REVIVED-BCIS2 **FAQs**

Version 2, July 2014

Contents

1. Screening and eligibility

1.1. Screening

Q. What is the best place to start looking for patients?

A. Begin with patients that have 2 of the 3 inclusion criteria known (e.g. known coronary artery disease and low LV function).

Q. What is the best way to approach patients found on heart failure databases?

A. Arrange their next clinic appointment so that they can be seen by both the PI and research nurse at the same time. It can help if the patient is spoken to face-to-face before they are given the information sheet.

Q. What is the best way to keep track of patients at different points in the work-up process?

A. This can be done in many ways and you will soon find what works best for you. From current experience, it has been found helpful to keep a folder or electronic log of potential patients that keeps track of which screening tests have been done, which are still needed and the next time the patient will be seen. An excel spreadsheet can be provided by the CTU that can be used to perform this task. Frequent meetings between the research nurse and PI are also useful to keep track of everything and ensure patients progress towards enrolment in REVIVED.

1.2. Viability

Q. Can patients who have viability but also have ischaemia be included? If so and ischaemia is present, is there a cut off for the amount of ischaemia that is present?

A. Yes, patients with ischaemia can be included. You only need to demonstrate viability for patients to be eligible for REVIVED but identifying ischaemia is encouraged where possible (i.e. progressing to high dose dobutamine on stress echo or adenosine perfusion MRI). There is no recommended ischaemia cut off but the MDT can use the information to make an informed judgement about the treatment that is best for the patient.

Q. Can myocardial perfusion scans be used to assess viability?

A. Yes, all modalities for viability assessment can be used.

Q. Can a FDG-PET scan be used to assess viability?

A. Yes, all modalities for viability assessment can be used.

1.3. Device implantation

Q. Is implantation of an ICD required for the trial?

A. No, ICD therapy is recommended by both NICE and ESC guidelines for standard care. Most patients will already have an ICD implanted. If a patient is due to have an ICD implanted, it is recommended that this is before randomisation. If a patient does not have an ICD, they can still be entered into the trial.

Q. Should there be a wait after implanting a CRT to see if LVEF is improved by CRT alone?

A. No, it has been decided not to include a mandatory delay between CRT implantation and randomisation. Although there is a chance that LVEF will be improved by CRT alone, given that the threshold has been set low there is little concern that it will result in a cohort whose risk have been improved by CRT. Even if there is some change over time, a delay should not introduce bias since new implants are likely to be balanced between the two arms.

1.4. MDT meetings

Q. Could the situation arise where all the screening is done, the patient is randomised and PCI is seen as unfeasible?

A. No, the patient must have been adjudicated as being an acceptable candidate for PCI by the MDT before randomisation.

Q. What is the advice on including patients with CTOs?

A. If there is a high risk of the procedure being a failure, do not include the patient but if it is likely that the procedure will be a success, there is no reason to exclude the patient.

Q. Can patients with left main stem disease (LMS) be enrolled?

A. Yes, if successful revascularisation is likely to be achievable, the patient can be included in the trial. It is important that eligible patients with LMS disease are not excluded as this could bias the outcome of the trial.

Q. Is there an upper time limit for the qualifying angiogram or viability assessment?

A. No. The MDT will assess the angiogram and viability assessments and if the information is considered to be clinically relevant it can be used. Only the qualifying echo has an upper time limit of 6 months.

2. Consent

2.1. Pre-screening

Q. Is there any provision in the trial for pre-screening consent?

A. Not at this time but please record on the screening log any patients that have been excluded because certain screening tests (specifically viability assessment or angiogram) could not be done as part of routine care.

2.2. Dealing with patient's preconceptions

Q. How do you deal with patients that have their mind set on one treatment or another?

A. Patients will sometimes have a preference for the treatment that they want but this is often based on what they have heard from friends and family. Patients need and want information to help them make the right choice. One important fact to get across is that this group would not get PCI if they are not in the trial as it is not a proven treatment for heart failure. If after talking to the patient and explaining their options, the patient is still set on a specific treatment, it is recommended not to include the patient as there is a greater chance they will withdraw if they are disappointed with their allocation.

2.3. After consent

Q. Once consent is taken, are we obliged to record events and if so, which arm are they counted in?

A. The patient is not officially in the trial until randomisation. Events do not need to be recorded until after patient is randomised.

Q. Is there any worry that the patient will change their mind about being in the trial between consent and randomisation?

A. From experience so far, this has not been an issue. By the time the patient is randomised, they will have been seen by either a trial doctor or nurse several times and hopefully will have built up a relationship with them.

3. Randomisation

3.1. Timescale for PCI after randomisation

Q. If a patient is randomised to PCI + OMT, how long after randomisation should the procedure occur?

A. It is important that the procedure take place no more than two weeks after randomisation to reduce the possibility of events occurring between randomisation and the procedure. It is suggested that a PCI slot is booked prior to randomisation and that the patient is randomised at most 2 weeks prior to that date. The best way is to always plan for the outcome of randomisation to be PCI + OMT. If the allocation is PCI + OMT, the patient has notice of the procedure. If the allocation is OMT alone, there is time to re-assign the slot. However, this is just a guide and things may work differently at your site.

4. Treatment

4.1. Patients undergoing PCI

Q. Is there any guidance on completeness of revascularisation?

A. It is strongly recommended that PCI is considered, and if feasible attempted, on all significant coronary lesions in major proximal coronary vessels subtending viable myocardium. It is up to the MDT to decide whether complete or nearly complete revascularisation is feasible in each patient. If not the patient should not be enrolled in the trial.

Q. If a patient is randomised to PCI + OMT and undergoes PCI but revascularisation is not possible, what action should be taken in regards to documentation and the patient continuing in the trial?

A. REVIVED is being analysed according to intention to treat, which means that the patient should remain in the trial and follow up should be conducted as normal. Any deviations from normal protocol will be documented in the eCRF.

Q. Could there be an element of the placebo effect at work for patients receiving PCI considering there is no sham procedure?

A. Possibly. There could also possibly be a degree of the placebo effect in all PCI procedures so this is no different from patients in the trial.

4.2. OMT

Q. Does the patient have to be optimised on optimal medical therapy before being randomised?

A. No. Patients recruited for REVIVED should in most cases already be optimised or on the trajectory for optimisation but are not required to be on the optimal doses. This is the responsibility of the treating physician and not stipulated by the trial other than the OMT treatment guidelines which are provided in an SOP.

Q. There are some doubts about the effectiveness of aspirin for heart failure. Should we be using Clopidogrel instead?

A. All concerns about aspirin in heart failure are currently only theoretical. Anti-platelet use in OMT will not be specified and should be dictated by usual local practice.

4.3. Crossover

Q. What are the rules for crossover?

A. Crossover will only be allowed in the protocol if patients meet class I indications for PCI, namely Acute Coronary Syndromes or the development of limiting (CCS class 3 or 4) angina.

5. Follow-up

5.1. SAEs

Q. What is the requirement for reporting adverse events?

A. **Expected** adverse events are reported on the eCRF. **Unexpected** adverse events are reported via an NSAE or SAE form and faxed in to the CTU, these forms are kept in the trial site file.

6. Data

6.1. Core labs

Q. How will the core lab information be transferred?

A. There will only be one essential core lab:

- **Echo core lab:** information will either be transferred using MEDCON or sent on an anonymised CD. For specific details on parameters, please contact the CTU. An SOP is in development, however please store images on site for the time being.

Q. What will happen to the echo sent to the core lab?

A. The secondary endpoint of LV function will be determined by the echos sent to the core lab.

Q. What are the other core labs?

A. These will be optional for sites that wish to participate in them.

- **ECG core lab:** the best way to store ECGs would be to make a photocopy and keep with the CRF. An SOP is in development which will describe the transfer procedure.
- **Viability core labs:** An SOP is in development which will describe the transfer of DSE/MRI data, until then this data should be stored on site.
- **ICD core lab:** this is being run by Jonathan Behar (jonathanbehar@gmail.com). If your site has expressed interest in contributing to the ICD core lab, Jonathan will be in contact shortly after the first patient has been recruited.

Please submit additional questions to Rebecca Matthews at the REVIVED CTU: rebecca.matthews@LSHTM.ac.uk