Quality Control Document:

Risk Assessment Report

# Purpose

The purpose of this document is to provide a template for the development of a project-specific risk assessment report. The risk assessment report will identify and evaluate the potential risks within the project, documenting the actions taken to mitigate and/or minimise these risks. This document has been designed for clinical trials and may be used as a tool to consider different aspects of the trial; however, the template may also be adapted for clinical studies. It should be used in conjunction with the Project Oversight and Quality Management SOP (UoB-POS-SOP-001).

This document has been produced with reference to the guidelines provided by the Medical Research Council (MRC) / Department of Health (DH) / Medical Healthcare Regulatory Agency’s (MHRA) ‘[Risk-adapted approaches to the management of clinical trials of investigational medicinal products](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/343677/Risk-adapted_approaches_to_the_management_of_clinical_trials_of_investigational_medicinal_products.pdf)’ (PDF – 4.5 MB). This document defines a simple risk categorisation for clinical trials based on the marketing information of the investigational medicinal product (IMP) and standard of care.

# Instructions

## Development of the risk assessment report

1. Remove these first two instruction pages.
2. Update the document’s header with the trial identifier.
3. Update the document’s footer with the version control details, retaining the reference to this quality control document (QCD).
4. Complete the trial information section (title, sponsor reference, IRAS number and REC number)
5. Complete section 1 ‘Risks to participant safety associated with intervention(s) being tests’ and section 2 ‘Other risks associated with the design and methods of the trial’.
* Instructions and guidance notes are given in red italic text.
* Where appropriate, carrying out the risk assessment will be performed in collaboration with the trial coordinator, statistician and programmer.
1. For CTIMPs, submit the risk assessment report as part of the initial sponsorship submission to the Research Ethics, Governance & Integrity Team (REGI). Note: for non-CTIMPs and studies, REGI may request a copy of the risk assessment.
2. Prior to finalisation, complete the ‘Document control sheet’ section. Refer to the Essential Document Development and Maintenance SOP (UoB-ESD-SOP-001) for guidance on a version control system.
3. As a minimum, ensure the chief investigator (CI) reviews and approves the finalised version of the risk assessment report.
4. File it in the trial master file.

## Review of the risk assessment report

1. Review the trial’s risk profile following any significant change(s) to the trial, including:
* a substantial amendment to the protocol
* a change to the organisation of the project
* a significant change to the summary of product characteristics/investigator’s brochure
* after a serious breach
* a change in risk identified during interim analysis.
1. Where the risk profile has not changed, complete section 3 ‘Risk assessment report review’.
2. Where the risk profile has changed, complete points 13-17 in ‘Amendments to the risk assessment report’.

## Amendments to the risk assessment report

1. Update relevant sections in the risk assessment report and retain a version containing the tracked changes for the audit trail.
2. Update the ‘Document control sheet’ and the document’s footer with the latest version control details.
3. As a minimum, ensure the CI reviews and approves each updated/new version of the risk assessment report.
4. For CTIMPs, forward a copy of the updated/new version of the risk assessment report to the REGI for information.
5. File the updated/new version of the risk assessment report in the trial master file.

# Related documents

* UoB-POS-SOP-001 Project Oversight and Quality Management
* UoB-ESD-SOP-001 Essential Document Development & Maintenance

Access to the full UoB QMS for clinical research is available via the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx).

# Reference and frameworks

* MRC/DH/MHRA joint paper: <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/343677/Risk-adapted_approaches_to_the_management_of_clinical_trials_of_investigational_medicinal_products.pdf>
* UoB IT policies and procedures (UoB login required): <https://bham.sharepoint.com/sites/IT/SitePages/Policies-and-procedures.aspx?csf=1&web=1&e=tcMkIY>

Risk Assessment Report

|  |  |
| --- | --- |
| Trial title: | <*insert full trial title>* |
| Sponsor reference: | <insert sponsor reference>  |
| IRAS number: | <insert IRAS number> |
| REC number: | <insert REC number> |

# Document control sheet

|  |  |
| --- | --- |
| Risk assessment version: | Reason for update: |
| <enter version number and date> | <enter reason> |
|  |  |
|  |  |

 Add or delete rows as required

1. Risks to participant safety associated with intervention(s) being tests

Tick the appropriate box below to indicate project type

[ ]  IMP trial

[ ]  Non-IMP trial/clinical study

* 1. Risk category

Tick the appropriate box below to indicate trial type:

|  |  |  |  |
| --- | --- | --- | --- |
| [ ]  | TYPE A |[ ]  TYPE B |[ ]  TYPE C  |
| Comparable to the risk of standard medical care | Higher than the risk of standard medical care | Markedly higher than the risk of standard medical care |
| **Examples**For CTIMPs:* Trials involving medicinal products licensed in any EU Member State if:
* they relate to the licensed range of indications, dosage and form, or
* they involve off-label use if this off-label use is established practice and supported by sufficient published evidence and/or guidelines.

For non-CTIMPs:* Projects involving skin prick tests, observational measures or quality of life assessments.
 | **Examples**For CTIMPs:* Trials involving medicinal products licensed in any EU Member State if:
* such products are used for a new indication,
* substantial dosage modifications are made for the licensed indication, or
* if they are used in combinations for which interactions are suspected.
* Trials involving medicinal products not licensed in any EU Member State if the active substance is part of a medicinal product licensed in the EU.

For non-CTIMPs:* Projects involving radiotherapy dose modifications or a new combinations of non-IMP treatment (e.g. surgery and radiotherapy).
 | **Examples**For CTIMPs:* Trial involving a medicinal product not licensed in any EU Member State.

For non-CTIMPs* Project involving a new surgery technique, a new radiotherapy technique or a new diagnostic technique
 |
| Justification for risk category: GuidanceList the intervention(s) and **briefly** justify the overall risk category selected (Type A, B or C). Consider the following: * 1. Phase of development
	2. Study population – healthy subjects or patients?
	3. Is the intervention licensed?
	4. Is the intervention being used outside of its licensed indication?
	5. Has the dosage regimen/route/surgical procedure/fractionation been modified? If so what are the implications of any modifications for participants?
	6. What is the safety profile of the intervention(s).
		1. What are the known/anticipated safety issues? Are they all addressed within normal clinical practice (standard care)?
		2. Anticipated risks/other effects based on pre-clinical data or knowledge of class of intervention?
		3. Is the duration of use compatible with previous experience? Is there a potential risk of dosing errors?
		4. May concomitant medication increase the risk i.e. interactions?
		5. Is there any published evidence – particularly for Type A trials intending to submit via the MHRA Notifications Scheme, or to support a risk category different to that indicated above?

<enter justification for risk category>  |

* 1. Risks related to the intervention

List below the key risks related to the intervention(s) and how these risks will be minimised. Consider all significant project-specific medical events. Examples are provided in red italic text. Add or delete rows as required.

|  |  |  |  |
| --- | --- | --- | --- |
| Intervention  | Body system/hazard | Mitigation/activity (including frequency) | Comments (including impact and likelihood where applicable) |
| Pazopanib | Gastrointestinal disorders / Diarrhoea | Sites will be prompted to collect data on toxicity on day one of each cycle (except first cycle and at end of treatment visit) and assess if/when the participant will have to cease the drug.The protocol specifies that participants who experience severe diarrhoea will stop pazopanib until symptoms resolve to grade 1.Detailed supportive care guidelines for management of diarrhoea are also provided in the protocol.Participants are also advised in the Participant Information Sheet to notify the study doctor immediately if they experience severe diarrhoea. |  |
| Medroxyprogesterone acetate | Neurological disorders / Depression | Participant is advised to contact local site if experiencing depression. Participants will be seen at the local site at least every 4 weeks and can visit their GP/use the details on the participant card if depression occurs.  | Depression is also monitored by the EORTC QLC-C30 at baseline and twice during therapy. However, this data is not looked at in real time. |
| Ch14.18/CHO Aldesleukin (IL-2) | Vascular disorders / Hypotension | Participant’s vital signs (including blood pressure) will be checked daily by site staff, while on treatment. |  |

* 1. Other risk mitigation processes

The project will be conducted in accordance with the UoB Quality Management System that is designed to mitigate generic risks for clinical research. The table below documents other project-specific risk mitigation associated with the intervention.

Examples are provided in red italic text. Add/delete rows as required:

|  |  |
| --- | --- |
| Mitigation/activity  | Comments |
| Treatment protocol  | 1. As this is such a complex treatment schedule, the protocol will contain considerable detail via description and flow diagrams of the treatment route for each randomisation group. In addition, checklists will be provided and referenced in the protocol.
2. Participants will be enrolled onto the trial in a staged process whereby the first participant in each cohort will complete the vaccination schedule prior to the enrolment of further participants. The subsequent two participants will be treated in parallel, provided there has been no evidence of Dose Limiting Toxicity (DLT). If a DLT occurs, the subsequent participant will also complete the vaccination schedule before further participants are treated.
 |
| Criteria for stopping or modifying trial treatment | 1. The 2-stage design will ensure that the trial is terminated after the first stage if there is insufficient evidence of therapeutic activity.
2. Any grade 4 toxicities will result in treatment being stopped immediately.
 |
| Trial-specific adverse event reporting strategy | 1. All adverse events will be collected for this trial which will be reviewed by an independent Data Monitoring Committee as defined by the protocol. Medically significant events as defined in the protocol will be captured on a serious adverse event form.
 |
| Trial oversight committees and independent data review | 1. A Trial Steering Committee (TSC), Trial Management Group (TMG) and Data Monitoring Committee (DMC) are in place for this phase I trial. The DMC will meet after 2 participants have completed 1 cycle of treatment and will review the study data and advise on the continuation of the trial. They will continue to meet per 2 participants recruited until all participants are recruited. The TMG will meet every 2 months and the TSC will meet every 3 months during the treatment period. The DMC will then meet annually to discuss the progress of the trial.
2. The trial will have a safety review committee who will meet a minimum of every 3 months during the recruitment phase and review all serious adverse events and evaluate the evolving safety profile of the trial. It will be formed of members from the TMG and an independent scientist and clinician.
 |
| Trial suspension between cohorts | 1. If any unexpected serious adverse events (CTC grade 3, 4 only) are encountered in the second arm, consideration will be given to suspending the entry of new participants into this arm, pending clarification of a causal relationship.
2. Toxicity will be closely monitored and if necessary, the study will be stopped in accordance with the early stopping rules, which include:
* the occurrence of grade 3 mucositis in 2 participants at 90 days
* grade >3 late radiotherapy induced complication in more than 2 participant at one year
 |

1. Other risks associated with the design and methods of the trial

Review the protocol to identify whether or not it contains any aspects that materially increase the risks in the areas outlined below. For each hazard identified, consider the appropriate mitigation, management and optimal monitoring strategy.

Under each category are some considerations when determining risk. For CTIMPS, further details can be found in Appendix 2 of the “[Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products”](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/343677/Risk-adapted_approaches_to_the_management_of_clinical_trials_of_investigational_medicinal_products.pdf) – MRC/DH/MHRA Joint Project.

Examples are provided in red italic text.

* 1. Risks to participants

| Category | Risk identified?  | If yes, list specific concerns | If yes, how will risks be minimised? Please specify any mitigations.  | If yes, could monitoring methods help to address concerns? Please specify |
| --- | --- | --- | --- | --- |
| Clinical proceduresE.g. Do they differ from standard care? If so, what is the likelihood of severity of harm to the participant? How will this harm be managed?  | [x]  Yes[ ]  No[ ]  N/A | Blood sampling 5 times a day - increased skin trauma to areas already bruised, discomfort and pain to patient of regular sampling. | Blood sampling will be performed by appropriately trained site staff. Where possible, samples will be taken when clinical blood samples are required. |  N/A; monitoring not required. |
| [x]  Yes[ ]  No[ ]  N/A | Additional CT scan required - increased exposure to radiation from increased frequency of scans. | An additional CT head scan is equivalent to about 1 year of average natural background radiation in the UK. The risk of developing another cancer as a result of an extra CT scan is considered very small.  | N/A; monitoring not required. |
| ConsentE.g. Is there any reason that the participants in the trial would not be able to give fully informed consent e.g. vulnerable groups, lack of capacity to consent, language difficulties?How will this be managed?  | [x]  Yes[ ]  No[ ]  N/A | The trial will involve patients aged from 12 – 25 years of age; <16 year olds are not legally able to consent for themselves. | Age specific Patient Information Sheets and a Parent Information Sheet will be produced. Informed consent will be received from parent(s)/legal guardian(s) for patients under the age of 16. | With explicit consent received from the parent/legal guardian (or patient where patient is under the age of 16) a copy of the Informed Consent Form will be sent to the Trials Office for in-house review. The Site Signature and Delegation Log will also be used to verify that the correct personnel are performing the consent procedures. The consent procedure will be reviewed during on-site monitoring. |
| [x]  Yes[ ]  No[ ]  N/A | This is an international trial involving 5 countries, with different language requirements. | The Patient Information Sheet and Informed Consent Form will be available in French, English, Spanish, Italian and Greek. Back translation of documents by a translation service will be performed.  | N/A; monitoring not required. |
| Data protectionE.g.Are particularly sensitive data being collected?Are personal identifiers associated with the data?Is there a need for data to be sent outside the country? Are data protection standards equivalent to those in the UK? *Note: staff are also required to comply with all associated UoB* [*IT policies and procedures*](https://bham.sharepoint.com/sites/IT/SitePages/Policies-and-procedures.aspx?csf=1&web=1&e=tcMkIY)*.*  | [x]  Yes[ ]  No[ ]  N/A | The patient’s full name and date of birth will be collected at randomisation (which is regarded as personal data in accordance with the Data Protection Act 2018 and GDPR). The patient’s full name is collected over the phone only and is entered directly into the trial database.In addition, copies of signed Informed Consent Forms will be collected and stored centrally by the Trials Office with the patient’s explicit consent.  | Personal data recorded on all documents will be regarded as confidential and will be handled and stored in a secure environment and in accordance with GCP, Data Protection Act 2018 and GDPR.Patients will be identified using only their unique trial number, initials and date of birth on the CRF and correspondence between the Trials Office and the participating site. | Patient’s signed Informed Consent Forms will be checked in-house to verify that patient has given explicit consent for patient’s full name, date of birth and copy of the Informed Consent Form to be provided to the Trials Office.  |
| [x]  Yes[ ]  No[ ]  N/A | With the patient’s explicit consent GP data will be submitted directly to the Trials Office. The GP data displays the patient’s full name and address. | At the Trials Office, the identifiers will be replaced with trial number and initials only.Personal data recorded on all documents will be regarded as confidential and will be handled and stored in a secure environment and in accordance with GCP, Data Protection Act 2018 and GDPR. | Patient’s signed Informed Consent Form will be checked in-house to verify that patient has given explicit consent for data to be collected from GP. |
| Target populationE.g.Phase of the disease, age range of the group, co-morbidities, prognosis of group, susceptibility to infections/complications, risk carrying intervention | [x]  Yes[ ]  No[ ]  N/A | Critically ill patients with a poor prognosis will receive multiple concomitant medications, making both the effect of the IMP and the relatedness of the IMP to any SAEs difficult to assess. | All concomitant medications will be recorded on the CRFs and analysed by the Investigator for both their interaction with the IMP and relatedness to SAEs. Regular monitoring of SAE categories will also be performed. | N/A; monitoring not required. |
| [x]  Yes[ ]  No[ ]  N/A | This target population is at high risk of graft versus host disease and is at greater risk of infection associated with the transplantation procedure. | Vital signs and adverse events will be assessed whilst patient is on trial treatment and for up to 28 days following completion of treatment. | N/A; monitoring not required. |

* 1. Risks to the reliability of results

| Category | Risk identified?  | If yes, list specific concerns | If yes, how will risks be minimised? Please specify any mitigations.  | If yes, could monitoring methods help to address concerns? Please specify |
| --- | --- | --- | --- | --- |
| Eligibility criteriaE.g. Does the trial require very precise assessment of eligibility?Are there any eligibility criteria that are not part of the clinical assessment and may need further highlighting? | [x]  Yes[ ]  No[ ]  N/A | The trial has a restricted eligibility criterion, where patients need to be specifically assessed to be ECOG performance status 2 at the time of registration. | The eligibility form will contain tick boxes containing individual statements taken from ECOG performance status scales and criteria. The form will also contain yes/no eligibility questions relating to ECOG status. This will be double checked by confirming at registration. | On-site monitoring will include source data verification to ensure ECOG performance status recorded in the medical notes is consistent with the ECOG status recorded on the eligibility form and registration form. |
| [x]  Yes[ ]  No[ ]  N/A | There is a risk of ineligible patients being enrolled as such a rare disease, symptoms may be misleading. | Only Investigators experienced in this disease site that have diagnosed and treated cases before will be able to randomise. | On-site monitoring will include checking patients meet eligibility criteria.  |
| Randomisation procedureE.g. Is there any possibility that the treatment allocation might be predicted prior to randomisation? Are there any aspects of the process surrounding randomisation that may cause errors to be made at site e.g. where site assigns next medication box number?Is there any possibility for randomisation not to be possible e.g. electronic systems go down? | [x]  Yes[ ]  No[ ]  N/A | External Sponsor has provided their own web-based randomisation service, concern with potential access issues/ system failure. | Sponsor assures a back-up server system is in place and that usernames/passwords are registered for the Trials Office. They also operate a 24-hour help line in the event of any access issues. | N/A; monitoring not required. |
| InterventionE.g. Is it a complex intervention/treatment regimen which might be applied incorrectly?If applicable, can process of dose escalation be easily followed? | [x]  Yes[ ]  No[ ]  N/A | The study involves the use of intensity modulated radiotherapy. The treatment is intensified i.e. radiotherapy dose delivered to the cancer is increased over 5 weeks. | Only Investigators with appropriate training will be treating patients. Treatment will occur at a single investigator site that has experience in approximately 100 cases using this technique. There will be strict adherence to the radiotherapy contouring protocol with a contouring review exercise prior to commencement.  | Monitoring will include checking that the contouring review exercise has been performed by consultants prior to any treatment of patients by reviewing the date the exercise was performed and the date the patient received treatment. |
| [x]  Yes[ ]  No[ ]  N/A | Complex treatment schedule requiring patients to attend 3 separate hospital departments on the first day of treatment. Delivery of a highly potent drug in the 2nd department that must also be given at an exact measure. Timing of chemotherapy agents is precise and will need close monitoring. | Sites will be trained on the importance of treatment timing at site initiation. A checklist will be provided so that each department will be able to see each time the treatment was administered, and each team will be required to sign off their treatment section (with start/finish times for the treatment given).  | This checklist along with treatment CRFs will be requested immediately after treatment and will be checked in-house to ensure that not only has the correct dose been delivered but that the timing was exact. The prescription forms and accountability logs will also be collected and cross-checked.  |
| [x]  Yes[ ]  No[ ]  N/A | This trial uses a dose schedule finding algorithm with 7 potential dose schedules. A maximum of 4 of these will be tested during the trial and clear communication between the sponsor and sites is essential to ensure patients receive the correct assigned dose. | Following patient registration, the Trials Office will inform sites of the assigned dose schedule for each individual patient which must be clearly documented and relayed to other members of the research team.  | *Monitoring will include checking prescription that correct dose prescribed for cohort.* |
| Management of interventionE.g. Consider any IMP supply, management, storage and dispensing requirements issues and impact/likelihood of non-adherence. | [x]  Yes[ ]  No[ ]  N/A | One arm of the trial treatment uses an IMP supplied by Belgium who use a company in China for the mechanism to deliver the IMP. If there are any supply issues from either country the particular treatment arm of the trial will not be available, and the arms will therefore be unbalanced. | Assurances have been sought from both suppliers that there is sufficient stock to supply the trial for its duration. | In-house monitoring to ensure that usability of the stock is efficient and not wasteful to ensure demand for new/additional supplies will not be required. |
| [x]  Yes[ ]  No[ ]  N/A | The IMP has to be temperature controlled and shipped at -10oC. It must also be at the site within 3 hours. | A specialist company that is already used by the supplier has been employed to transfer the IMP to sites.  | Monitoring will include checking the shipment and delivery times to ensure that the protocol requirements are being adhered to. |
| BlindingE.g. If it is required is there any risk that it could be ineffective? Does the unblinding method provide 24-hour cover with the appropriate level backup and failover processes?Is blinding to be performed by local pharmacies? Could there be any unblinding during the course of the trial? | [x]  Yes[ ]  No[ ]  N/A | As this is a small trial (recruiting 100 patients), unblinding procedures will be performed by local pharmacies. This could affect objectivity and result in inappropriate unblinding.  | Local pharmacies have been assessed to ensure they can provide this service. The provision of this service is included within the site agreement. Staff at sites will be trained that unblinding must only occur where knowledge of the treatment is essential for the correct clinical care of the patient or where a person other than the patient has taken trial medication.Site-specific instructions will be provided.  | Quality checks on unblinding process will be performed.Monitoring will include checking that all sites are familiar with the process and the reasons for unblinding. |
| [x]  Yes[ ]  No[ ]  N/A | This is a placebo controlled, double blinded trial. Unblinding will occur in the event of disease progression or an SAE where knowledge of the trial treatment is essential for patient care. Disease progression is known to be high and therefore there is a risk that frequent unblinding may occur and could lead to the site becoming aware of which patients are receiving the placebo and active drug. Disease progression is also an end point and this could lead to results being available early and visible to sites. | A 24-hour unblinding service will be provided and controlled by the Trials Office (office hours) and an external service provider outside of office hours. The caller will be asked to provide a brief reason for the unblinding requirement. Details of the unblinding procedures are located within the protocol, pharmacy file and on the patient card. | Reasons for unblinding will be monitored in-house as will the number of patients unblinded.  |
| Outcome measures(these should be defined in the grant application, ethics and the protocol)E.g. Are any key outcomes subjective, or require complex assessment? Is there potential for standardised assessment or external verification (e.g. death certificate)? | [x]  Yes[ ]  No[ ]  N/A | One of the outcome measures for the trial is complete pathological response. | An in-house review of all pathology reports will be performed by two independent assessors to conclude if complete Pathological Response has occurred. A standard form will be completed for each patient and compared. Where there is disagreement a third independent assessor will make the final decision.  | In-house monitoring will include checking that each patient report has been reviewed by two assessors and any differences concluded. |
| [x]  Yes[ ]  No[ ]  N/A | One of the secondary outcome measures for this trial is complete resection. Local surgeons and radiologists will be asked to judge the resectability of the tumour based on imaging. | In order to assist sites in the decision-making process, an Advisory Radiology Panel has been established which will review and provide a final opinion on a specific patient’s imaging for cases where it is difficult to ascertain if the tumour has been resected. | N/A; monitoring not required. |
| Sub-studiesE.g.Are there any issues with sample collection, storage, transfer of materials?Obtaining consent for the sub-study?Sending data to patients? | [x]  Yes[ ]  No[ ]  N/A | Sites will be asked to send different types of blood samples identifying the patient only by trial number via special delivery using Royal Mail containers. There is a risk that the samples may be lost in the postal system. | Sites will be asked to divide the samples equally across two boxes to minimise the risk of 1 box becoming lost.  | Deliveries will be centrally monitored and alternative transportation methods identified and used if there is an issue with this system. |
| [x]  Yes[ ]  No[ ]  N/A | The trial examines the welfare of the patient by using booklets sent directly to them for 7 years. This is a long period in which patients may move address or cease to want to participate. | Patients have to provide explicit consent for their GP to be advised of their participation in the study, through which reminders will be sent if no response or “addressee unknown” post is returned to the Trials Office.  | N/A; monitoring not required. |
| Follow-upE.g. Is the follow-up schedule difficult? (e.g. long and different from standard care) What is the likelihood and impact on the trial results of non-adherence? | [x]  Yes[ ]  No[ ]  N/A | This study has a 20 year follow up period. Patients may become lost to follow up or discharged to GP care. There is also the possibility that given the length of follow up, original research staff will leave and be replaced with staff members unfamiliar with the trial and its requirements, creating a danger of forms being incorrectly filled out or not completed.  | To maintain follow-up compliance, a simple CRF will be used in addition to comprehensive guidelines for completion to ensure that new staff members have supporting information to work on the trial. Mail shots containing forms, reminders and queries will be sent along with ad hoc newsletters to ensure that trial awareness is maintained. The Informed Consent Form will request that patient data can be collected from the GP and Data Access Request Service. A GP letter will be produced to advise them of the trial and request for their assistance in cases of patients discharged to GP care. Sites will be advised that they may also telephone the patient for follow-up. | The Trial Coordinator and Trial Statistician will monitor returns of data from sites, to identify any underperforming sites.  |
| Statistical considerationsE.g. Is there any concern that the trial may have insufficient power to detect the anticipated effect of the intervention?Any other risks associated with trial design/outcome measures/analysis plans? | [x]  Yes[ ]  No[ ]  N/A | There is a concern that there will be insufficient power to detect the anticipated effect of the intervention due to lower than anticipated patient numbers.  | Research and feasibility questionnaires indicate that there should be sufficient numbers in this disease population to achieve recruitment targets. The scenario has been factored into the statistical analysis plan and alternate options are available if this occurs. | N/A; monitoring not required. |
| Data collectionE.g. Is there any particular cause for concern over the data collection (e.g. volume and complexity of the data)?Potential for fraudulent data? | [x]  Yes[ ]  No[ ]  N/A | This trial is not part of the NIHR Portfolio so research nurse time may be limited which may impact on data return/quality. | A modest payment is available to Trust R&Ds to cover nurse time. The Trials Office is aware that this may be an issue and will be proactive in ensuring data is returned in a timely fashion. | In-house monitoring of data return may identify any issues |

* 1. Other risks

| Category | Risk identified? | If yes, list specific concerns | If yes, how will risks be minimised? Please specify any mitigations.  | If yes, could monitoring methods help to address concerns? Please specify |
| --- | --- | --- | --- | --- |
| FinanceE.g. Availability of the appropriate resources.  | [x]  Yes[ ]  No[ ]  N/A | Funding has been provided by GSK for 2 years. There are multiple targeted requirements that have to be met within this timeframe in order for finance to be renewed at the end of this period. One of the set criteria is that 50% of the recruitment target must be met within this period. Given the nature of the disease site, this is a challenging target which may require the initiation of additional sites to meet the target. | Recruitment will be monitored frequently with sites being encouraged by the Trial Coordinator to enter patients. Screening logs will also be collected and reviewed.Investigator meetings will be held to promote awareness of the disease site and the trial and to encourage referrals from non-participating centres. | N/A; monitoring not required |
| Investigator sitesE.g. Education and experience, existence of quality systems | [x]  Yes[ ]  No[ ]  N/A | A significant proportion of the Primary Treatment Centres (PTCs) will work with Shared Care Centres (SCCs) to deliver the trial treatment.  | The SCCs will be managed through their respective PTC which will be provided with all relevant trial documentation. The site agreement with each PTC includes the PTC’s responsibilities with regards to its SCCs. The PTC will fax a checklist to the Trials Office confirming activation of each SCC; on receipt Trials Office will activate drug shipment. To ensure that all SCCs understand the trial, the Trials Office will perform pharmacy initiations for each SCC in addition to the PTC and will also provide them with a pharmacy manual and abbreviated site file.  | Quality checks on PTC’s oversight of its SCCs will be performed. |
| **Sponsor/coordinating centre**E.g. Education and experience, existence of quality systems | [x]  Yes[ ]  No[ ]  N/A | This is an international trial. The trial will operate from National Coordinating Centres (NCC) in each country to manage the trial in accordance with the protocol and relevant laws.  | The contract with the NCC specifies which aspects of trial management are to be taken on by the NCC.Each NCC will be assessed for its suitability.NCC will be consulted regarding any changes to trial documents in order to comply with local regulatory/ legislative requirements and translation of documents. Trial Coordinator and Monitor will visit NCC to provide training.NCCs will perform site initiation and on-site monitoring of sites in their country. | Trials Office will employ methods of oversight of each NCC e.g. via site visits/audits and collection and review of key documents such as monitor visit reports. |
| Trial governanceE.g. Influence upon/ interference with trial governance by a private organisation. Consider requirements placed on Trials Office by drug company if supply of drugs is provided free of charge or grants are provided. | [x]  Yes[ ]  No[ ]  N/A | The device used within the trial is only available through the current manufacturer. The device manufacturer also has interests in the results of the trial.  | Responsibilities will be clearly defined in contracts between the Sponsor and the device manufacturer. This will include what trial data the device manufacturer has access to.  | N/A; monitoring not required. |

1. Risk assessment report review

The below table indicated that this risk assessment report has been reviewed and no update was required. Review performed by chief investigator (or delegate).

|  |  |  |  |
| --- | --- | --- | --- |
| Name |  Signature | Date  | Reason for review\*  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

\*A review may be conducted, for example, following:

* a substantial amendment to protocol or participant information sheet/informed consent form
* significant changes in trial organisation (e.g. resource allocation, governance) and/or external funding, or
* any other changes that may alter risk. See Project Oversight & Quality Management SOP (UoB-POS-SOP-001) for further examples.