 27] Any inkling of preferential treatment combined with the patient's belief that doctors and nurses act in the patient's best interest, could lead to patients feeling they have been given false hope.[3 18]

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A few patients reported feeling rushed to make a decision; these patients had anxieties that if they did not decide quickly they may lose the trial to another patient. It is crucial patients are given the time and information they require, to make a fully informed decision about trial participation. The patient's anxieties may be due to their therapeutic misconceptions or unrealistic expectations about the benefit, combined with their knowledge of small recruitment numbers across multiple sites.[13 22] Clinical trial teams should consider these factors when discussing trial participation. In addition, the wording used to inform patients they are "eligible" could affect patient's decision-making regarding trial participation. Patients frequently report feeling "lucky" or "honoured" they were eligible for the trial, as it gave them another chance for a cure.[26 28] Therefore it was important to capture patients' experiences who were ineligible for clinical trials.[3 4] Those who were ineligible felt disappointed and were out of treatment options. Brown et al. found patients suggested the phrase "the trial is suitable for you'' could be used instead of "eligible", as the phrase was perceived to objectify the study and highlight the possibility of other treatment options. In addition the use of "unsuitable" may minimise the disappointment felt by those ineligible for the study.[26]

To aid decision-making regarding continued participation in early phase clinical trials, patients desired regular updates about their response to trial treatment. Patients desired information about other patients' experiences of side effects while on the trial and response to the trial and more detailed feedback about the trial progress (i.e. recruitment and retention). This is in line with previous studies, which also found patients frequently shared information with each other about side effects and their experience on the trial.[24 29 30] Providing information about other patients' experiences will depend on the information received from the trial sponsor. However, it is crucial information is presented in a way that does not lead to false hope emphasising there are no guaranteed benefits or side effects, and patients have different reactions to treatment.

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The main aim of the majority of early phase trials is to investigate the safe dosage range and side effects experienced by patients.[3] Therefore to ensure patients' safety and validity of the trial, it is crucial patients are honest about side effects and their severity.[13] Yet many patients admitted holding back information about side effects due to fear of being taken off the trial.

The disclosure of side effects is likely influenced by patients' beliefs.[13 28] Previous studies found trial patients believed higher doses were more effective and side effects were caused by effective treatment.[31 32] To reduce fear and address any misconceptions (regarding dose level and effectiveness, and withdrawal of trial if they disclose the trial), these misconceptions could be incorporated into a question prompt list (a list comprised of standard questions to prompt discussion between patient and doctor) highlighting dose reduction as an option if side effects are disclosed.[14 33] However, further research is required to see if providing this information would reduce the under-reporting of side effects.

Another possible option to improve the accuracy of reporting side effects is the integration of electronic Patient Reported Outcomes (ePROs) in clinical trials. Patients often delay reporting side-effects leading to their effect being minimised.[16 33 34] The integration of ePROs enables regular monitoring of patients' side effects and can improve the accuracy and timing of reporting side effects.[35 36] EPROs aid real-time data collection, which can be used to notify their clinical trial team of adverse events, allowing for earlier clinical decisions, and provide relevant medical advice, tailored to patients' responses.[37] Therefore, enhancing the patients' quality of care and communication with their clinical team.[35]

Participation in clinical trials led to a reduced QoL for some patients and not all were aware their poor health was due to treatment toxicity and attributed it to their cancer instead. Some of these patients may have a limited life expectancy and their quality of time left may be more important than staying on the trial.[3] Therefore, clinical trial teams should have ongoing discussions throughout the trial about the patient's trial response, risks and benefits

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of trial continuation, and other treatment options including palliative care. These discussions will enable patients to make fully informed choices and find a balance between trial participation and QoL.[3 38]

As well as impacting patient's QoL, patients can experience undesirable side effects, which can have a negative impact on patient's psychological wellbeing.[5] Yet the majority of patients felt they did not need emotional/psychological support. Despite this perception, patients experienced psychological distress (anxiety and/or depression) at various points throughout the trial (initial screening to determine if patients were eligible or awaiting test results). Patients, who are physically or psychologically impacted, may benefit from specialist palliative care.[39] However, due to the conflicting beliefs (palliative care is for end of life whereas the trial provides hope for another treatment option) patients were less likely to access specialist palliative care.[39] The clinical trial teams may need to provide more information and education about the supports available to patients and the potential benefit of specialist palliative care alongside trial treatment.[39]

Trial participation can require both the patient and their families' time, physical and emotional energy, and some parts of their lives to be put on hold.[40] Therefore, patients felt it was important their family had psychological, financial, and/or practical support. Family/friends acting in a caregiver role (including managing medications, appointment schedules, finances, and/or providing emotional support and/or physical care) commonly experience burden and depression.[41] Patients with advanced cancer also perceived their caregivers' lives were on hold when the caregiver was their child.[41] Additionally, caregivers of trial patients experience greater distress and anxiety when compared with the population norms of caregivers of cancer patients.[42] Untreated anxiety and depression can lead to poor physical and mental health, as well as reduced QoL for carers and potentially patients as well.[41] Despite this, very few patients knew if there was any support available to their family and friends, other than the medical support provided by the clinical trials team. The clinical

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trial team should provide information about various support services available to patients and their families throughout the trial. However, there is minimal literature on the most effective support for carers of cancer patients and further research is required to identify the support needs of carers.[41 42]

Limitations

One limitation is the cross-sectional nature of the study, as experiences and perspectives may vary throughout the trial. Future studies should use a longitudinal design targeting people at various stages throughout the trial. A second limitation is the study's sample. All participants are from a single comprehensive cancer centre, patients' experiences may vary across hospitals and clinical trial units. However, the study has a large sample size and heterogeneous population in terms of cancer diagnosis, duration of trial participation, and stage of the clinical trial (only two patients interviewed were "screen fails", but it was still important to capture their experiences). The ethnic diversity of the sample was limited and therefore not representative of the area where the data was collected. However, recruitment levels for clinical trials are lower for ethnic minority groups. The majority of trial patients are white British, therefore the sample used was representative of people who usually participate in clinical trials.[43 44]

Conclusion

Patients require the simplification of trial information and want more information regarding side effects, available support, their response to trial treatment, and overall trial progress throughout the trial, to make fully informed decisions about ongoing trial participation. Due to the trial burden, ongoing discussions are required to help patients find the balance between quality of life and trial participation. Patients were unaware of the support available for their family and wanted more support for their family.

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Contributors: J.Y and S.T developed the study design. J.Y has supervised the study. C.S and JY analysed the materials. CS and LP wrote the manuscript. J.Y, S.T, L.C, N.C, M.K, D.G, F.T, and M.D, have given substantial input throughout the development and writing of the paper. J.T (patient representative) was involved with the study design and discussion of main themes.

Funding: The study was funded by Manchester Experimental Cancer Medicine Centres (ECMC) and The Christie CRF Charity, the grant number for this award is A01008. The study was supported by the NIHR Manchester Biomedical Research Centre.

Conflicts of Interest: The authors declare that they have no conflict of interest.

Ethics approval: Ethical approval was gained from the appropriate Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.

Data sharing statement: The interview transcripts are available to show proof of the paper. However, they would only be available for legal purposes. They are confidential and can only be given access to in case of legal Requirements

Acknowledgements: Patients, Carer's, the Christie Experimental Cancer Medicine Team. We would also like to thank Elaine Blowers, Rana Lee, Grant Punnett, and Sarah Bellhouse for their help with the study. We would also like to thank J.T for all their help with the study.

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Figure Captions

Figure 1. Study flow diagram

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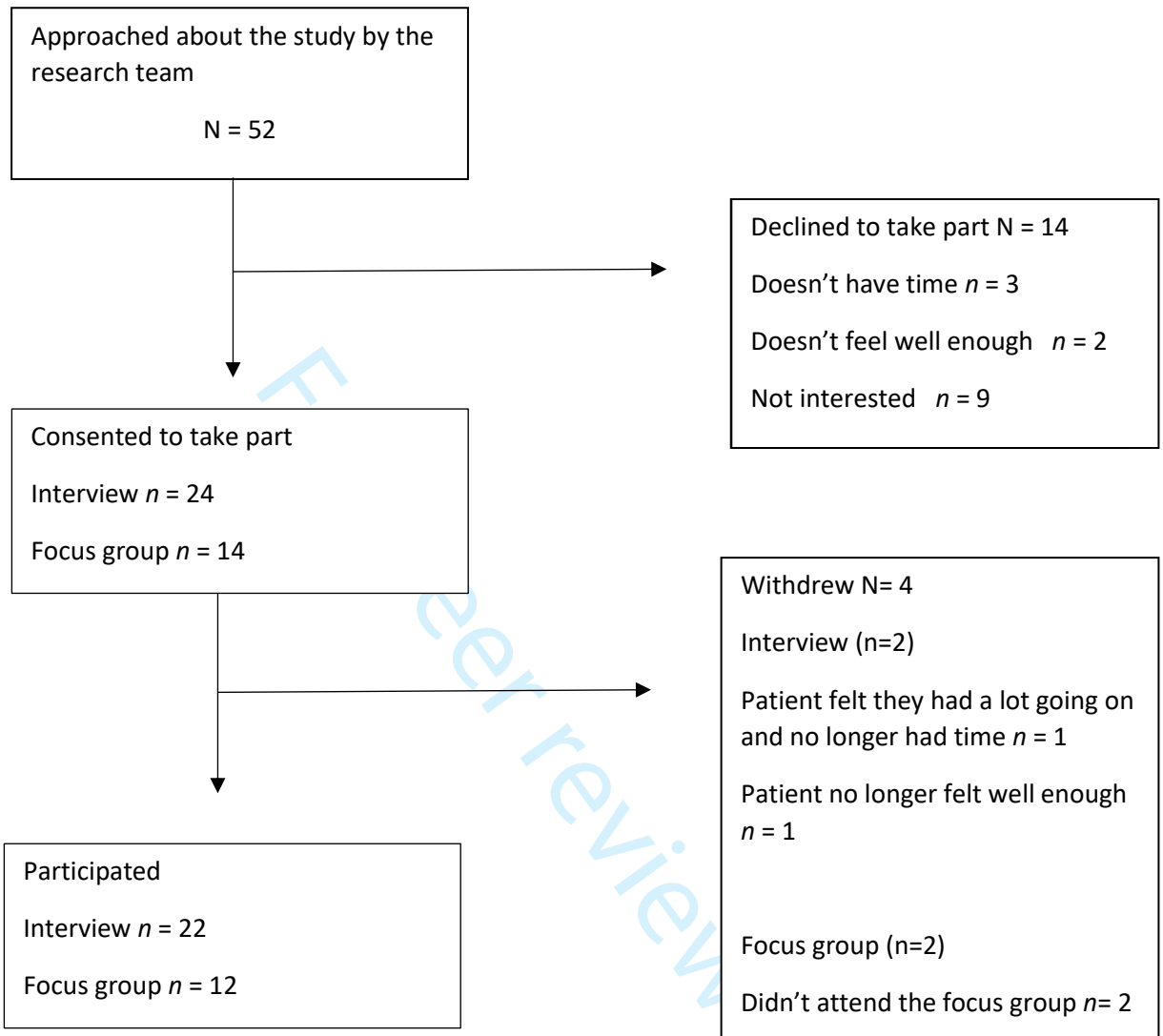
Figure 1. Study flow diagram



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Questions

Pre Trial

1. At diagnosis, how were you informed about your illness?
   - Was there anything that could have been done differently?
2. What was your understanding of the treatment?
   - Was there a discussion about different options for treatment?
   - Was there a discussion about if the treatment didn't work, how was that approached?
3. How were you involved in decisions about your treatment?
4. How did you feel after your first meeting with the doctors at the Christie?
   - Was this for a trial or standard of care?
   - Were you seen by different teams for trial and non-trial visits?
   - If so how were the visits different?
5. How was the subject of a clinical trial approached?
   - At what point was this done?
   - Was the timing appropriate for you?
6. Was there a discussion about side effects and management?
   - How was this approached?
   - What advice and information was given?
   - Did this change your decision making and how?
7. Was there a discussion about supportive care?
   - When did this take place?
   - What was discussed?
   - How did this make you feel?
   - Would you like this to have been approached differently or at a different time?
   - How did this information impact your decision making going onto a trial?
8. Were your family and friends involved if you wanted them to be?
9. Was there anything you would have like to be prioritised more?

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10. When you were told that a trial was the next option, how were you supported?
    - How was the care pathway explained to you?
    - Was it consistent across all members of staff?
    - Was the pathway updated to suit your needs? Can you give an example?
    - What could have been done differently?
11. What was your impression of communication between your clinical team?
    - Was everyone you spoke to aware of your care path?
12. Was everything explained to you in a way that you understood, how was this done?
13. Were you given time to ask questions?
    - How did you feel about asking questions?
14. Did you know who to contact if you had questions or needed support?
    - How were you told about this?
    - Who were you told to contact?
    - What information were you given about when and why to contact?
15. Going onto a clinical trial, what were your expectations?
    - What did you expect from the treatment?
    - What did you expect from your doctors and nurses?
    - Were these expectations met?
16. Did the care you receive feel personal?
    - What was/could have been done to make it feel personal?
17. Was there anything that detracted from your care?
18. How were the visits organised?
    - Did they run on time?
    - What were some problems you encountered?
    - Were you waiting for long periods of time?
    - If so were you kept informed?
    - Do you think this would have been different if you weren't on a trial and how?

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19. In a questionnaire – what questions would allow you to get your experience across?

    - What would you like to be/have been asked?

20. What would you like to see change?

21. Based on your experience, would you go onto another trial in the future and why?

22. *Do you worry about your carers?*

    What support do you think they need?

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Standards for Reporting Qualitative Research (SRQR)*

http://www.equator-network.org/reporting-guidelines/srqr/

	Page/line no(s).
Title and abstract	
Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	1/ 1-2
Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	2/ 22-39
Introduction	
Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	5/ 67-89
Purpose or research question - Purpose of the study and specific objectives or questions	5/ 88-90
Methods	
Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	8/ 124-125
Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	8-9/141-151
Context - Setting/site and salient contextual factors; rationale**	5/ 103
Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	5/ 103-106
Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	6/ 115-116
Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	6/ 107-116

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Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	5/95-96 & 6/ 114
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	Table 1
Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	8/128-132
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	8/ 124-134
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	7/ 129-132 7/136-138

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	9/ 153-159
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Page 10-11

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	16-17/ 275-281
Limitations - Trustworthiness and limitations of findings	21/ 390-402

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	22/ 419
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	22/ 416-418

*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

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**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Reference:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. **Standards for reporting qualitative research: a synthesis of recommendations.** *Academic Medicine*, Vol. 89, No. 9 / Sept 2014
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