<Study Acronym + Logo>

<Full study title>

ISRCTN
NCT *(clinicaltrials.gov)*

<Version number and date>

<Amendments and previously approved versions>

SPONSOR:
FUNDERS: xxx
STUDY COORDINATION CENTRE: xxx

Ethics reference: xxx

Protocol authorised by:

Name:	**Role:**	Chief Investigator
Signature:	**Date:**	
Name:	**Role:**	<if coordinated at another centre>
Signature:	**Date:**	
Name:	**Role:**	Sponsor Representative
Signature:	**Date:**	

Main Contacts

Trial Management Group
[give name, address and contact numbers for each member of the trial management team, eg:]

Chief Investigator:
Co-investigators:
Statistician:
Trial Manager:

Trial Coordination Centre
[give name, address and contact numbers for whoever is responsible for managing the day-to-day aspects of the study, eg trial manager or data manager]

For general queries, supply of trial documentation, and collection of data, please contact:

Trial Manager and/or Data Manager:
Address:
Tel:
Fax:

Clinical Queries
Clinical queries should be directed to xxx who will direct the query to the appropriate person.

Sponsor

[Name and address with a supporting statement of the organisation which is taking on the legal responsibilities of the study. 'Sponsor' does not necessarily mean the same as 'funder' as a funder may only provide the financial resources for a project, particularly in the case of charity. A sponsor is the organisation that takes responsibility for project initiation, administration and management]

Funder
[Who is funding the study]

This protocol describes the xxx study and provides information about procedures for entering participants. The protocol should not be used as a guide for the treatment of other participants; every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study, but centres entering participants for the first time are advised to contact the trials centre to confirm they have the most recent version.

Problems relating to this trial should be referred, in the first instance, to the study coordination centre.

This trial will adhere to the principles outlined in the International Conference on Harmonisation Good Clinical Practice (ICH GCP) guidelines, protocol and all applicable local regulations.

Table of Contents

GLOSSARY OF ABBREVIATIONS

KEYWORDS

[Insert a list of keywords]

STUDY SUMMARY

TITLE

DESIGN

AIMS

OUTCOME MEASURES

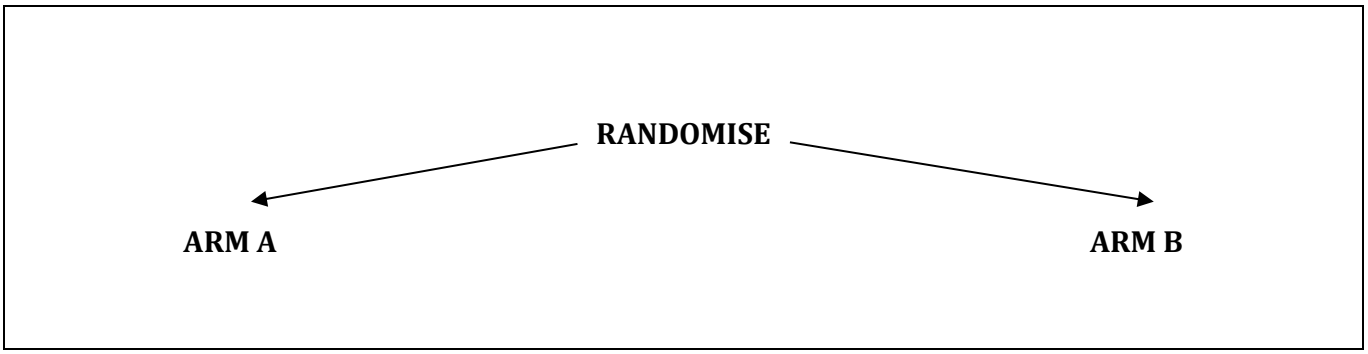
POPULATION

ELIGIBILITY

TREATMENT

DURATION

REFERENCE DIAGRAM



1. INTRODUCTION

1.1 BACKGROUND

[To include: review of previous studies, disease or area particulars, incidence, current treatment options, risks and benefits]

1.2 RATIONALE FOR CURRENT STUDY

[To include: research question and hypothesis, as well as potential risks and benefits]

2. STUDY OBJECTIVES

[List the primary, secondary and other study objectives]

3. STUDY DESIGN

[Type of study: eg randomised, double-blind, placebo, controlled, open, public health intervention, drug, cluster etc.]

[Duration: ie what constitutes the treatment phase and the follow-up phase of the study]

[Number and type of participants to be recruited: eg 800 participants, 400 in control and 400 in experimental arm]

[Study setting (multicentre or single centre, multi-country (provide country list)), type of site (e.g. recruiting, treating, continuing care etc) and what the specific requirements are for each]

3.1 STUDY OUTCOME MEASURES

What are the endpoints of the study? [eg: disease-free survival, toxicity etc]

3.2 RISKS AND BENEFITS

[Summarise known and potential risks and benefits, if any, of the intervention]

4. SELECTION AND WITHDRAWAL OF PARTICIPANTS

4.1 PRE-RANDOMISATION OR PRE-REGISTRATION EVALUATIONS

[What tests need to be included before a participant can enter the study? Eg, FBC, LFT, biopsy, CT scan. All screening procedures should be included]

4.2 INCLUSION CRITERIA

[Include justifications, if necessary]

4.3 EXCLUSION CRITERIA

[Include justifications, if necessary]

4.4 WITHDRAWAL CRITERIA

[Describe procedures for stopping early]
[Describe proceduresfor participants should they wish to withdraw their consent, ie will all data to date be held, will all date be destroyed]

5. RANDOMISATION AND ENROLMENT PROCEDURE

5.1 RANDOMISATION OR REGISTRATION PRACTICALITIES

[Describe procedures enrolling participants and what needs to be completed prior to randomisation. Give numbers to ring, or websites to access for randomisation]

5.2 UNBLINDING (IF APPLICABLE)

[Unblinding is discouraged during the study. Give details on how this will be done (if applicable).]

[Systems for SUSAR and SAR reporting should, as far as possible, maintain blinding of individual clinicians and of trials staff involved in the day to day running of the trial. Once all the information for the assumed SUSAR has been collated, the unblinding procedure detailed in the trial protocol should be followed. It is very important that details of the unblinding process are included in the trial protocol. For example, when reporting adverse events for blinded trials that involve two active drugs, the person responsible for the evaluation for causality and expectedness might be able to state that if the patient was on drug A, the event would be causal and/or unexpected, but if on drug B, it would be expected. If the event were unexpected for either of the active drugs, the case should be unblinded.]

6. TRIAL MEDICATION

6.1 Name and description of investigational medicinal product(s)
[Give a full description of each IMP]

6.2 Legal status of drug
[Is drug licensed for use in the intended country (ies) and what is its indication]

[If unlicensed or ring-fenced commercially supplied IMP then the following statement can be used:
The trial is being carried out under a Clinical Trial Authorisation (CTA). The drug is therefore only to be used by the named investigators, for the patients specified in this protocol, and within the trial.]

6.3 Summary of Product Characteristics (SmPC) or Investigator Brochure (IB)
[Detail if an SmPC or IB is going to be used, what version and how updated versions will be incorporated into the trial.]

6.4 Drug Storage and Supply
[Describe the procedures for shipment, receipt, distribution, return and destruction of the IMP, including placebo.]

6.5 Preparation and labelling of IMP
[Provide a precise and complete description of the preparation and labelling of the IMP.]

6.6 Dosage schedules/modifications
[Give a precise and complete description of the dosage schedules and any required dose modifications.]

6.7 Known drug reactions and interaction with other therapies
[Identify any know drug reactions or interactions with other therapies.]

6.8 Concomitant medication
[Provide a full description of con meds – permitted/not permitted etc.]

6.9 Trial restrictions
[Provide a full description of any trial restrictions – dietary requirements, contraception etc.]

6.10 Assessment of compliance
[Describe how compliance will be assessed – monitoring of participants taking meds, acceptable level of IMP compliance, how this information will be recorded, follow up for non-compliant participants etc.]

6.11 Name and description of each Non-Investigation Medicinal Product (NIMP)
[Provide a full description of each NIMP – products supplied to trial participants according to the protocol but are not under investigation, including dosage, treatment duration and administration.]

7(I). SAFETY REPORTING FOR DRUG TRIALS

[This section is applicable to drug studies only. For non-drug trials, please see section 7(II)]

7.1 DEFINITIONS

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational medicinal product (IMP), whether or not considered related to the IMP.
Adverse Reaction (AR)	Any untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant. The phrase "response to an investigational medicinal product" means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out. All cases judged by either the reporting medically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the trial medication qualify as adverse reactions.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • Results in death • Is life-threatening • Requires inpatient hospitalisation or prolongation of existing hospitalisation • Results in persistent or significant disability/incapacity • Consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting investigator, believed with reasonable probability to be due to one of the trial treatments, based on the information provided.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse reaction, the nature and severity of which is not consistent with the information about the medicinal product in question set out: • In the case of a product with a marketing authorisation, in the summary of product characteristics (SmPC) for that product • In the case of any other investigational medicinal product, in the investigator brochure (IB) relating to the trial in question.

7.2 CAUSALITY

Most adverse events and adverse drug reactions that occur in this study, whether they are serious or not, will be expected treatment-related side effects due to the drugs used in this study. The assignment of causality should be made by the investigator responsible for the care of the participant using the definitions in the table below.

If any doubt about the causality exists the local investigator should inform the study coordination centre who will notify the Chief Investigators. The pharmaceutical companies and/or other clinicians may be asked to advise in some cases.

In the case of discrepant views on causality between the investigator and others, all parties will discuss the case. In the event that no agreement is made, both points of view are to be reported.

Relationship	Description

Unrelated	There is no evidence of any causal relationship
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial medication). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatment).
Possible	There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the trial medication). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant treatments).
Probable	There is evidence to suggest a causal relationship and the influence of other factors is unlikely.
Definitely	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.
Not assessable	There is insufficient or incomplete evidence to make a clinical judgement of the causal relationship.

7.3 REPORTING PROCEDURES

Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the study coordination centre in the first instance. A flowchart is given in appendix xx to aid in the reporting procedures.

7.3.1 Non serious Adverse Reactions (ARs)/Adverse Events (AEs)

[The CI can decide how to record and report adverse events/reactions, whether expected or not. It may be decided that all or only some non-serious AEs/ARs are to be recorded. All that are important to safety monitoring in the research and to the evaluation of the intervention, therefore consistent with the purpose of the research must be collected.]

[All AEs reported at a trial visit should be recorded unless otherwise specified. This is part of routine data collection. The AE should be recorded in the participant's medical records where appropriate. They are usually collected and recorded on CRFs, often on specific AE logs that should be kept along with the other CRFs for the study. It should be clearly stated in the protocol and the local SOP what will be recorded and how the reporting is to be managed.]

7.3.2 Serious Adverse Reactions (SARs)/Serious Adverse Events (SAEs)

Serious Adverse Events (SAEs) and Serious Adverse Reactions (SARs) should be reported to the study coordination centre within 24 hours of the local site being made aware of the event.

An SAE form should be completed and submitted to the study coordination centre with as much detail of the event that is available at that time. If awaiting further details, a follow up SAE report should be submitted promptly upon receipt of any outstanding information. The CI (for a single-centre trial) or PI (for a multi-centre trial) must record the event with an assessment of seriousness, causality and expectedness.

[Expected SAEs for the disease and/or trial drug/intervention should be listed in the protocol. It should be stated that these would not require reporting or be considered to be SUSARs unless the severity of the event was considered to be unexpected. Where SAEs are listed but happen rarely then an explanation of the likely risk of an event may be considered of value.]

Any events relating to a pre-existing condition or any planned hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

7.3.3 SUSARs

All SAEs assigned by the PI or delegate as both suspected to be related to IMP-treatment and unexpected will be classified as SUSARs and will be subject to expedited reporting to the Regulatory Authority (RA).

The Sponsor (or delegate) will inform the RA, and the ethics committee of UK-relevant SUSARs within the required expedited reporting timescales (as per the Sponsor's Standard Operating Procedure for recording, managing and reporting of adverse events for IMP studies).

For blinded trials, all SUSARs must be reported assuming the active compound is involved.

[SUSARs occurring in all other countries (EU and non EU), the reporting requirements depend on the national regulations. The protocol should specify procedures for both the timing and format of reports of SUSARs.]

In the case of a suspected, unexpected, serious adverse reactions (SUSAR), the staff at the site should:

1. Contact the study coordination centre immediately by phone or email to inform them of the event.
2. Submit a completed SAE form (signed and dated) within 24 hours, together with relevant treatment forms and anonymised copies of all relevant investigations.
3. Submit any additional information promptly upon request.

Contact details for reporting SAEs and SUSARs
Fax: xxx, attention xxx
Please send SAE forms to: xxx
Tel: xxx (Mon to Fri 09.00 – 17.00)

7(II). SAFETY REPORTING FOR NON-DRUG TRIALS

[This section is applicable for non-drug trials only. All drug trials should follow safety reporting procedures in section 7(I)]

7.1 DEFINITIONS

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or study participant
Serious Adverse Event (SAE)	A serious event is any untoward medical occurrence that: Results in death Is life-threatening Requires inpatient hospitalisation or prolongation of existing hospitalisation Results in persistent or significant disability/incapacity Consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.

7.2 REPORTING PROCEDURES

Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

7.2.1 Non serious AEs

[The CI can decide how to record and report adverse events, whether expected or not. It may be decided that all or only some non-serious AEs are to be recorded. All that are important to safety monitoring in the research and to the evaluation of the intervention, therefore consistent with the purpose of the research must be collected.]

[All AEs reported at a trial visit should be recorded unless otherwise specified. This is part of routine data collection. The AE should be recorded in the participant's medical records where appropriate. They are usually collected and recorded on CRFs, often on specific AE logs that should be kept along with the other CRFs for the study. It should be clearly stated in the protocol and the local SOP what will be recorded and how the reporting is to be managed.]

7.2.2 Serious AEs

Serious Adverse Events (SAEs) should be reported to the study coordination centre within 24 hours of the local site being made aware of the event.

An SAE form should be completed and submitted to the study coordination centre with as much detail of the event that is available at that time. If awaiting further details, a follow up SAE report should be submitted promptly upon receipt of any outstanding information.

[Expected SAEs for the disease and/or trial drug/intervention should be listed in the protocol. It should be stated that these would not require reporting or be considered to be SUSARs unless the severity of the event was considered to be unexpected. Where SAEs are listed but happen rarely then an explanation of the likely risk of an event may be considered of value.]

Any events relating to a pre-existing condition or any planned hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

Contact details for reporting SAEs
Fax: xxx, attention xxx
Please send SAE forms to: xxx
Tel: xxx (Mon to Fri 09.00 – 17.00)

8. ASSESSMENT AND FOLLOW-UP

[How long will the participant be followed up for? When and what will their assessments consist of? Efficacy assessments should also be included]

8.1 LOSS TO FOLLOW-UP

[list procedures for participants lost to f/up, eg if flagging through Office of National Statistics or equivalent]

8.2 TRIAL CLOSURE

[list procedures for closing a trial, whether early or after end of recruitment.]
[Definition of end of trial]

9. STATISTICS AND DATA ANALYSIS

[Statistical plan, eg sample size calculation and data analysis, methods of randomisation.]

[Describe interim analyses, if planned]

Data and all appropriate documentation will be stored for a minimum of 5 years after the completion of the study, including the follow-up period.

10. MONITORING

10.1 RISK ASSESSMENT

[Describe the risk assessment that has taken place for the study. Is the study considered high, medium or low risk? How does this justify level of monitoring provided?]

10.2 MONITORING AT STUDY COORDINATION CENTRE

[eg data entry checks, double data entry, consent form checks, missing or unusual data values]

10.3 MONITORING AT LOCAL SITE

[based on risk assessment, how many site visits, what level of source data verification]

11. REGULATORY ISSUES

11.1 CTA (APPLICABLE IF A DRUG TRIAL)

This study has Clinical Trials Authorisation from the relevant RA name. Reference: xxx

[this will change if the study is conducted overseas, include other competent authorities as required]

11.2 ETHICS APPROVAL

[The protocol should state where approval has been sought for the trial protocol, informed consent forms and other relevant documents (e.g. advertisements and GP information if applicable).]

The Study Coordination Centre has obtained approval from the Research Ethics Committee name, as well as the xxx (local ethics committee).

[The protocol should demonstrate that the trial will receive continuous ethical review and approval.]

[For example, how substantial amendments will be managed e.g. will not be implemented until a favourable opinion has been granted from the ethics committee (as well as any other applicable regulatory bodies). How correspondence with ethics committee will be filed – in TMF/ISF. Submission of annual progress reports and notification of end of study.]

11.3 CONSENT

Informed consent must be obtained prior to the participant undergoing procedures that are specifically for the purposes of the study.

Consent to enter the study must be sought from each participant only after a full explanation has been given, an information leaflet offered and time allowed for consideration. Signed participant consent should be obtained.

The right of the participant to refuse to participate without giving reasons must be respected.

All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

The PI is responsible for ensuring that all vulnerable participants are protected and participate voluntarily in an environment free from coercion or undue influence.

[Where the participant population is likely to include a significant proportion of participants who cannot read or write, require translators or have cognitive impairment, appropriate alternative methods for supporting the informed consent process should be employed.]

11.4 CONFIDENTIALITY

Any participants' identifiable data collected by the Study Coordination Centre will be stored securely and their confidentiality protected in accordance with the Data Protection Act 1998.

[Describe how participant confidentiality will be maintained and how the trial is compliant with the data protection act.]

11.5 INDEMNITY

The Sponsor's name holds Public Liability ("negligent harm") and Clinical Trial ("non-negligent harm") insurance policies which apply to this trial.

11.6 SPONSOR

The Sponsor's name will act as the main sponsor for this study. Delegated responsibilities will be assigned locally.

11.7 FUNDING

xxx are funding this study. [Any per patient payments, investigator payments should be detailed here]

11.8 AUDITS AND INSPECTIONS

The study may be subject audit by the Sponsor's name under their remit as sponsor, the Study Coordination Centre and other regulatory bodies to ensure adherence to GCP.

12. TRIAL MANAGEMENT

A Trial Management Group (TMG) will be appointed and will be responsible for overseeing the progress of the trial. The day-to-day management of the trial will be co-ordinated through the xxx Study Coordination Centre.
[Describe whether an oversight committee, eg Trial Steering Committee or Data Monitoring Committee or Data Monitoring Safety Board will be convened]

13. PUBLICATION POLICY

The study's publication policy should be described in full. Below is an example paragraph.
All publications and presentations relating to the study will be authorised by the Trial Management Group. The first publication of the trial results will be in the name of the Trial Management Group, if this does not conflict with the journal's policy. If there are named authors, these will include at least the trial's Chief Investigator, Statistician and Trial Coordinator. Members of the TMG and the Data Monitoring Committee will be listed and contributors will be cited by name if published in a journal where this does not conflict with the journal's policy. Authorship of parallel studies initiated outside of the Trial Management Group will be according to the individuals involved in the project but must acknowledge the contribution of the Trial Management Group and the Study Coordination Centre.

14. REFERENCES

[List of useful and relevant references for the study]

EXAMPLE APPENDICES

[Appendices should be additional information to the protocol and can consist of:]

- Eligibility/Assessment Criteria (e.g. ECOG, RECIST, CTCAE etc)
- PIS, Consent form, GP letter (although may be more practical to have them separate)
- Expected side effects
- Schedule of procedures/events table
- Safety Reporting Guidelines/Flowchart