Observational study investigating Tolerance Of Anticancer Systemic Therapy In the Elderly (TOASTIE): a protocol

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ABSTRACT

Introduction The number of older adults diagnosed with cancer is increasing. Older adults are more likely to have pre-existing frailty, which is associated with greater chemotherapy-related toxicity. Early identification of those at risk of toxicity is important to reduce patient morbidity and mortality. Current chemotherapy toxicity prediction tools including the Cancer and Ageing Research Group (CARG) tool exist but are not in routine clinical use and have not been prospectively validated in a UK population. This study is the first prospective study to investigate the CARG tool in a UK population with cancer.

Methods and analysis Tolerance Of Anticancer Systemic Therapy In the Elderly is a prospective observational study of patients, aged >65 years, commencing first-line (any indication) chemotherapy for a solid-organ malignancy. Patients receiving other systemic anticancer agents or radiotherapy will be excluded. The primary objective will be to validate the ability of the CARG score to predict grade 3+ toxicity in this population. Secondary objectives include describing the feasibility of screening for frailty, as well as the prevalence of frailty in this population and assessing patient and clinician perception of chemotherapy toxicity risk. 500 patients will be recruited over a two year period. Baseline assessments will be recorded. At the end of the 6-month follow-up period, toxicity data will be retrospectively collected. A descriptive analysis of the recruited population will be performed. The validity of the CARG model will be analysed using receiver-operating characteristic curves and calculation of the area under the curve (c-statistic).

Ethics and dissemination The study has received ethical approval from the East of Scotland Research Ethics Service 20/ES/0114. Results will be reported in peer-reviewed scientific journals and disseminated to patient organisations and media.

INTRODUCTION

The number of adults of age >65 years diagnosed with cancer is increasing rapidly and is expected to treble by 2040 in the UK.1

Randomised controlled trials poorly represent the general oncology population, with only 20% of patients being eligible to participate and fewer than 3% participating in clinical trials.2 Certain groups are commonly under-represented, including older patients and those with multiple pre-existing health conditions, and thus frailty.3 This results in large disparities between the data collected in clinical trials and that seen in the real-world clinical environment.4 The provision of clear and accurate information relating to both potential benefits and potential harms of treatment is an essential factor in assisting both clinicians and patients to make informed evidence-based decisions.

Frailty in cancer has been extensively described in the literature and has been found to correlate with an increased risk of chemotherapy intolerance and death.5 Although considered as distinct entities, the prevalence of frailty increases with age.

The decision to offer chemotherapy is made by the treating physician following an assessment of patient suitability. Clinicians commonly use the Eastern Cooperative
Oncology Group performance status as a crude assessment tool for this purpose in patients of all age groups, despite it being shown to poorly correlate with frailty.\(^6\)

Research into the utility of frailty scores in aiding chemotherapy decision-making is limited. Therefore, most clinical decisions are underpinned by heuristic learning obtained through clinical practice despite clinicians having a tendency to overestimate benefit and underestimate harm.\(^7\) Studies have highlighted that oncologists’ predictions of grade 3 chemotherapy toxicity poorly correlated with actual treatment toxicity.\(^8,9\) Both underestimation and overestimation of risk of significant toxicity from chemotherapy may lead to changes in patient decisions, highlighting the need to provide accurate information.\(^10\)

Failure to take account of patient frailty may result in inappropriate selection of patients for chemotherapy, a neglect to make appropriate alterations to treatment, such as dose reduction, and a lack of patient-centred intervention, culminating in adverse patient experience.\(^11\) Incorporation of frailty screening within oncology has been under review for some time and several different tools have been appraised to help predict mortality and chemotherapy toxicity,\(^12\) including the International Society of Geriatric Oncology Geriatric Screening Tool (G8)\(^13\) and Rockwood Clinical Frailty Score (CFS).\(^6\) Although these tools have all been demonstrated to have utility in identifying frailty, none have been studied as predictive markers of chemotherapy toxicity.

Two chemotherapy prediction tools that have been studied are the Cancer and Ageing Research Group (CARG) score and the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score.\(^14,15\) The CRASH score takes 20–30 min to complete and due to time constraints it may not be practically feasible to incorporate this tool into non-trial National Health Service (NHS) clinical practice.

The CARG score can be used to predict grade 3–5 chemotherapy-related toxicity in patients >65 years of age undergoing treatment of solid-organ cancers and lymphomas.\(^16\) It considers 11 domains and takes approximately 5 min to complete. The results of the assessment can be used to assign the risk of developing grade 3–5 chemotherapy toxicity which is expressed as both a percentage and low, intermediate or high risks.\(^15\) This information can subsequently be used in providing more personalised information related to treatment risks, which can better inform discussions and decision-making between the clinical team and the patient.\(^11\)

The score was initially developed in the USA and has subsequently been adapted to include tumour specific factors relating to breast cancer.\(^16\) Subsequent research at centres in Australia questioned its ability to predict risk and it has thus far failed to enter routine clinical practice there.\(^9\) The variation in the tools utility by geographical area may be due to differences in thresholds of patient selection for chemotherapy and variation in treatments delivered, coupled to the availability of support networks.

To date, the CARG score has not been evaluated prospectively in a UK population.

In summary, we know that frailty is associated with chemotherapy intolerance and while many scoring systems exist to evaluate frailty, in practice it is rare that formal scoring assessments are utilised. Physician estimates of chemotherapy tolerance are poorly correlated to objective risk and clinical outcomes, further supporting the case for developing a validated scoring system.

This study aims to address the gap in much needed information regarding frailty and chemotherapy tolerance in the older cancer population within the UK. To our knowledge, no frailty scoring system predicting for chemotherapy toxicity has been evaluated for feasibility and validity in the UK population.

The Tolerance Of Anticancer Systemic Therapy In the Elderly study aims to validate the CARG scoring system in a UK real-world older aged population across a range of solid-organ tumour groups. Through the information we collect, we will also be able to assess the utility of other commonly used geriatric assessment tools in predicting risk of severe chemotherapy toxicity, namely the G8 and Rockwood CFS.

The CARG score was specifically chosen owing to the fact it has already been validated in the USA, and in view of its simplicity and length, it is more likely to be able to fit in to a time-constrained new patient NHS consultation. If the CARG score is validated as a tool to predict high-grade chemotherapy-induced toxicity in our UK cohort and can easily be integrated into routine clinical practice there will be significant implications for both patients and cancer services. Decisions on starting chemotherapy will be better informed by a more accurate risk assessment of toxicity. This will allow more refined dose and regimen choices ultimately leading to fewer high-grade toxicities, benefiting patients’ quality of life and reducing the strain on health services that would otherwise have had to manage these toxicities.

If we are unable to validate the CARG score, we will look at the utility of G8 and CFS in predicting chemotherapy toxicity in our study population.

We will also describe the prevalence of frailty in patients aged >65 years who are commencing first-line chemotherapy in our population and demonstrate the feasibility of implementing frailty assessment in routine practice. This will help inform future NHS service development.

Finally, this study will assess the value of risk prediction tools compared with clinicians’ estimates of toxicity risk, as well as exploring patients’ perception of risk associated with chemotherapy in this population.

**METHODS AND ANALYSIS**

This is a UK multicentre prospective observational study (non-randomised) which will recruit patients aged >65 years who are commencing first-line neoadjuvant, adjuvant or palliative chemotherapy for a solid-organ malignany with a prognosis of >3 months.
The study plans to recruit 500 patients over the course of 24 months using centres which are part of the National Oncology Trainee Collaborative for Healthcare research (NOTCH) network. 17 A prestudy survey sent to 21 centres indicated this number is feasible to recruit. Further details on sample size calculations can be found in the Statistical Analysis Plan below. Participants will be followed up over a period of 6 months or until completion of treatment—whichever is earliest. Recruitment will commence in April 2021 and is anticipated to complete in April 2022.

The CARG score has not been validated in a UK population therefore the study does not alter treatment decision. Participants will not be required to undergo any additional investigations or treatments. The local clinical team responsible for the patient will be able to access and use the additional information gathered, and address any issues as needed.

Study population
Participants will be ≥65 years old commencing first-line chemotherapy with any treatment intent for a solid-organ malignancy. The inclusion and exclusion criteria are shown in box 1.

Recruitment process
Potential study participants will be identified by the care team in each participating site. Each participating site will develop their own strategies for identifying participants. Participant advertising material can be distributed for local promotion. Potential participants will be provided with a patient information sheet (PIS) to read prior to their clinic review where possible or given time to read this literature after the clinic in all other cases (online supplemental file 1).

Consent and registration
Consent to participate in the study will take place during a standard clinic appointment. During the new patient clinic review, an authorised member of the research team will discuss participation in this study and seek consent once the participant has had sufficient time to consider the PIS and ask any questions. Questions regarding the study will be answered to the satisfaction of the potential participant in a language understandable to them. As this is an observational study only, it is deemed reasonable to discuss the study and consent during a single clinic visit if that fits the pathway of the centre. In the current climate, returning for additional study visits also puts participants at greater risks given that hospitals are known to act as a reservoir for SARS-CoV-2, the causative agent for COVID-19. In some centres where patients are consented for chemotherapy at a second appointment, the participant could consent to the study at this visit.

Assenting participants will be asked to document their consent by initialling the boxes on the consent form, printing and signing their name, and dating the form. The investigator must complete the header details on the consent form and check that the participant has completed the consent form correctly. The investigator will also print and sign their name and date the form contemporaneously.

The participant will be assigned a study number. All study IDs will be of the format XXXYYY where XXX is the centre code and YYY is the participant number.

The original consent form will be filed in the investigator site file. A copy of the consent form will be given to the participant and a copy will be retained in the participant’s notes.

The principal investigator (PI) retains overall responsibility for the informed consent of participants at their site and must ensure that any person delegated responsibility to participate in the informed consent process is duly authorised, trained and competent to do so according to the ethically approved protocol, principles of good clinical practice (GCP) and Declaration of Helsinki 1996.

The right of a participant to refuse participation without giving reasons must be respected. The participant must remain free to withdraw at any time from the study without giving reasons and without prejudicing his/her further treatment. If after consenting to participate, the patient opts not to have treatment or is deemed not suitable for treatment, this will be recorded and no further data will be collected. At no point during the process of obtaining informed consent must the researcher or any member of the research team coerce or unduly influence the participant to take part in the study. None of the oral or written information concerning the study should contain any language that causes the participant to waive or appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor or their agents from liability for negligence.

The PIS and consent form given to the participant must be the most current versions approved by the Research Ethics Committee. The version number and date must be printed on the document.

Study assessments
Data will be collected by the direct care team via structured forms which will be completed during the delivery
of routine care to the participants enrolled within the study. The study flowchart is shown in figure 1. The CARG score will be calculated using the established predefined scores and standardised toxicity severity definitions (Common Terminology Criteria for Adverse Events (CTCAE) V.5). This will limit variation in intersite and interuser assessment.

Documents will be locally collected at each of the study sites and manually inputted into the relevant case report form (CRF). The input information will remove all patient identifiable information and will be stored against a unique study specific ID. On completion of the data collection at each site, the data will be securely transferred to the analysis environment where the data will be collated prior to analysis.

**Study pathway**

During a standard clinic appointment, following consent for chemotherapy, each participant will be asked additional health questions (AHQ) (online supplemental file 2). This is estimated to take <10 min. This information is of additional clinical value and available to the treating physician. Information collected in the AHQ should be recorded in the BASELINE AHQ CRF. Information should be collected prior to commencing cycle 1 of chemotherapy.

After completion of the clinic visit the participant will be provided with a participant questionnaire (PQ) (online supplemental file 3) to complete. This is estimated to take <10 minutes to complete. This will be returned to an authorised member of the research team. Information collected from the PQ should be recorded in the BASELINE PQ CRF. Information should be collected prior to commencing cycle 1 of chemotherapy. The CARG score will be calculated retrospectively from the baseline data at the end of the study period.

The authorised member of the research team collecting the information in the AHQ will complete BASELINE RE CRF (online supplemental file 4). This information should be collected following the end of the clinic consultation, and prior to receiving the results of the PQ.

The results of routine assessments and investigations performed prior to cycle 1 of chemotherapy should be recorded in the BASELINE DATA CRF once consent has been obtained. This may be after treatment has commenced. Where an investigation listed on the CRF has not been performed as part of routine care this should be documented, but an investigation should not be ordered for the purpose of this study if it has not been performed during routine care.

Participants will be assessed during treatment as per local standard care. Toxicity will be assessed according to CTCAE V.5 and only grade 3 or above toxicities will be recorded in the progress CRF. Details of hospital admissions will be obtained from the medical records retrospectively.

The PROGRESS CRF should be completed by the time of chemotherapy completion or by 6 months—whichever is earliest.

**Outcome measures**

**Primary outcome**

1. To validate the CARG score’s ability to predict grade 3–5 toxicity in patients aged ≥65 years who are receiving first-line chemotherapy in the UK national health system.

**Secondary outcomes**

1. Describe the prevalence of frailty in patients of age ≥65 years commencing first-line chemotherapy in the UK.
2. Assess the utility of the G8 frailty assessment and Rockwood frailty score in predicting the occurrence of grade 3–5 toxicity.
3. Demonstrate the feasibility of implementing frailty assessment in routine practice.
4. Describe patient and clinician perception of toxicity risk associated with chemotherapy.

Statistical analysis plan
As the study is an observational study, the sample size calculation has been made based on precision as opposed to power as is typical for interventional studies. This attempts to estimate the population size needed to gain a specified level of precision of the CIs. This calculation has been made using the R Shiny web application ‘precisely’. Calculations used risk rates derived from the original 500 patient development cohort of the CARG study. The lowest pairwise difference in risk for grade 3 or more toxicity was between the low CARG (30.47%) and intermediate CARG (51.54%) groups with a risk difference of 21.07%. The same study also identified 50% of patients as being in the intermediate-risk group and 25% each in the other two groups. Based on a 500 patient cohort, this would yield on average 125 low-risk and 250 intermediate-risk groups. Based on these numbers, precision of the 95% CI would be estimated at 0.2. Even assuming a 15% dropout rate of participants this would give a precision of 0.23. Both of these would be sufficient to identify the expected scale of risk difference and the majority of clinically relevant risk differences.

Prior to commencing analysis, a detailed statistical analysis plan will be produced. The CARG score will be calculated from 11 prechemotherapy variables. Patients will be categorised into low (0–5), intermediate (6–9) and high (10–19) risk. Observed grade 3–5 toxicity rates between groups will be compared using a \( \chi^2 \) test of proportions. We will then assess the validity of the model by composing receiver-operating characteristic curves and calculating the area under the curve (c-statistic) for the CARG score.

A descriptive analysis of the prevalence of frailty in the population and the feasibility of implementing frailty assessment will be performed. Patient and clinician perception of risk will be compared using a paired t-test of the baseline perceived percentage risk.

Data missing from the CRF will, where possible, be completed retrospectively from written records.

Patient and public involvement
The PIS, consent form and patient questionnaire have been reviewed by older adult patients (265 years as per inclusion criteria of study) who are either receiving systemic anticancer treatment or have previously received treatment (for any tumour type and with all intents, for example, neoadjuvant, adjuvant and palliative).

ETHICS AND DISSEMINATION

Ethical approval
This TOASTIE study has been approved by the East of Scotland Research Ethics Service 20/ES/0114 with protocol V.1.2 dated 16 November 2020.

The study will be conducted in accordance with the principles of GCP as applicable under UK regulations, the NHS Research Governance Framework and through adherence to study standard operating procedures. All members of the research team will be GCP-trained. The study will also be performed in accordance with the recommendations guiding physicians in biomedical research involving human participants adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964, amended at the 52nd World Medical Association General Assembly, Edinburgh, UK, October 2000.

Patients will be pseudoanonymised. The care team will be responsible for assigning study numbers to consented participants as per the protocol. No patient identifiable data will be transferred to the research team. Paper questionnaires completed by participants will be kept securely in a locked drawer in a locked security-controlled office, in the investigator site file at each recruiting site by the care team.

Electronic data will be stored at each site in a designated password-protected folder, on secure password-protected NHS servers. Only relevant study personnel on the delegation log will have access to this.

Linked-anonymised data will be shared via nhs.net (which is a secure mail system regularly used by clinicians to share patient data) to a secure mailbox to which only one person has access. It will be transferred to a secure, password-protected study-specific domain on a high-secure tertiary centre NHS Trust (The Leeds Teaching Hospitals NHS Trust) server, to which only relevant study personnel will have access. The master Microsoft Excel document within this domain will additionally remain password-protected.

Data storage and security
All information collected during the course of the study will be kept strictly confidential. Information will be held securely on paper and electronically. The research team will comply with all aspects of the 2018 Data Protection Act.

Investigator site files, including copies of CRFs and eligibility/link-anonymisation forms, will be stored securely at NHS sites by each PI for a period of 10 years. This may be either in physical or electronic form as per local NHS policy. The Leeds Teaching Hospitals NHS Trust will store link-anonymised ‘Confirmation of Consent’ forms and CRFs for 10 years. After 10 years, arrangements for confidential destruction of data and documents that are due to be disposed of will be made by the sponsor.

This study is conducted within the framework of information governance (IG) good practice.

The data analysis will be undertaken in two settings: either within the NHS by employees of the organisation or university researchers within NHS-approved secure data environments. All staff will have undergone appropriate training on IG and will be given access to the research data files for the
purposes of this study. Research data files will be stored on password-protected NHS computers on secure networks or other NHS-approved secure cloud infrastructure.

University colleagues may have access to increased resources for delivering this work, in particular human capital that will allow the fastest route to realising the potential patient benefit of this research data. This process will follow the formal data release process in place at Leeds Teaching Hospital Trust.

Statement of indemnity

This study is sponsored by the Leeds Teaching Hospital Trust who will be liable for negligent harm caused by the design of the study. The NHS has a duty of care to participants, whether or not the participant is taking part in a study, and the NHS remains liable for clinical negligence and other negligent harm to participants under this duty of care.

Dissemination of results

Following completion of follow-up and analysis of data, results will be communicated in academic forums such as presentation at academic meetings and publication in journals. Results will also be communicated to the public through patient networks. Publication will be under joint authorship on behalf of NOTCH. We used the Standard Protocol Items: Recommendation for Interventional Trials (SPIRIT) checklist when writing this report.20

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Contributors HD: designed the study and wrote the protocol; MAB: drafted the manuscript, assisted in the study design and writing of the protocol; KZ: designed the statistical analysis plan for the study; SM, MR, CMJ, ACO-B, RDP, DS: assisted in the study design and writing of the protocol. All authors approved the final version.

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Competing interests ACO-B has received honoraria from BMS, MSD and Roche outside the scope of this work. MR has received honoraria from MSD, Servier and Astellas Pharma outside the scope of this work. RDF has undertaken speaking, consulting and advisory roles for Eli Lilly, SMS, Pfizer, Sanofi, Servier; and received research funding (not related to the work in this manuscript) from Astra Zeneca, Roche, MSD, Merck serrano, Eli Lilly, Five Prime Therapeutics, Clovis, Boston Biomedical and Janssen.

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Tolerance Of Anti-cancer Systemic Therapy In the Elderly (TOASTIE)  v1.3 (16.11. 20) IRAS ID: 281443

INSTITUTION LETTERHEAD HERE

Participant Information Sheet

Tolerance Of Anti-cancer Systemic Therapy In the Elderly (TOASTIE)

National Oncology Trainee Collaborative for Healthcare (NOTCH)

We are inviting you to take part in this research study

Before you choose whether or not to take part, we want you to understand why we are doing the study. We also want to tell you what it will involve if you agree to take part. Please take time to read this information carefully. You can ask us any questions you have and talk to other people about it if you want. We will do our best to answer your questions and give you any more information you ask for. You do not have to decide straight away.

Why is the study being done?

- The number of people over the age of 65 years who have cancer and are treated with chemotherapy is going up. As you get older, some people start to have problems with their health. This means they can take longer to get better after they have been ill. Doctors call this ‘frailty’.

- We know people who are living with frailty can be more likely to fall or have to go into hospital. Not all people over 65 are living with frailty, but it becomes more common as you get older.

- It can be hard to tell if people are living with frailty. Sometimes we don’t ask the right questions. If we find people who are living with frailty, we might be able to put extra help in place to try and prevent problems from happening.

- All patients having chemotherapy (which we also call Anti-cancer Systemic Therapy), are at risk of having side effects. Some people have bad side effects and might even need to go into hospital. At the moment, it is hard to know in advance which people are at higher risk of side effects from chemotherapy.
• We think people who are living with frailty might be more likely to struggle with the side effects of chemotherapy.

• There is something called a CARG score which might help us find people who are more likely to have side effects. It is a mix of simple questions and the results of blood tests (which you will have anyway).

• The CARG score was tested in America and was helpful. It didn’t work so well in Australia. We want to find out if it will be helpful for patients receiving chemotherapy in the UK.

• We also want to know how many people over 65 who have chemotherapy are living with frailty. This will help us to provide the right support for these people.

• We will also assess whether you and your doctors are good at predicting the likelihood of side effects.

• As the CARG score has not been proven to be helpful in the UK we will not change your treatment based on your CARG score. Your doctor will know how you answered the questions and will try to help with any problems that are raised as a result.

**Do I have to take part?**

No. You can choose if you want to take part or not.

If you do decide to take part, you can stop at any time.

You do not need to give a reason and the doctors and nurses will still look after you in the same way.

If you do decide to take part, you will be given this information sheet to keep and will be asked to sign a consent form.

**Why are you being asked to take part?**
You are being asked to participate because you are over the age of 65 years and are about to start treatment with chemotherapy.

**How many people will take part in the study?**

Approximately 500 people around the UK will take part in this study.

**Description of Research Study**

This study is an observational study, which means your treatment will not change and we will merely look at what happened to you during and after treatment.

We will ask you some questions about frailty and what you think is your risk of side effects from treatment. This will be done on your first clinic visit. Your doctor will use this information to calculate a CARG score.

We will look at your medical records to collect some health information about you that is relevant to your cancer diagnosis and treatment. We will also look to see if you have had side effects from chemotherapy or have had to go into hospital during your chemotherapy treatment.

We will see if this helps us to find people who are more likely to have side effects from chemotherapy. We will also see how many people older than 65 and having chemotherapy are living with frailty.

**What will happen if you take part?**

After your clinic visit, we will ask you some extra questions about your general health. This should take less than 5 minutes.

We will also ask you to fill in a simple questionnaire. This should take less than 10 minutes. Your doctor will be able to see what you have said.

You only have to do this once.
We will look at your medical records to see if you have had side effects from treatment or had to go into hospital during treatment. A member of the team who is not your own doctor may look at the records.

This information will be shared with other members of the research team, who may be outside this hospital. The information we collect will be labelled with a unique study number (not your name) so that your information is anonymised.

**Will taking part in the study affect my usual care?**

No. Your treatment will not be in any way affected by participating in this study.

**What are the possible benefits of taking part?**

This study will not change your treatment in any way.

Your doctor will spend slightly longer than usual with you finding out about your general health in a little more detail.

We hope that the results from this study will be helpful to future patients when making decisions about their treatment.

**What are the possible disadvantages and risks of taking part?**

This study will make your clinic visit today a bit longer and you will need to fill in a questionnaire. We should be able to do both these things in less than 15 minutes.

As no changes to your treatment or follow-up are necessary for this study, we do not anticipate any significant risks or disadvantages to you.

**What if something goes wrong?**

In the event that something does go wrong and you are harmed during the research and this is due to someone’s negligence then you may have grounds for a legal action for compensation against the Leeds Teaching Hospitals NHS
Trust but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

(insert local PALS or PASS information here)

**How will the results of the study be shared?**

We hope to publish the results of the study in an academic journal and at medical conferences so other doctors can learn from the results. The results will not affect your care but we can provide you with a summary of them if you wish. You will not be personally identified in any report or publication on this study.

If you want to find out the results of the study you can contact the research team as detailed below.

The results will be shared on the website:  www.uknotch.com

**Who is organising this research?**

This project has been organised by the collaborative NOTCH  - National Oncology Trainee Collaborative for Healthcare Research.

The sponsor (controller) of the study is the Leeds Teaching Hospitals NHS Trust.

**What will happen with the information collected about me?**

The study will be conducted in compliance with the Data Protection Act, 2018. All information that is collected about you during the course of the study will be kept strictly confidential. All information about you that is shared with the study will be stored on an NHS secure computer, only by a study number, and not by your name, so that your information is pseudo-anonymised.

If you consent to take part in this study, you will also be agreeing to allow authorised staff from the research team to inspect your medical records to

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update the study. Under no circumstances will your name or address be disclosed outside the clinic.

We would like you to let us tell your GP and any other doctors looking after you that you have entered this study to help us ensure we collect the health information we need.

Leeds Teaching Hospitals NHS Trust (LTHT) is the sponsor for this study. The trust will be using information we gather from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. LTHT will keep this information about you for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting your local study investigator above.

Your treating hospital will collect information from you and your medical records for this research project in accordance with instructions from LTHT. This information is kept securely in a locked drawer in locked security controlled office, in the investigator site file at each recruiting site by the care team. The team at the hospital will keep your name, NHS number and contact details confidential and will not pass on this information. The hospital team will use this information as needed to contact you about the research study and make sure that relevant information about the study is recorded in your care records, and to oversee the quality of the study. The link anonymised data will be transcribed onto an electronic form which will be submitted to the research team. NHS.net email will be used for transfer and excel documents will be password protected.

Certain individuals from LTHT and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. The hospital team will keep identifiable information about you from this study for 10 years after the study has finished.
Who has reviewed this study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. The East of Scotland Research Ethics Service REC 1, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of research ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from Leeds Teaching Hospitals NHS Trust whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

Contact details for further information.

If you have any questions regarding this study please contact:

Local Principal Investigator details: (insert details here)

Central Research Team: Dr H Dearden, helen.dearden1@nhs.net
CONSENT FORM

Title of Project: Tolerance Of Anti-cancer Systemic Therapy In the Elderly (TOASTIE)

Name of Researcher:

Please initial box

1. I confirm that I have read the information sheet dated.......... (version..........) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the research team, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.

5. I agree to my General Practitioner being informed of my participation in the study.

6. I agree to take part in the above study.

Name of Participant  Date    Signature

Name of Person  Date    Signature
taking consent

When completed: 1 for participant; 1 for researcher site file; 1 to be kept in medical notes.
Additional Health Questions - Guide for Physician

1. How is the patient’s hearing? 0. normal 1. impaired?

2. Has the patient had any falls in the last year? 0. No 1. 1-2 2. 3+

3. In the past 4 weeks has patient’s physical or emotional health interfered with social activities eg visiting friends?
   1. all the time 2. most of the time 3. some of the time 4. a little of the time 5. none of the time

4. Can the patient take their own medications?
   1. without help 2. with some help (pre-prepared eg blister pack/reminders) 3. Unable

5. Does patient’s health limit them walking 100m?
   1. Unable to 2. With breaks 3. no limitations

6. How many regular medications does the patient take? .................

7. Has the patient had any weight loss past 3 months?
   1. >3kg 2. 1-3kg 3. don’t know 4. no weight loss

8. Please describe the patient’s mobility
   1. bed/chair bound 2. gets around the home 3. gets out of the home

9. Has the patient’s food intake declined in the past 3 months?
   1. severe decrease 2. moderate decrease 3. no decrease

10. Does the patient have any psychological issues?
    1. moderate or severe dementia or depression 2. mild cognitive impairment
    3. Mild depression 4. no problems

11. Please score the Rockwood CFS (see attached guide) (1-9) ..........................

Time taken to answer these questions ............... mins
Researcher Evaluation - Guide for Physician

1. Have you already calculated the CARG score to estimate risk? Yes No

2. How likely do you think this patient will experience significant (G3+) toxicity
   a. Unlikely  b. Not very likely  c. Quite likely  d. Very likely

3. Please quantify this risk estimation as a percentage (see scale below)

0 means I think it definitely won’t happen to the patient → 100 means I think I will Patient will definitely experience significant toxicity

0-----10-----20-----30-----40-----50-----60-----70-----80-----90-----100
Tolerance Of Anti-cancer Therapy In the Elderly (TOASTIE): Patient Questionnaire

Patient ID: …………………………………

Thank you for agreeing to take part in this research study. These questions will let us know more about your general health and your thoughts regarding the risks of your treatment.

If you have any questions or need help to fill in the questionnaire please ask your oncology doctor or another member of the oncology team.

Please circle all options that apply to you for each question below:

1. Marital Status
   a. Single
   b. Married/living with partner
   c. Widow/widower
   d. Other (please describe)…………….

2. Please describe who you live with:
   a. I live alone
   b. I live with my partner/family member
   c. I am a carer for my partner/family member
   d. I live in a residential or nursing home
   e. Other - please describe here ………………………………..

3. If you need help, for example someone to help you with your shopping or take you to a hospital appointment, do you have someone you can count on to help you with this?
   a. Always
   b. Sometimes
   c. Never
   d. I never need help

4. Do you smoke?
   a. Yes
   b. No – I used to smoke
   c. No – I have never smoked

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5. How many times have you had to stay in a hospital (for one night or longer) in the last 12 months?
   a. 0
   b. 1-2
   c. 3 or more

6. If you compare yourself with most people the same age as you, how do you think your health is?
   a. Not as good as someone else my age
   b. As good as someone else my age
   c. Better than someone else my age
   d. Don’t know

7. How likely do you think it is that a side effect from chemotherapy will cause you to have to stay in hospital for one night or longer or have to stop treatment?
   a. Unlikely
   b. Not very likely
   c. Quite likely
   d. Very likely

Please mark your answer on the scale below:

0 means I think it definitely won’t happen to me → 100 means I think I will definitely need to stop treatment or stay hospital at some point during my treatment

0-----10-----20-----30-----40-----50-----60-----70-----80-----90-----100

8. We would like to know how good or bad your health is TODAY

Please mark on the scale to indicate how your health is TODAY.

0 means the worst health you can imagine → 100 means the best health you can imagine

0-----10-----20-----30-----40-----50-----60-----70-----80-----90-----100

Thank you for your help answering these questions
Please return it to the receptionist, your specialist nurse or the doctor you have just seen.
**Researcher Evaluation - Guide for Physician**

Please enter your answers to the questions below in the RE section of the CRF.

Thank you.

1. Have you already calculated the CARG score to estimate risk?  
   - Yes  
   - No

2. How likely do you think this patient will experience significant (G3+) toxicity?  
   a. Unlikely  
   b. Not very likely  
   c. Quite likely  
   d. Very likely

3. Please quantify this risk estimation as a percentage (see scale below)

   0 means I think it definitely won’t happen to the patient → 100 means I think I will  
   Patient will definitely experience significant toxicity  

   0----10----20----30----40----50----60----70----80----90----100