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Study protocol for a randomised controlled trial of enhanced informed consent compared to standard informed consent to improve patient understanding of early phase oncology clinical trials (CONSENT)

Abhijit Pal ,[1,2,3] Sarah Stapleton ,[2] Christina Yap ,[4,5] Julia Lai-Kwon,[1,2] Robert Daly,[1,2] Dimitrios Magkos,[1,2] Bindumalini Rao Baikady,[1,2] Anna Minchom,[1,2] Udai Banerji,[1,2] Johann De Bono,[1,2] Deme Karikios,[3] Frances Boyle,[3] Juanita Lopez[1,2]

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For numbered affiliations see end of article.

Correspondence to
Dr Abhijit Pal;
abhijit.pal@sydney.edu.au

ABSTRACT

Introduction Early phase cancer clinical trials have become increasingly complicated in terms of patient selection and trial procedures—this is reflected in the increasing length of participant information sheets (PIS). Informed consent for early phase clinical trials has been contentious due to the potential ethical issues associated with performing experimental research on a terminally ill population which has exhausted standard treatment options. Empirical studies have demonstrated significant gaps in patient understanding regarding the nature and intent of these trials. This study aims to test whether enhanced informed consent for patient education can improve patient scores on a validated questionnaire testing clinical trial comprehension.

Methods and analysis This is a randomised controlled trial that will allocate patients who are eligible to participate in one of four investigator-initiated clinical trials at the Royal Marsden Drug Development Unit to either a standard arm or an experimental arm, stratified by age and educational level. The standard arm will involve the full length trial PIS, followed by electronic or paper administration of the Quality of Informed Consent Questionnaire Parts A and B (QuIC-A and QuIC-B). The experimental arm will involve the full length trial PIS, exposure to a two-page study aid and 10 online educational videos, followed by administration of the QuIC-A and QuIC-B. The primary endpoint will be the difference (using a one-sided two-sample t-test) in the QuIC-A score, which measures objective understanding, between the standard and experimental arm. Accrual target is at least 17 patients per arm to detect an 8 point difference (80% power, alpha 0.05).

Ethics and dissemination Ethics approval was granted by the National Health Service Health Research Authority on 15 June 2020—IRAS Project ID 277065, Protocol Number CCR5165, REC Reference 20/EE/0155. Results will be disseminated via publication in a relevant journal.

Trial registration number NCT04407676; Pre-results.

Strengths and limitations of this study

- Innovative, prospective clinical trial examining informed consent for patients considering participation in currently open and active early phase clinical trials— enhanced validity and ability to translate results to clinical practice (as opposed to a simulated design).
- Multiple focus groups with patients with advanced cancer on early phase trials used to design the experimental interventions (two-page study aid and educational videos) to ensure they are as patient focused as possible.
- Truly informed consent is a topic of significant ethical and scientific importance in the current era of early phase clinical trials which are becoming an increasingly common part of the cancer journey for many patients, but for which there is a paucity of modern day research in the era of mandatory research biopsies, complex biomarker selected trial designs and increasing expectations of efficacy.
- Interventions are in English so results may not be directly applicable to patients from non-English speaking background.
- This study is running concurrently only with investigator-initiated early trials which as a group have slightly different characteristics to industry sponsored early phase clinical trials which may impact the generalisability of the results.

INTRODUCTION

Early phase oncology clinical trials are becoming increasingly complex with a rapidly increasing array of investigational agents, combinations of these agents and a variety of trial designs which incorporate the importance of personalised approaches

and the hope of fast tracked drug discovery. Informed consent for early phase oncology trials has always been a contentious area, and now it continues to be of relevance for the wider oncology community and the phase I trial community. A 2018 study demonstrated significant gaps in understanding of patients regarding the nature and intent of early phase oncology trials.[1] There has been a longstanding debate in the medical oncology community about the nature of phase I trials and the ethics of allowing vulnerable patients to participate in clinical research where the primary purpose is to establish the safe dose. Opponents of the argument point to the need to understand both sides and that patients need to understand enough to consent, which is not necessarily full comprehension.[2] The fact that this group of patients is hopeful, optimistic and desperate has been well characterised[3] and no doubt plays a role in their ability to process information presented to them by the clinical research team. It is also important to recognise that consent for early phase trials deals with many of the same issues that are faced by clinicians considering consent in complex standard of care settings (eg, refusal of transfusion of blood components) with a focus on the key themes of preserving patient autonomy, protecting patient rights, ensuring jargon-free information and incorporating shared decision-making.[4–6]

Empirical research showing patients misunderstand early phase clinical trials

Multiple studies have shown that advanced cancer patients (ACP) misunderstand the nature and purpose of phase I oncology trials. Most recently, Hlubocky *et al*[1] demonstrated through audiotaping clinical encounters between 101 ACPs and 29 oncologists, that ACPs had a poor understanding. Only 26% were able to recall the primary purpose of the trial as safety and only 7% were able to recall that there was a risk of major adverse effects such as organ damage. The study also demonstrated deficiencies in clinician communication, with only 40% of encounters containing a direct statement on the research purpose being to establish safety, toxicity and dosage. In 2010, a similar study of 17 oncologists and 52 patients in the UK showed that several key areas of information including prognosis were omitted from the clinical encounter.[7] Joffe and colleagues also conducted a survey of trial participants (including phase I, II and III clinical trials) and investigators and showed significant deficits in understanding.[8] Furthermore, in a survey of 95 patients on phase I trials, Pentz and colleagues demonstrated that 68.4% of patients had a therapeutic misconception by failing to answer two core questions correctly ((1) 'Is the research study mostly intending to help research and gain knowledge or mostly intending to help you as a person?' (2) 'Does the research study or your doctor decide the treatments?').[9] There was also a misunderstanding of the risk associated with participating in an early phase clinical trial and that they did not correctly grasp the key difference between individualised care and clinical research. In addition, there was a correlation between lower education and lower family incomes with therapeutic misconception. Overall, there is extensive empirical evidence to suggest that a significant proportion of ACPs considering early phase oncology clinical trials harbour misconceptions about the nature and design of these trials.

Participant information sheets are too long, too complex and fail to meet the information needs of patients

It has long been recognised that participant information sheets (PIS) or informed consent forms (ICF) are highly complex and lengthy across all the phases of oncology clinical trials. In 2007, Beardsley and colleagues showed that PIS were increasing in length and that an objective measure of informed consent (the Quality of Informed Consent Questionnaire Part A (QuIC-A)), understanding decreased as PIS's increased in length[10]. There have been no published studies on the PIS used in phase I studies specifically. However, in the era of combination trials, Bayesian adaptive design and seamless phase I/II designs, the PIS for phase I trials can be particularly complex and lengthy. While there is regulatory requirement for disclosure, these documents have ultimately become unwieldy, disliked by investigators and anecdotally, not read at all by some participants. This further magnifies the issues on therapeutic misconception that were highlighted earlier. We note that the Hastings Center has published a three-page phase I consent form with guidance on assessment of readability, but to the best of our knowledge this is not in widespread practice.[11] Overall, in this era of increasingly sophisticated trial design, PIS are becoming lengthier and are becoming less useful as adjuncts to the informed consent process.

Paucity of interventional research to improve understanding

We performed a review of the literature looking at interventions that have been tested to improve participant comprehension of phase I trials which yielded two relevant studies. The first, a simulated teaching intervention to improve clinician confidence by Fallowfield *et al*[12] showed that an intensive 8-hour educational intervention for clinicians involved in early phase trials improved their self-confidence along with patient simulator ratings of understanding. Second, Kass *et al*[13] randomised 288 participants to receive either a 20-minute educational computer based presentation or a standard pamphlet on clinical trials and showed that they could improve patient understanding of trial purpose from 16% to 34%[13] and also showed that there was no significant differences in likelihood of enrolment. We note that there have been multiple efforts directed towards empowering patients with cancer in later phase trials including audiovisual techniques such as multimedia presentations,[14] question prompt lists[15] and decision aids.[16] Promisingly, sponsors are already taking steps towards improving their information sheets and there are already attempts to incorporate audiovisual materials and electronic assessment of patient understanding.

Justification for CONSENT

CONSENT will be a randomised controlled trial examining the effect of both a short (2 page), jargon-free, plain language participant information sheet and a suite of online educational videos, for participants considering consenting to an investigator-initiated trial (IIT) within the Royal Marsden Drug Development Unit. Early phase trials have dramatically changed over the last decade and there have been no interventional studies published in this area in this time and consequently this is a significant area of unmet need for both patients and investigators. This trial will use a validated measure of informed consent (Quality of Informed Consent—Part A).[17] It is powered to test a statistical hypothesis of whether providing both a short summary PIS and a link to these online video modules will improve patient understanding as compared with a control group who are provided only the normal PIS. It will also examine the acceptability of the two interventions for patients. While the trial will employ a randomised design, it will ensure all participants including those randomised to the control group will be provided access to the enhanced consent materials prior to their actual consent visit to ensure fairness.

This trial will also assess user acceptability and feasibility of the two interventions for patients.

METHODS AND ANALYSIS

Study aims

The primary aim of this study is:

- To establish whether the experimental arm can result in improved patients' objective understanding (measured by the QuIC Part A) of early phase oncology clinical trials as compared with the standard PIS.

The secondary aims of this study are as follows:

- To establish whether the experimental intervention can result in improved subjective (QuIC Part B) patient understanding of clinical trials between the control group and the experimental group.
- To establish whether the experimental intervention can result in improved objective (QuIC Part A) and subjective patient understanding within the same patient as measured on the QuIC Part B.
- For the glioblastoma multiforme (GBM) cohort—to establish whether the experimental intervention can result in improved objective (QuIC Part A) and subjective patient understanding within the same patient as measured on the QuIC Part B.
- To confirm acceptability, uptake and utility of enhanced experimental interventions in this trial population.

Study materials

The first part of this enhanced consent will be a study aid (see online supplemental appendix 1) which contains the absolutely necessary information for patients—the design of this aid has been based on a qualitative study of patients on phase I trials and their informational needs.[18] The top three priorities identified patients were

1. Will this trial work for me?
2. What are the side effects?
3. How often do I have to come? This will consist of an easy to understand flowchart.

The second part of this enhanced consent, based on the same data, will be an online link to 10 video modules (summary provided in table 1 and transcripts attached in online supplemental appendix 2) covering key areas of the consent. We asked about the key areas that need to be communicated, common areas of misunderstanding and preferred ways forward of improving patient understanding. We also used the feedback of the Royal Marsden Hospital Patient and Carer Research Review Panel to design these materials.

Study design and setting

Patient and public involvement

In 2019 we conducted a qualitative study[18] of the key stakeholder groups in our early phase clinical trials unit in order to work out the design of the interventions used for this study. As part of that process we conducted two focus groups and gathered data on the key pieces of information that patients wished to know and ensured that these were incorporated into the design of the two-page study aid and also the content of the video. This protocol was presented to the Royal Marsden Hospital Patient Review Panel on multiple occasions and feedback was obtained about the nature of the study.

Endpoints

The primary endpoint of this study

- To determine the QuIC Part A scores following administration of a standard PIS alone, and compare it to the QuIC Part A score following administration of a standard PIS along with a study aid and a suite of online educational videos.

The secondary endpoints of this study are as follows:

- To determine the QuIC Part B scores following administration of a standard PIS alone, and compare it to the QuIC Part B score following administration of a standard PIS along with a study aid and a suite of online educational videos.
- To determine the changes in QuIC Part A and Part B scores before and after administration of enhanced consent materials in the control group only.
- GBM cohort—to determine the changes in QuIC Part A and Part B scores before and after administration of enhanced consent materials in patients recruited to the GBM cohort in the Ice-CAP study.
- To confirm the acceptability and utility of the study aid and educational videos with a user feedback survey (online supplemental appendix 3).

Table 1 List of educational videos and description of key themes covered. Please see online supplemental appendix 2 for transcripts

Lay description	Key themes to be covered
What are early phase clinical trials?	Safety and dose finding Eligibility, potential for screen fail Early phase clinical trials ► Dose escalation ► Dose expansion
Will being in an early phase clinical trial shrink my tumour?	Uncertainty Difference between trial and treatment Individualised conversation for each patient
Will I get side effects by being on an early phase clinical trial?	Uncertainty Difference between trial and treatment Potential for serious side effects
Do I have any other options? Am I missing out by not being on a phase I trial?	Alternatives to trial participation including best supportive care
What is it like to be on an early phase trial?	Time commitment, research burden, length of trial, costs
Why are biopsies part of many early phase trials?	What is a research biopsy and how is tissue handled?
What is involved in a biopsy and what types of imaging will I undergo?	What imaging procedures do we use? Deep versus superficial biopsies
What will you do with my data?	How is my data handled? Data sharing with sponsors
What is it really like #1?	Patient video #1—dose escalation
What is it really like #2?	Patient video #2—dose expansion

Inclusion/ exclusion criteria

Inclusion criteria

- Eligible for an IIT within the drug development unit (RAF-MEK—NCT02407509, FRAME—NCT03875820, Ice-CAP—NCT03673787, ACE—NCT03177187).
- Patients with GBM eligible for Ice-CAP will not be randomised but assigned to a separate cohort.
- English is patient's primary language.

Exclusion criteria

- Pre-existing visual, non-cancer related cognitive impairment or reading impairment.
- Patients who have already consented to a trial or have prior consent knowledge.

Study processes

This is a prospective, randomised trial running concurrently with our current standard of care for informed consent for our patients considering clinical trials—the design is summarised in figure 1. As per our normal standard operating procedure, patients are identified at a patient allocation meeting as potentially suitable for one of the four investigator-initiated clinical trials included in this study (RAF-MEK—NCT02407509, FRAME—NCT03875820, Ice-CAP—NCT03673787, ACE—NCT03177187). At this point, we will consider whether the particular patient would be suitable for CONSENT, and if suitable, the subinvestigator responsible for discussing the trial will also discuss whether the patient would be interested in participating in CONSENT. If the patient is interested then we will send the CONSENT PIS to the patient.

The study setting is the population of patients who are considered eligible for one of our investigator-initiated clinical trials at the Drug Development Unit, Royal Marsden Hospital, Sutton. Patients with GBM will be included in the study but will not be randomised. They will only be enrolled into the control arm and we will recruit up to 15 patients from the Ice-CAP trial. They are expected to have higher rates of baseline cognitive impairment and will be analysed separately.

As future IITs open in our unit, we will submit amendments in order to include them in CONSENT.

At this point after the patient has received the CONSENT PIS, they will confirm during the follow-up phone call and can return the CONSENT ICF (online supplemental appendix 4) via email, post or during the next visit to hospital. Once they have consented, we will randomise the patient to either the control or experimental arm. The randomisation algorithm will be set up and managed by the Institute of Cancer Research Cancer Trials and Statistics Unit.

On the experimental arm, the patient will be provided the standard PIS, along with a link to the 10 online educational video modules and also a copy of the study aid for the IIT they have been allocated to. They will have at least 24 hours to review these materials, and they will then be asked to complete the demographic data collection form, the QuIC (Parts A and B) (please see[17] for details on the

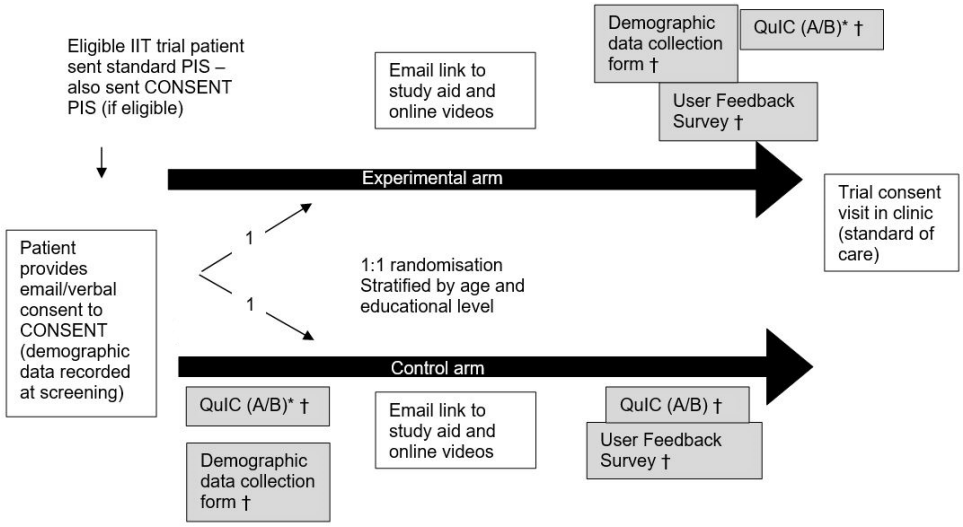

Figure 1 Schema of study design of CONSENT. *Primary endpoint is being undertaken. †Questionnaire will be delivered and received via encrypted email, or paper version. IIT, investigator-initiated trial; PIS, participant information sheets; QuIC (A/B), Quality of Informed Consent Questionnaire Parts A and B.

instrument and scoring) and the feasibility questionnaire (online supplemental appendix 3). They have the option of completing the surveys and demographic data form (online supplemental appendix 5) via encrypted email or paper. They will then arrive for their consent visit as per standard of care .

On the control arm, patients will be provided the standard PIS, given at least 24 hours and then asked to complete the QuIC (Parts A and B) and demographic data form. Once this is completed, we will send the link to the online videos and also the study aid for their trial (as per the experimental arm). After at least 24 hours, the participants will then repeat the QuIC (Parts A and B) and the feasibility questionnaire. They will then arrive for their consent visit as per standard of care.

We will recruit a small cohort of patients with GBM from Ice-CAP (NCT03673787) to this study but they will not be included in the primary analysis due to the high prevalence of cognitive impairment in this group. This is a rare tumour that may stand to specifically benefit from enhanced consent and we thought it prudent to include these patients in a non-randomised fashion to obtain preliminary data on the efficacy and feasibility of enhanced consent in this group.

Statistical plan

Analysis population

The primary analysis in this trial will be comparison of the QuIC-A scores in the experimental group after exposure to the enhanced informed consent materials in addition to the standard PIS (standard of care) as compared with the control group after exposure to the standard PIS (standard of care). We will include all randomised patients for whom we have data on the initial QuIC-A (the primary endpoint). The patients recruited to the GBM cohort will not be included in the primary analysis.

Background on the QuIC-A instrument

The QuIC-A has been validated through rigorous testing as a tool for measuring the quality of informed consent in research participants. We performed testing within our unit and found it performed similar to the level expected in the literature[19] The average score on the QuIC-A among patients was 76.8/100 with a SD of 9.1.

We have consulted with the primary author of the QuIC[17] and also looked at other literature using the QuIC Part A as a measure of informed consent and have found that a clinically meaningful score would be an improvement in score of at least 5 points.

We have also observed the statistical analysis for three other trials using the QuIC-A as a primary endpoint to test the effectiveness of an intervention to improve patient understanding of clinical trials. Tattersall *et al*[20] aimed to detect a difference of 5 points with the addition of a question prompt list, Hoffner *et al*[21] aimed to detect a difference of 5 points with an educational video about clinical trials and Spellecy *et al*[22] aimed to detect a difference of 4 points using an easy to read informed consent sheet.

In contrast to these studies, the experimental arm has two interventions we expect to be active—a two-page study aid, and also a suite of 10 jargon-free videos and we expect them both to have a significant impact on patient understanding of clinical trials and we expect this to be reflected in the QuIC Part A score to justify looking for a larger effect size (at least 8 points) between the experimental and control arms. Both interventions have been developed after an extensive qualitative analysis of our various stakeholder needs and requirements.

Randomisation

Once suitable patients are identified, consented and screened, they will be randomised in a stratified manner by two factors that we expect to impact on trial comprehension—age (over

65 or below) and educational level (university educated or otherwise). This will be performed with a minimisation approach and will be performed by the Institute of Cancer Research Clinical Trials Statistics Unit Randomisation Team—investigators will provide this team with the stratification factor information and will be informed of the allocation. Once informed, the study team will email the required interventions and questionnaires to participants. Participants and investigators will not be blinded once they have been randomised.

Analysis methods

We will use a one-sided two-sample t-test to determine whether there is a difference in the mean QuIC-A score between the control and experimental arm QuIC-A scores. We will use the same software to analyse the difference between the QuIC-B scores and also use the same method to compare the before and after QuIC-A and QuIC-B scores in the control arm using a paired t-test. If the distribution cannot be assumed to be normally distributed, a non-parametric unpaired and paired t-test using Wilcoxon rank-sum test and Wilcoxon signed-rank test, respectively, will be considered. The user feedback survey will be reported using descriptive statistics.

The primary and secondary endpoints of QuIC-A and QuIC-B will also be compared between the two arms using standard multiple linear regression models, with adjustment for the stratification factors of age and educational level. The model assumptions will be checked and if they do not hold, alternative modelling approaches will be explored as appropriate.

We will use Microsoft Excel (Office 365) or R to perform the analysis.

Sample size calculation for primary endpoint

We also understand the pragmatics of early phase clinical trials which have smaller numbers of patients and doing non-interventional studies on large groups of patients will not be feasible in this situation. We will aim to recruit at least 17 patients per arm, but we will recruit up to a maximum of 22 patients per arm. To detect an improvement of 8 points in the QuIC-A scores, we would require 17 patients per arm to give 80.6% power with a significance level (alpha) of 0.05 using a one-sided two-sample t-test (assuming SD of 9.1 for each group). If we recruit up to a maximum of 22 patients per arm, this will provide a higher power at 88.9% under the same test statistic and design parameters (difference of 8 points, one-sided alpha of 0.05 and SD of 9.1). We do not expect dropout from this study given the period of participation is short (between 24 hours after randomisation and up to a week), but if it does occur, we will recruit additional patients as appropriate.

Ethics and dissemination

Ethics

Ethics approval was granted by the National Health Service (NHS) Health Research Authority on 15 June 2020—IRAS Project ID 277065, Protocol Number CCR5165, REC Reference 20/EE/0155.

Safety considerations

Both the two-page study aid and the educational videos have been co-produced with patients so we have a minimal expectation of harm arising from participation in this trial. Anxiety due to the additional information may be possible and we will be formally studying this on the Brief User Feedback Survey (Item 1) but we will also escalate any concerns noted by investigators in this study to the principal and chief investigator so that they can be addressed quickly and safely.

Data handling and record keeping

We will permit trial related monitoring, audits, Institutional Review Board (IRB)/Independent Ethics Committee (IEC) review and regulatory inspections and provide direct access to source data/documentation. The trial will be conducted within the standard operating procedures of both the Royal Marsden Hospital and the Drug Development Unit and the conduct of the trial will be regularly reviewed by both the principal investigator and the chief investigator.

The online data will be kept securely on a password protected database and participants will be provided with a secure link to access the survey data.

A key step will be the online questionnaires that need to be completed by study participants. Participants will complete this questionnaire online and then email it back to the secure clinical trial (NHS) email address, to which only the principal investigator or their specified delegate when they are on leave can access. The study participants will be informed that given their personal email addresses are not secure, there is a small risk that their personal data may be compromised when it is being sent to our email address. Patient demographic data will be stored on a password protected Microsoft Excel database.

Publication plan

Results will be disseminated via publication in a relevant journal.

DISCUSSION

To our knowledge, CONSENT is the first randomised controlled trial to test the efficacy of an intervention to improve patient comprehension of early phase clinical trials in cancer.

Informed consent is an extremely complex area to study due to the paucity of research, the vulnerability of this patient group and the heterogeneity of patient informational needs. The vast amount of literature[1 3 9 23–25] documenting a lack of understanding juxtaposed with the stringent ethical demands of good clinical practice demands further efforts to actively seek to improve our consenting methods. Phase I trials, and the PIS accompanying them, are becoming more complex to understand

and we are obliged to convey this information as simply as possible. We felt that a trial of simple and pragmatic interventions embedded within a real world setting will advance the field and provide information for both our unit and other phase I centres.

The study has multiple strengths. The intervention arm employs two novel interventions for patients considering early phase clinical trials—a two-page study aid and the set of 10 online educational videos. These have been created based on the results of an exhaustive qualitative analysis of all the key stakeholders in the informed consent process for early phase clinical trials including patients.[18] Patient co-production is a particularly strong aspect of this study as patient input has played a pivotal role in the design of the experimental interventions and delivery of this trial. Second, this trial has a quantifiable primary endpoint which will objectively measure patient's understanding of clinical trial. We have previously discussed the importance of measuring quality of informed consent[19] and we are employing the QuIC-A as the primary endpoint for this study. Informed consent is a crucial component of good clinical practice and we believe measuring it, and particularly in studies such as these to examine the effectiveness of interventions is crucial.

Third, this trial is being conducted in a live setting running concurrently with patients considering on whether to participate in an early phase clinical trial. Performing a randomised study in this setting is additionally challenging but we believe this is the best way to isolate the effect of the interventions. It is crucial to note that all patients in CONSENT will receive the study specific ethics committee approved PIS up front so will not be disadvantaged by any 'alternative' information compared with those who do not take part in CONSENT. Additionally, to ensure equality within patients who take part in CONSENT, the standard arm will also receive the enhanced consent materials after completing the primary endpoint (QuIC-A). Given we anticipate this study will be completed electronically by the majority of the participants, we anticipate this trial will represent only a small additional burden for patients.

There are several limitations to this study. First, the early phase clinical trials included as part of this study are all investigator-initiated clinical trials—it is recognised in the literature and anecdotally that, on average, industry-sponsored studies will have longer PIS and more complicated schedules than IITs. Second, there is no baseline data on quality of informed consent as measured by the QuIC-A in the early phase clinical trials and this trial will be important in establishing this but it will make it difficult to benchmark. Additionally, the study is powered to detect a large difference in QuIC-A scores and it may miss a smaller effect size—this was a pragmatic decision based on the recruitment rate to early phase clinical trials and the complexity of managing recruitment to this study in parallel with recruitment to four clinical trials which have their own tempo of patient recruitment. Third, while the online and electronic nature of this study is a key benefit there remains a small risk of patient data being compromised. We have taken every effort to ensure our communications are encrypted via the NHS encrypted email system (nhs.net) but there remains a potential vulnerability in patient-sided technology —this is part of our consent sheet for this trial so patients are advised about this. Finally, we recognise that additional information may cause anxiety or distress for patients—we are recording this in our final survey as we seek to understand this but preliminary data from a separate project indicates that this is unlikely. We also provide the contact details for our clinical nurse specialists to all patients and we will provide support and clarification if required.

Results from CONSENT will help to inform the manner in which informed consent for early phase clinical trials is performed and will provide valuable information as to whether enhanced consent materials can impact on objective trial comprehension. We also hope that the focus on producing jargon-free and easy to understand information will be of relevance to other areas where consent is performed—for example, in standard of care settings in medicine. This is a key study in the broader effort to improve patient–clinician communication surrounding entry into early phase clinical trials, protect and enhance patient autonomy and ultimately better support patients with advanced cancer to make the decisions that are most congruent with their own values at the end of their life.

Author affiliations
[1]Institute of Cancer Research, London, UK
[2]Drug Development Unit, Royal Marsden Hospital Sutton, London, UK
[3]The University of Sydney, Sydney, New South Wales, Australia
[4]Cancer Research UK Clinical Trials Unit, University of Birmingham, Birmingham, UK
[5]Clinical Trials and Statistics Unit, Institute of Cancer Research, London, UK

Twitter Abhijit Pal @DrAbhiPal, Sarah Stapleton @staplehedge and Christina Yap @ChristinaBYap

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Patient consent for publication Not required.

Ethics approval Ethics approval was granted by the NHS Health Research Authority on 15 June 2020 – IRAS Project ID 277065, Protocol Number CCR5165, REC Reference 20/EE/0155.

Provenance and peer review Not commissioned; externally peer reviewed.

Author note The study sponsor is the Royal Marsden Hospital and the contact email address is RDCCR@rmh.nhs.uk. The Royal Marsden Hospital Committee for Clinical Research provided initial review and feedback for this protocol—analysis and interpretation of data will be left to the study team.

ORCID iDs
Abhijit Pal http://orcid.org/0000-0002-4600-6569
Sarah Stapleton http://orcid.org/0000-0002-1579-9447
Christina Yap http://orcid.org/0000-0002-6715-2514

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