



SITS OPEN STUDY GUIDANCE

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INTRODUCTION

This is a guide for SITS Open centres to get started with the study and prepare and perform the procedures.

ROLES – RESPONSIBLE PERSONS/TEAMS

(Contact details are found in Investigator Folder)

KI

The sponsor of the study.

Coordinating investigator: Professor Nils Wahlgren, M.D., Ph.D.

Co- Coordinating investigator: Professor Olav Jansen, M.D., Ph.D.

SITS Open Coordination Team

SITS Open Coordination team is coordinating the network of study centres. Local PI and the SITS Coordination team will collaborate through the study. The SITS Coordination team will provide Local PI with ongoing updates, including newsletter, amended documents etc.

The electronic Case Report Form (eCRF) is based on the SITS register.

Study Coordinator UKSH Kiel (German sites only)

Coordinator for German sites. The Coordination team in Kiel will provide Local PIs in Germany with ongoing updates and be the main contact for questions regarding the study in Germany.

Study Coordinator NHS Greater Glasgow and Clyde (UK centres only)

Coordinator for the UK centres. The Coordination team in Glasgow will provide Local PIs in UK with ongoing updates ongoing updates and be the main contact for questions regarding the study in UK.

mRS Adjudication Team

The Stroke Research team in the institute of Cardiovascular and Medical Sciences at the University of Glasgow will arrange for video recordings of patient interviews to be securely stored within the Robertson Centre for Biostatistics at the University of Glasgow and will analyse all video recordings of patient interviews on their functional status at three months after onset of symptoms.

Imaging Core Lab

The Department of Neuroradiology at the University Hospital at Dresden, Germany, will analyse all computer tomography (CT-scans), both native and angiographic images, magnetic resonance imaging (MR-scans), native and angiographic, if supplied by centres, and angiographic images from the endovascular procedures.

University of Edinburgh (Neurosciences Imaging Group)

This group will handle the review, logistics and archiving of all images in the study

The Local Coordinator (Local PI) at the centre

In the “delegation list” (filed in Investigator Folder) the Local PI should fill in the responsibilities, contact details of your team members in the study. Site team members has to sign and date this delegation list. Send the list to the SITS Open Coordination team: open@sitsinternational.com. If the delegation log is updated with new information, please resend it to the SITS Coordination Team.

Local PI - Responsibilities

- Primary contact with the SITS Open Coordination team regarding all clinical matters
- Inform and remind all relevant staff about the study and will be available to answer questions
- Provide the site staff with study documents and ensure they are trained in the protocol and related documents
- Ensure that new study team members are informed and trained in the study.
- Update the study team member with amendments of study protocol and related documents.
- Inform primary stroke centres submitting patients to your clinic about the study
- Ensure that all eligible patients will be included in the study with the highest data quality
- Authorise (delegate according to the delegation list) other clinical study doctors to decide about enrolment of patients, receive and sign informed consent and enter study data.
- Ensure that the study team (e.g. a research nurse) will enter clinical study data as soon as they are available. The first study data should be entered as soon as informed consent is provided to achieve an enrolment number for your patient.
- Ensure that the clinical study doctor who perform the NIHSS is certified for NIHSS (link provided)
- Ensure that CT images for each time point (Baseline, 24h and Intervention) are sent to SIRS according to Procedure Imaging Manual.
- Ensure experienced member of the study team will be responsible for the 3 months follow ups which will include a video interview.
- Ensure that the person who perform the mRS is trained and certified for mRS (link provided)

STUDY DOCUMENTS

- Study protocol
- Project plan
- User's guide for SITS Open CRF
- mRS training material
- Imaging Procedure Manual
- Physicians Verification Form
- Additional Logs (e.g. Delegation log, Enrolment log)
- Additional instructions

Local PI ensure that all site team members are trained and follow those documents.

If the documents are amended, Local PI will ensure that centre staff are trained and follow these new documents.

TRAINING

Protocol

See Study Protocol and related slides form Initiation call in Investigator Folder

NIHSS Certification link:

<https://secure.trainingcampus.net/uas/modules/trees/windex.aspx?rx=nihss-english.trainingcampus.net>

Please archive the certificate in the Investigator Folder

mRS Certification

<http://europeanacademictrials-sits-open.trainingcampus.net>

Please archive the certificate in the Investigator Folder

Additional training is available in the investigator Folder

Training will be provided by Adjudication team in Glasgow

Images

See separate Imaging Procedures Manual

CRF

See separate User's guide

GCP

It is highly recommended that site team member are educated in Good Clinical Practice.

Please file your certificate of GCP education in Investigator Folder (if applicable)

LOGS

Delegation log

This log has two purposes:

1. Documentation of signatures and initials of all staff that collect and record data, study documentation attributed to specific staff members may be verified.
2. List of study related activities that staff members may do per delegation by the Local Clinical PI.

Enrolment log

This log is a record of all enrolled patients in the study at your centre. This log should stay at the clinic and archived in Investigator Folder according to local regulations.

SITS REGISTER AND SITS OPEN CRF

How to join the main SITS register

Each user that is going to enter patient data into SITS registry need to have an account. If the user is not already a member, please go to this page:

<https://sitsinternational.org/join-now>

Press "Become a s SITS centre" button and follow the steps for joining SITS registry.

How to get access to the SITS OPEN CRF - log in

When you have created an account in the registry, you will receive an automatic email with a link to create a password. Log in to the database when you have created your password, and notify us as soon as this is done. We will then activate your account so that you are able to enter SITS Open patients.

After you have gain access to the CRF please create a test patient (see separate instructions).

Register the patient in the CRF

For detailed information please see user´s guide

When you have a patient fulfilling the criteria of the study you register the patient by clicking on "New patient" in the SITS registry and thereafter the "SITS Open" box.

It is preferable that all other patients not fulfilling criteria for SITS Open, will be registered in SITS registry.

The patients registered in the SITS Open study can be seen in the registry report section when the inclusion of patients at the centre is completed.

Please note that all patients once entered into the eCRF will be documented as study patients even a thrombectomy procedure has not been done. Intention to treat (ITT) patients should follow all procedures according to protocol and CRF should be completed accordingly.

STUDY PROCEDURES

Inclusion of patients

Please follow inclusion/exclusion criteria from protocol.

Patients which will be considered for inclusion can either have been initiated on thrombolysis at the study centre or at a primary centre and then referred to the study centre (drip and ship). This also apply for patients that not are treated with thrombolysis.

In both situations, if patients are treated with thrombolysis it is important that treatment is according to generally accepted criteria and that the NIHSS obtained before initiation of thrombolysis is correct and documented for the study. Furthermore, the first CTA showing the required occlusion should be used as the study baseline examination. Only if the first CTA is of unacceptable quality, a second CTA showing a relevant occlusion may be considered. If a second CTA is considered, it should be performed within 15 minutes after IVT initiation. For a patient to be included in the study, the baseline CTA should not be performed later than 15 minutes after IVT initiation, if given. If IVT is not given, the baseline CTA should be performed within 15 minutes from the plain CT.

If the NIHSS is obtained by a non-certified person, it is important that a certified study person will discuss directly with the examiner to ascertain that the value is correct.

A very important point to make to the radiologist for the baseline non-contrast CT, is to not discard thin slices but to save at least 2.5 mm slices. This is of importance for evaluation of the clot size

It is important to remember that all patients fulfilling the entry criteria will be considered for the study, also if they have been improving or even recovered since initiation of thrombolysis. The decision to register the patient is taken early during the infusion, as soon as a relevant occlusion has been identified on CTA.

It is of outmost importance that all these patients are registered, since otherwise the study will build in an imbalance between the active group and control, and a benefit of thrombectomy may be more difficult to prove.

Remember to document information about the participation in the study in the Medical Record for the patient. This information should include: Study description, enrolment number for the patient, date when Informed Consent was obtained, version of Informed Consent used, confirmation that patient is eligible for the study (Inclusion and Exclusion Criteria considered).

Registration call

As soon as the decision is taken that the patient is eligible for the study (usually when the patient is still on the CT table), a Registration Call (free of charge, open 24/7) must be done.

The number is +46 8 5177 6114

You will be asked the following questions:

Your name?

Your Centre (if possible the centre code)

Patients age and gender

Time of initiation of thrombolysis (hh.mm)

Before you enter the first patient, please perform a test call (state your name and centre and that it is a test). If there are any problems to call from your hospital inform the SITS Open Coordination team immediately.

Thrombectomy (ONLY - Active centres)

It is recommended that the thrombectomy procedure is being initiated as soon as the patient has been found to meet entry criteria. However, additional neuroimaging may be done on the investigators discretion on clinical grounds, and they may result in cancellation of the thrombectomy if it is found that recanalization has occurred after thrombolysis initiation or if it is found that the patient has developed extensive ischaemic lesions or other conditions and is unlikely to benefit from the procedure.

Whether proceeding to thrombectomy or not, the patient will remain in the active group and will follow all planned study related procedures.

Informed consent

Collect the Informed Consent from the patient within 20 h after initiation of IVT or the baseline CT. If a patient cannot consent themselves, a routine for how to consent these patients need to be approved from the local ethic committee.

Archive the Informed Consent according to local regulations.

NIHSS

Time points to perform NIHSS

Before IVT or CT

2h (control centres)

Before Thrombectomy (Active centres)

12h

24h

7 days or at discharge (whichever is later)

Imaging

For detailed information, follow the separate Imaging Procedures Manual

The neuroradiology images should be saved on DVD disks (all patient identity information will be removed and replaced by ENROLMENT NUMBER) (Each time point on separate DVD discs); DVD:s will be sent to the SIRS and sequentially forwarded to the core lab:

- Baseline CT (first done before IVT with thin slices ≤ 2.5 mm)
- Baseline CTA (first done before IVT, if acceptable quality, otherwise second one within 15 minutes at latest after IVT)
- DSA including TBY procedure (ACTIVE Centres)
- Follow up CT
- Follow up CTA
- Any additional imaging which may be of importance for understanding of clinical decisions
- A transmittal sheet will be completed for each CD

Three months follow up - mRS

All patients will be seen by a clinical study doctor at three months for final follow up. The data required by the eCRF will be collected and modified Rankin Score will be evaluated based on the structured interview. The interview will be documented by the video camera provided by the study organisation. Instructions for the interview will be distributed separately. As soon as the interview has been documented, it will be transferred through the USB connection via the SITS Open homepage to the mRS Adjudication team. The investigator's own evaluation of mRS will be documented in the eCRF.

Physician verification form

Treating principle or sub investigator complete “Physician verification form” to confirm the accuracy and validity of patient data for each patient.

AE/SAE/Death and SUSARS

Please report SAE/AE’s on the “Adverse Events” page in the eCRF. In case of death, please report this both on the “Death” page in the eCRF and also in the “Adverse Events” page, since death is an adverse event. SAE should be reported within 24 hours!

There is no obligation to report AE/SAE beyond the eCRF.

SUSARS should be reported according to clinical practise to health authorities.

Medical Record/Patient record

Remember to document information about the participation in the study in the Medical Record for the patient. This information should include: Study description, enrolment number for the patient, date when Informed Consent was obtained, version of Informed Consent used, confirmation that patient is eligible for the study (Inclusion and Exclusion Criteria considered).

All changes made in the record should be trackable.

The medical record needs to be signed by the person who enter the data.

Archive

Archive relevant study documentation e.g. Investigator Folder and Patient files (Including Informed Consent) according to local regulations. Older versions will remain and to be possible to retrieve.

Changes made to documentation needs to be verified and dated by the persons who make the change.

SUPPORT

The SITS Coordination team will be available over email and telephone daytime for support:

Open@sitsinternational.org

Telephone: +46 76 945 96 70