

# SOP: Randomization, Follow-up and Data collection of patients in the CASES trial

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## Contents

1. Aim.....	3
2. Range.....	3
3. Definitions and abbreviations .....	3
4. Responsibilities.....	4
5. Study Characteristics .....	4
6. Procedures.....	6
6.1 Check eligibility for participation.....	6
6.2 Randomization.....	6
6.3 Patient interview and deferred informed consent .....	8
6.4 Study Actions .....	8
6.4.1. NIHSS score.....	8
6.4.2. Requesting imaging studies.....	9
6.5. CRF.....	9
6.5.1. CRFs on paper.....	9
6.5.2. eCRF in Castor EDC .....	10
6.6. Transfer to another hospital .....	15
6.7. Discharge .....	15
6.8. (S)AEs.....	16
Adding (S)AEs in Castor EDC.....	17
6.9. Follow-up.....	20
6. Related documents .....	20
8. Contact Information Study team.....	21
9. Appendices .....	23
10.1 Appendix 1: NIHSS.....	23

## 1. Aim

This standard operating procedure (SOP) contains an overview of all steps required to enroll a patient in the Carotid Artery Stenting during Endovascular treatment of Stroke (CASES) study, and the course of the further study processes. This SOP will ensure the quality and the uniformity of the data.

## 2. Range

This SOP applies to the local Principal Investigator (PI) and for all qualified research assistants (including research nurses), who are involved in screening and enrolling patients, conducting study actions, completing information in the Case Report Forms (CRFs), and reporting serious adverse events (SAEs) within the CASES trial.

## 3. Definitions and abbreviations

CAS	Carotid Artery Stenting
CEA	Carotid Endarterectomy
CONTRAST	Collaboration for New Treatments of Acute Stroke
CRF	Case Report Form
eCRF	Electronic Case Report Form
CT	Computed Tomography
CTA	Computed Tomography Angiography
CTP	Computed Tomography Perfusion
DSA	Digital Subtraction Angiography
EHR	Electronic health record
EQ-5D-5L	EuroQol five-dimension five-level
EVT	Endovascular treatment
GCP	Good Clinical Practice
ICA	internal carotid artery
ICF	Informed Consent Form
ICH	Intracranial hemorrhage
ISF	Investigator Site File
METC	Medical Ethics Review Committee
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
PI	Principal Investigator
PIS	Patient information sheet

PROBE	Prospective Randomized Open, Blinded Endpoint
RA	Research Assistant
(S)AEs	(Serious) Adverse Events
SOP	Standard Operating Procedure
WMO	Dutch Law pertaining to medical scientific research with human subjects
2FA	Two Factor Authentication

## 4. Responsibilities

It is the responsibility of the local PI to ensure that all study procedures are performed within the CASES as described in the study protocol (and any amendments).

In practice, the research staff (e.g., involved co-/sub-investigators or research nurse/study coordinator) will usually conduct the research activities. In this SOP, these employees are referred to as the delegates.

It is the responsibility of the local PI to ensure that all delegates involved in conducting study procedures are trained accordingly.

Delegates must be listed on the “Delegation Log of Authority”. It is expected that all parties involved are demonstrably aware of the sub-objectives of the national applicable legislation and regulations, ICH-GCP guidance, Declaration of Helsinki and the research protocol that are relevant to their research activities.

## 5. Study Characteristics

Title: Carotid Artery Stenting during Endovascular treatment of Stroke trial (CASES)

Study design: phase 3 international multicenter randomized clinical trial with open label treatment and blinded outcome assessment (PROBE design). The study will have a non-inferiority design.

Objective: To investigate the effectiveness and safety of carotid stenting during EVT in people with acute ischemic stroke caused by a tandem lesion.

Participants: Patients with acute ischemic stroke due to proximal intracranial arterial occlusion and an ipsilateral cervical carotid artery stenosis of more than > 50% and of presumed atherosclerotic origin, who are eligible for EVT.

Intervention: In the intervention group, the carotid artery lesion will be treated with CAS during EVT. In the control group, the carotid artery lesion will be treated according to the current guidelines: with CEA or CAS within two weeks after the initial event or medical management alone, based on functional recovery after stroke.

Outcome (O): The primary outcome is the degree of disability at 90 days (modified Ranking Scale Score).

Sample Size: 600 patients

Trial duration: 48 months (from first patient in till trial report)

Sponsor: University Medical Center Groningen

Chief Investigators: dr. Maarten Uyttenboogaart (UMC Groningen), dr. P.J. Nederkoorn (UMC Amsterdam) and prof. dr. Robin Lemmens (UZ Leuven)

Participating sites:

17 EVT centers in the Netherlands (Amsterdam AMC, Erasmus MC Rotterdam, Haaglanden Medisch Centrum The Hague, Haga Ziekenhuis The Hague, Maastricht University Medical Center, Leiden University Medical Center, Radboud UMC Nijmegen, St-Elisabeth Ziekenhuis Tilburg, Catharina Ziekenhuis Eindhoven, St Antonius Ziekenhuis Nieuwegein, Rijnstate Ziekenhuis Arnhem, University Medical Center Utrecht, Isala Klinieken Zwolle, Medisch Spectrum Twente Enschede, Amphia Ziekenhuis Breda, Albert Schweitzer Ziekenhuis Dordrecht, University Medical Center Groningen)

9 EVT centers in Belgium (UZ Gent, UZ Antwerpen, AZ Groeninge Kortrijk, AZ Sint Jan Brugge, UCL Brussel, ULB Erasme, Hopital Civil Marie Curie, CHC Liège and UZ Leuven).

For a complete overview of the study design and study procedures of the CASES trial we refer to the study protocol, which can be found on the CASES website: <https://cases-trial.eu/>

## 6. Procedures

### 6.1 Check eligibility for participation

To be eligible to participate in the CASES trial, a patient must meet all the inclusion criteria listed below. A potential participant who meets one of the exclusion criteria will be excluded from participation.

#### Inclusion criteria:

- Age > 18 years
- Baseline NIHSS  $\geq 2$
- Acute ischemic stroke due to proximal intracranial occlusion in the anterior circulation (intracranial ICA, M1, proximal M2) on the CT angiography
- Stenosis >50% according to the NASCET criteria<sup>16</sup> or initial occlusion of the ipsilateral cervical carotid artery of presumed atherosclerotic origin on baseline CT angiography
- Eligible for EVT according to the guidelines: EVT within 6 hours of onset or EVT between 6-24 hours after onset based on perfusion CT imaging selection (conform current guidelines)
- (Deferred) Informed Consent

#### Exclusion criteria:

- Any intracranial hemorrhage
- Cervical carotid artery stenosis or occlusion with other causes than presumed atherosclerosis (e.g. carotid artery dissection, floating thrombus, carotid web)
- Any exclusion criterion for EVT according to the guidelines
- Pre stroke disability (defined as a modified Rankin Scale score >2)
- Recent gastro-intestinal or urinary tract hemorrhage (<6 weeks)
- Recent severe head trauma (<6 weeks)
- Recent infarction on baseline brain CT in the same vascular territory (< 6 weeks)
- Known allergy to aspirin and/or clopidogrel
- Pregnancy

### 6.2 Randomization

If a patient meets all inclusion criteria and has no exclusion criteria for participation in the CASES trial, a patient can be included and randomized:

1. Go to the CASES website: [CASES - randomize](#)
2. Click on 'click HERE to randomize a new patient'
3. Login with your center-specific login information (provided by you at the beginning of the trial)
  - a. Username
  - b. Password
4. Complete the next screen with your email address and patient information, and check the in- and exclusion criteria:

Specific explanation of certain items:

- "Email": enter here the email address of the person including the patient.
- "Patient ID of your center/Center ID": enter here the ID of your center (provided to you at the beginning of the trial), followed by the number of the patient in the CASES trial at your center.

Should there be an error in the count, the randomization tool will correct you after randomization.

- E.g. UZL-001 for the 1<sup>st</sup> patient included in UZLeuven
- E.g. UZL-010 for the 10<sup>th</sup> patient included in UZLeuven

5. If all the information is complete and correctly filled in, click on 'Submit form'.

A screen will then appear with a:

- CASES study number *example: Study ID: 30001*
- Center specific number *example: Center ID: UZL-001*
- Randomization result *example: immediate CAS (study intervention)*

This screen should be printed and saved in the ISF.

You will receive confirmation of inclusion at the email address provided. A copy of the inclusion with encrypted inclusion data will be sent to the CASES mailbox.

6. Fill in both numbers (study and center ID) from the confirmation of inclusion into the patient's EHR and treat the patient according to the assigned study arm.

**Key file (subject identification log).**

Keep the data of the included patients in the key file, in which the personal data is noted together with the study numbers, so that this can be used as a code table. Consequently, only pseudonymized data needs to be entered in the eCRF.

### 6.3 Patient interview and deferred informed consent

We work with a deferred informed consent procedure, similar to many other studies within the CONTRAST consortium. This means that after randomization and the intervention procedure, consent will be sought from the subject or his/her legal representative.

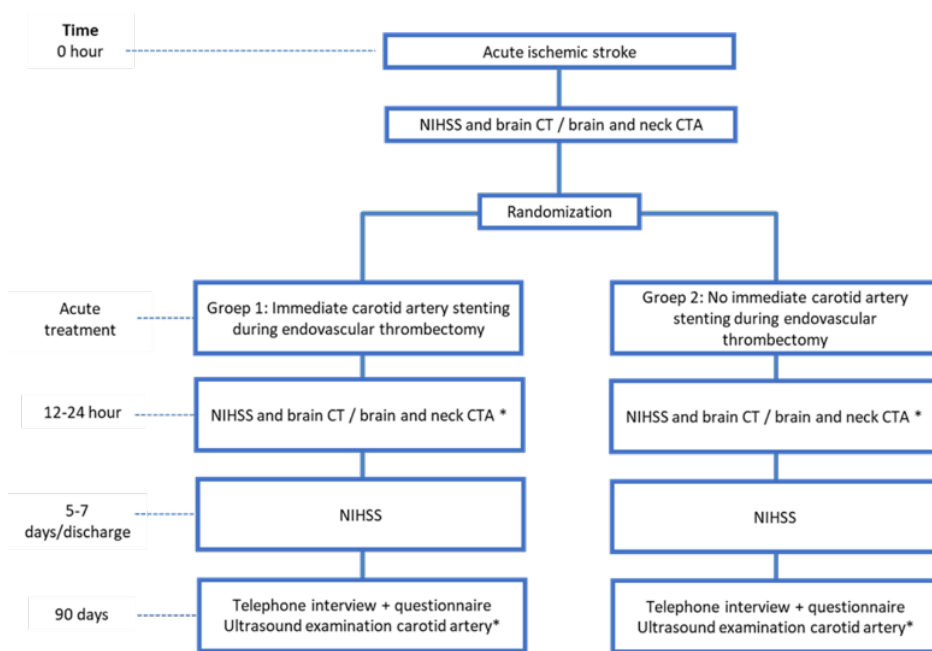
For more information about the deferred informed consent, we refer to the SOP 'patient information and deferred informed consent'.

For the CASES trial, all patient information sheets and informed consent forms can be found on the CASES website: [CASES - trial protocol and trial documents](#). All paper CRFs are also available here.

Provide a PIS and ICF in duplicate: 1 copy for the patient (and/or legal representative), and 1 copy for the ISF. Signed consent forms should be stored and archived by the local study site as per applicable laws and regulations.

### 6.4 Study Actions

The current checklist of all study actions is available on the CASES website: [CASES - trial protocol and trial documents](#).



#### 6.4.1. NIHSS score

At baseline, after 24h and after 5-7 days (or upon discharge), the NIHSS score is administered. For further explanation on the NIHSS scoring system in comatose or difficult to instruct/confused patients, see *Appendix 1*.



A couple of tips here:

- Item 11 (extinction/inattention): should only be scored if it is also testable. If this item is not testable (e.g. in case of reduced consciousness, loss of sensibility and/or hemianopsia), always score it as 0.
- In comatose patients, specific agreements exist regarding the score of certain items. For example, item 9 (aphasia) is scored as 3 and item 10 (dysarthria) as 2. See *appendix 1* for an overview of all instructions.
- Please note: 'untestable' for item 5/6 (motor arm/leg) may only be used if someone has an amputation, for example, and for item 10 (dysarthria) only if there is a physical barrier such as an endotracheal tube.

#### 6.4.2. Requesting imaging studies

At baseline, a NCCT and CTA are performed for all patients participating in the CASES trial.

During endovascular treatment, DSA images are obtained.

Additionally, at 24 hours, a NCCT and CTA is performed in all patients at 24 hours ( $\pm$  6 hours). During follow-up, at 90 days, a carotid duplex ultrasound is performed.

After randomization, request these follow-up scans and ultrasound promptly, so that they can be scheduled by the radiology department.

#### 6.5. CRF

##### 6.5.1. CRFs on paper

After the endovascular treatment on the ward, source data will be completed on paper. Centers can use the worksheets provided by the sponsor. Some centers choose to use the EHR or their own worksheets as the source document. This is allowed, provided that all requested data entered in the eCRF can also be found in the EHR.

Indicate the study numbers (CASES number and center-specific number) on the CRF forms.

Blank CRF forms can be found on the CASES website: [CASES - trial protocol and trial documents](#).

The following visits must be filled in by the local study team (also see checklist of all study actions):

- Inclusion & Randomization
- Informed Consent
- Baseline
- Endovascular treatment
- Study treatment (depending on randomization arm)
- Clinical follow-up
- Deferred treatment (depending on randomization arm)
- Follow-up 3 months (unblinded)
- (S)AE
- End of study

Report SAEs immediately via [cases-trial@umcg.nl](mailto:cases-trial@umcg.nl) and/or on the CASES phone: +31 6 5272 4593 and complete a SAE CRF (in Castor EDC).

### 6.5.2. eCRF in Castor EDC

For all CASES participants, a record in Castor EDC is created by the national coordinating centers (UMC Groningen for the Netherlands, UZ Leuven for Belgium), within one business day after inclusion. In this participant-specific record, the data entered online in the randomization module (such as age, assigned treatment arm, ...) are already entered by the clinical trial coordinators.

Informed consent should be obtained prior to data entry. To enter the collected data, go to Castor EDC.

1. Go to Castor EDC production environment: [Castor EDC - Login](#)
2. Log in with your personal Castor EDC account with two factor authentication:
  - a. If you do not yet have a Castor EDC account or 2FA enabled yet, please see the following link for more information: <https://academy.castoredc.com/p/getting-started-with-castor-free>
  - b. If you do not yet have access to the CASES Castor EDC production environment with your email address, you can request it through our mailbox: [cases-trial@umcg.nl](mailto:cases-trial@umcg.nl)
3. If you are working with Castor EDC for the first time, we recommend taking the online course "Data entry in Castor EDC" (sections "Adding data" and "Reports"; total duration 15 minutes), through the following link: <https://academy.castoredc.com/p/dataentry-free>
4. Click on "CASES". An overview screen of all CASES participants from your center will then open.

Participant...	Site	Randomiza...	Progress	Last opene...	Created on	Updated on	Status			
000001	Test Site	-	<div style="width: 100%;"></div>	Louise Maes	30 Jan 2023	22 May 2023	Not Set	🔒	🔔	⋮
000002	Test Site	-	<div style="width: 100%;"></div>	Theodora van Elk	23 Mar 2023	23 Mar 2023	Not Set	🔒	🔔	⋮
000003	Test Site	-	<div style="width: 100%;"></div>	Theodora van Elk	27 Mar 2023	12 Apr 2023	Not Set	🔒	🔔	⋮
000004	Test Site	-	<div style="width: 100%;"></div>	Louise Maes	13 Apr 2023	05 May 2023	Not Set	🔒	🔔	⋮
110001	UMC Groningen	-	<div style="width: 100%;"></div>	Theodora van Elk	16 Mar 2023	16 May 2023	Not Set	🔒	🔔	⋮
120001	Erasmus MC	-	<div style="width: 100%;"></div>	Louise Maes	14 Apr 2023	22 May 2023	Not Set	🔒	🔔	⋮
120002	Erasmus MC	-	<div style="width: 100%;"></div>	Louise Maes	17 Apr 2023	22 May 2023	Not Set	🔒	🔔	⋮

5. Click on the participant's study ID to open that participant's record and start filling in the eCRFs.
6. The left side menu shows an overview of all eCRF to be completed for this participant. Click on the name of the eCRF ('visit') and then on a subpart ('form'), to open the corresponding part of the eCRF.

Participant ID: 30050 (Not Live (v.66.41)) Participant status: Not set

### 1. Checklist in-and exclusion criteria

**Inclusion criteria**

- 1.1 Acute Ischemic stroke due to proximal intracranial occlusion in the anterior circulation (intracranial ICA, M1, proximal M2) on the CT angiography  Yes  No
- 1.2 Stenosis >50% according to the NASCET criteria or initial occlusion of the ipsilateral cervical carotid artery of presumed atherosclerotic origin on baseline CT angiography confirmed by digital subtraction angiography  Yes  No
- 1.3 Eligible for EVT according to the guidelines: EVT within 6 hours of onset or EVT between 6-24 hours after onset based on perfusion CT imaging selection  Yes  No
- 1.4 Baseline National Institute of Health Stroke Scale (NIHSS) score ≥ 2  Yes  No
- 1.5 Age >18 years  Yes  No

**Exclusion criteria**

- 1.6 Any intracranial hemorrhage  Yes  No
- 1.7 Cervical carotid artery stenosis or occlusion with other causes than presumed atherosclerosis (e.g., carotid artery dissection, floating thrombus, carotid web)  Yes  No
- 1.8 Any exclusion criterion for EVT according to the guidelines  Yes  No
- 1.9 Pre stroke disability (defined as a modified Rankin Scale score >2)  Yes  No
- 1.10 Recent gastro-intestinal or urinary tract  Yes  No

7. Required fields are indicated with a ● before the field (*required*). When a required field is completed, the bullet changes to ● (*completed*). If fields are not completed according to the appropriate format, this is indicated with a comment and the bullet changes to (*invalid*).

Participant ID: 30050 (Not Live (v.66.41)) Participant status: Not set

### Baseline 9. Lab results

9.1 Date of laboratory results: 2023-06-14

9.2 Time of laboratory results: 07:30 (hh:mm)

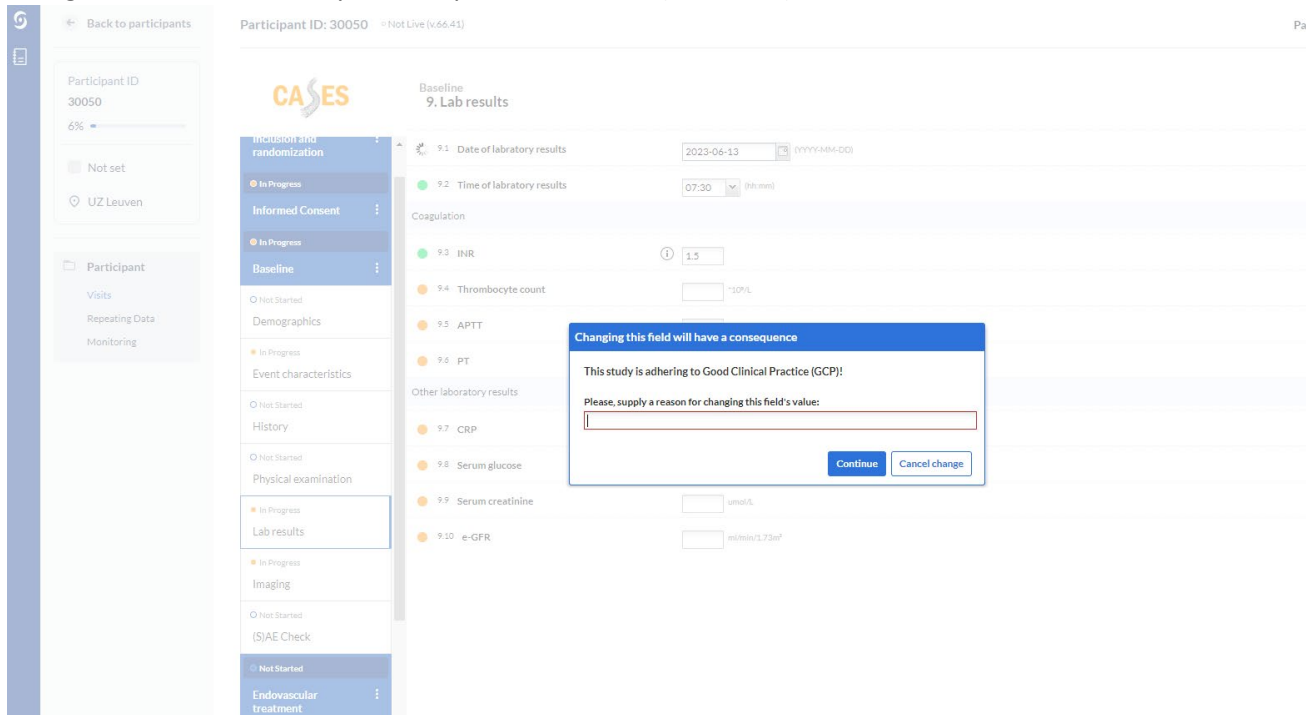
**Coagulation**


- 9.3 INR:  ● The maximum value for this field is 21
- 9.4 Thrombocyte count:  /L
- 9.5 APTT:  sec
- 9.6 PT:  sec

**Other laboratory results**

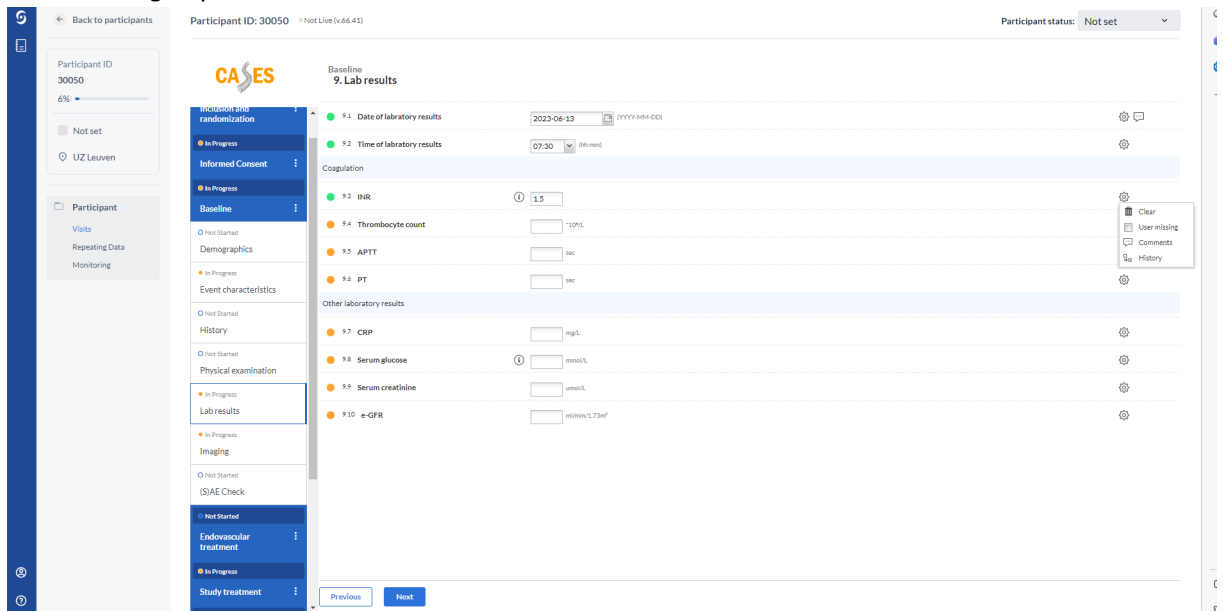
- 9.7 CRP:  mg/L
- 9.8 Serum glucose:  mmol/L
- 9.9 Serum creatinine:  umol/L
- 9.10 e-GFR:  ml/min/1.73m<sup>2</sup>

- During completion of the various forms, all answers are saved immediately. If you want to change an answer later on, you must provide a reason (audit trail).



Entries that are changed later on are marked with a  on the right side, with the audit trail displayed when you click on this icon.

- If an item cannot be answered due to missing data or some other known reason, it is necessary to specify this in Castor. To do this, use the icon on the right side to select the "user missing" option.




Then indicate the reason for missing data in the dialog box and briefly explain this reason in the text box. The default reasons are:

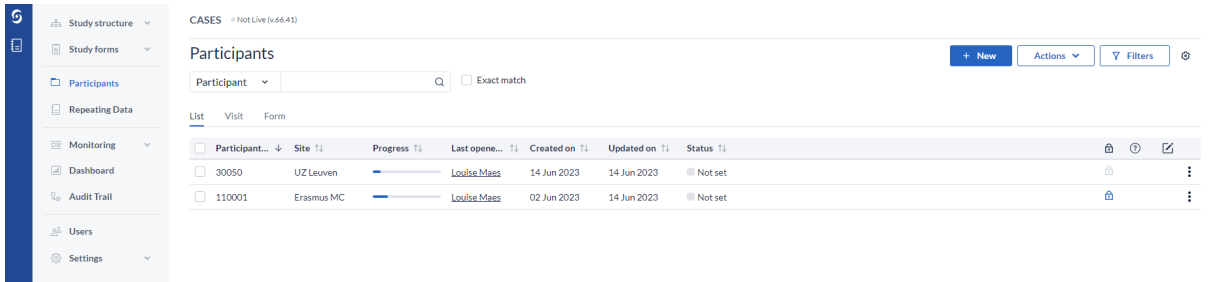
- a. **Measurement failed (-95):** enter this reason if a measurement was carried out but the determination failed (e.g., in case of a haemolytic sample at lab collection).
- b. **Not applicable (-96):** enter this reason if a certain question is not applicable for this participant.
- c. **Not asked (-97):** try to avoid this reason. If possible, still ask the item in question.
- d. **Asked but unknown (-98):** enter this reason if an item has been asked, but the answer to the question is unknown (e.g. unknown number of 'falls in the past year').
- e. **Not done (-99):** enter this reason if a study action was not performed (e.g., a lab value not determined, or a blood pressure measurement not taken).

The field marked as missing is displayed faded/gray in the form, but the status icon is updated to indicate that the field has been completed. A comment is added to the field indicating the reason entered

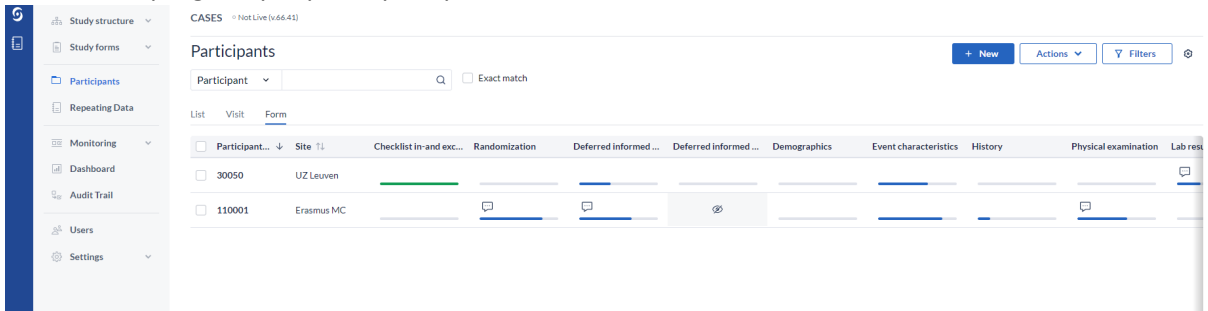
10. The progress of completing a form is displayed in the left side menu above the appropriate section of the eCRF by " Not started" if the eCRF is still empty, " In progress" if the eCRF is partially completed, and " Completed" if the eCRF is fully completed.

Participant ID: 30050

11. You can navigate between the different parts of the eCRFs by clicking on them in the left side menu, or by using the 'previous' or 'next' buttons in the bottom left of the screen to go to the previous or next eCRF part.
12. To return to the overview screen of all CASES participants from your center, click on  , at the top left of the screen.
13. In the overview screen, the progress of completing all eCRFs for one participant is shown via the progress bar.



To view the progress per participant per eCRF item in one view, click on 'Visit' or 'Form'.



There are multiple 'Visits' in Castor EDC with different 'Forms' underneath. Below are the nine relevant 'Visits' for local researchers:

Visit	Forms
<b>Inclusion and randomization</b>	Checklist in- and exclusion criteria, Randomization arm
<b>Informed Consent</b>	Deferred informed Consent (BE/NL)
<b>Baseline</b>	Demographics, Event characteristics, History, Physical examination, Lab results, Imaging, (S)AE check
<b>Endovascular treatment</b>	General information, Anesthetic management, Pre-treatment, Treatment, Attempt 1, Attempt 2-10
<b>Study treatment*</b>	Immediate CAS
<b>Clinical follow-up</b>	24 hour follow-up, 14 hour imaging, Day 6 +- 1 day follow-up, discharge intervention center part 1 & 2, (discharge second hospital (transfer) part 1 & 2)
<b>Deferred Treatment*</b>	Deferred Treatment
<b>Follow-up 3 months (unblinded)</b>	General patient information, Carotid ultrasound
<b>(S)AE check</b>	(S)AE form
<b>End of study</b>	End of study

\* Depending on whether the study treatment (immediate carotid artery stenting) is performed or not

## 6.6. Transfer to another hospital

Patients with acute ischemic stroke are usually sent to the nearest hospital. There, a NCCT/CTA and/or CTP is made. Should a patient qualify for EVT, he/she can be transferred to an EVT center. At the EVT center, the patient's eligibility for inclusion in the CASES trial will be evaluated. If eligible, the patient will be randomized.

Patients will remain in the EVT center at least until after the 24-hour follow-up. Thereafter, patients can be transferred back to a referring center or discharged to another care facility. This must be done after the deferred consent has been obtained. In case of transfer, the referring hospital is requested to provide the NIHSS score at discharge (5-7 days).

In both cases, the discharge letter should state that the patient is participating in a clinical trial.

Below are some drafts that can be included in the discharge letter.

### Patients presented at primary EVT center:

- This patient is participating in the Carotid Artery Stenting during Endovascular treatment in Stroke trial (CASES).
- A telephone interview with the study participant or his/her designated contact person will take place after approximately 90 days by a research assistant from the national coordinating center (UMC Groningen for the Netherlands or UZLeuven for Belgium).

### For referred/transferred patients:

- This patient is participating in the Carotid Artery Stenting during Endovascular treatment in Stroke trial (CASES).
- Please perform an NIHSS score on day 5-7 (or earlier at discharge).
- We would like to receive the patient's discharge letter and a copy of the paper CRF form 'discharge second hospital transfer', part 1 & 2
- In the event of complications, we would like to receive feedback.
- A duplex ultrasound of the carotid arteries will take place after 90 days
- A telephone interview will take place after approximately 90 days by a research assistant from the national coordinating center (UMC Groningen for the Netherlands or UZLeuven for Belgium).

## 6.7. Discharge

Upon discharge of the patient, additional information about the patient should be filled in on the discharge form to enable (blinded) telephone follow-up at 90 days after randomization.

1. Go to the CASES website: [CASES - discharge form](#)
2. Click on "Click here to submit patient discharge information".
3. Login with your center-specific login information (provided by you at the beginning of the trial)

4. Complete the screen below

5. If all information is completely and correctly entered, click 'Submit data'

6.8. (S)AEs

An Adverse Event (AE) is an undesirable experience occurring to a subject during the study, whether or not it is considered related to trial procedure. All adverse events reported spontaneously by the subject or observed by the investigator or his staff will be recorded in Castor EDC, using the (S)AE form.

A serious adverse event (SAE) is an adverse medical event in a patient or subject that is not necessarily causally related to the study and that:

- Results in death;
- Is life threatening (at the time of the event);
- Requires hospitalization or prolongation of hospitalization;
- Results in permanent or significant disability or incapacity;
- Is a congenital anomaly or birth defect;
- Any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been based upon appropriate judgement by the investigator.

An elective hospital admission will not be considered as a serious adverse event.



The investigator will report all AE to the sponsor by completing an AE form in Castor

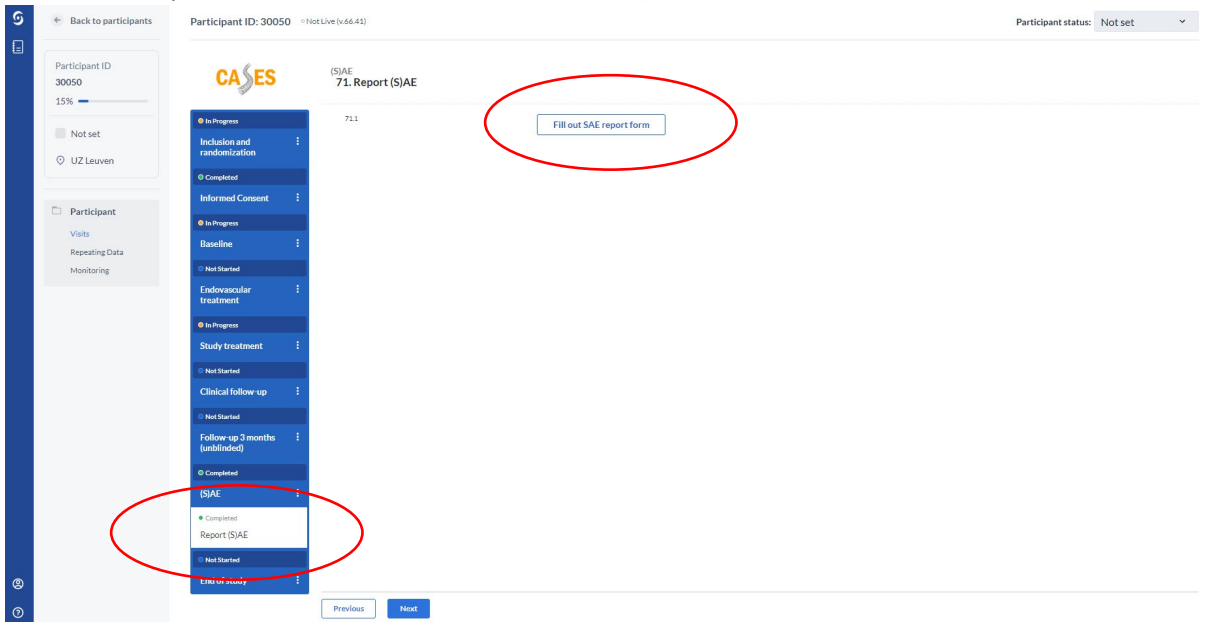
The investigator will report all SAEs to the sponsor without undue delay (< 24 hours) after obtaining knowledge of the events.

- Report all SAEs via [cases-trial@umcg.nl](mailto:cases-trial@umcg.nl) and/or +31 6 5272 4593 **AND**
- Complete an SAE form (in Castor EDC)

The sponsor will report the SAEs through the web portal to the accredited METC's in the Netherlands and the Research Ethics Committee UZ/KU Leuven (Central Committee) that approved the protocol, within 7 days of first knowledge for SAEs that result in death or are life threatening followed by a period of maximum of 8 days to complete the initial preliminary report. All other unexpected SAEs will be reported within a period of maximum 15 days after the sponsor has first knowledge of the serious adverse events.

### Adding (S)AEs in Castor EDC

1. Log in to Castor EDC. Click on "CASES". Click on the participant's study ID to open that participant's record (see also [eCRF in Castor EDC](#)).
2. Click on visit '(S)AE' and on form 'report SAE'. Then, click on 'Fill out SAE report form': a new window will open. Click on 'create' to create a new (S)AE form.



3. The (S)AE CRF opens (under 'repeating data'). Please fill out the form as completely as possible.

Participant ID: 30050 (Not Live (v.66.41)) Participant status: Not set

**SAE**

- Date of (S)AE report
- Name of investigator
- Description of the (S)AE (please create a short report)
- Date of (S)AE onset
- Neurologic deterioration of 4 points or more on NIHSS?
- Neurologic deterioration of 2 points or more on one NIHSS?
- Was there neuro-imaging performed for this SAE?
- SAE category
- (S)AE expected
- Select most likely cause for (S)AE
- Was there another cause for (S)AE selected?
- Relationship with the study procedures

Buttons: Close repeating data, All repeating data, Add another

4. The distinction between an AE and an SAE is made at question 8 'SAE category'. For an AE, select 'Not listed above (i.e. not a serious adverse event)'.

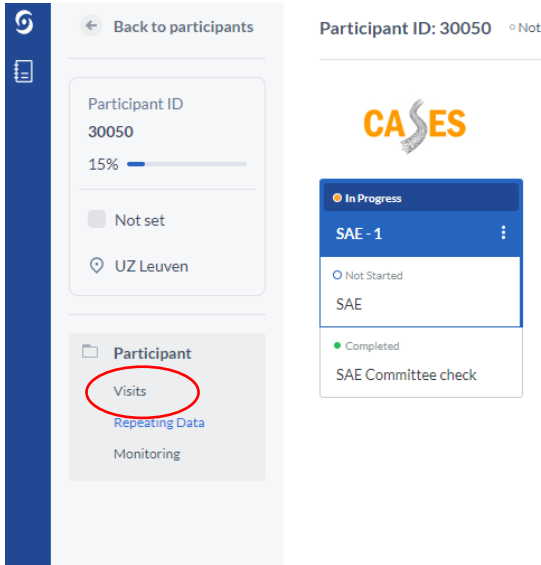
Participant ID: 30050 (Not Live (v.66.41)) Participant status: Not set

**SAE**

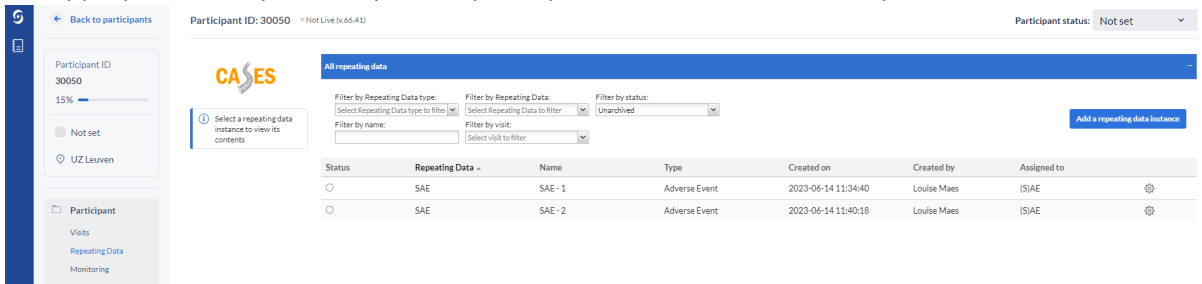
- Description of the (S)AE (please create a short report)
- Date of (S)AE onset
- Neurologic deterioration of 4 points or more on NIHSS?
- Neurologic deterioration of 2 points or more on one NIHSS?
- Was there neuro-imaging performed for this SAE?
- SAE category
- (S)AE expected
- Select most likely cause for (S)AE
- Was there another cause for (S)AE selected?
- Relationship with the study procedures
- Actions regarding study participation
- Outcome

Buttons: Close repeating data, All repeating data, Previous, Next

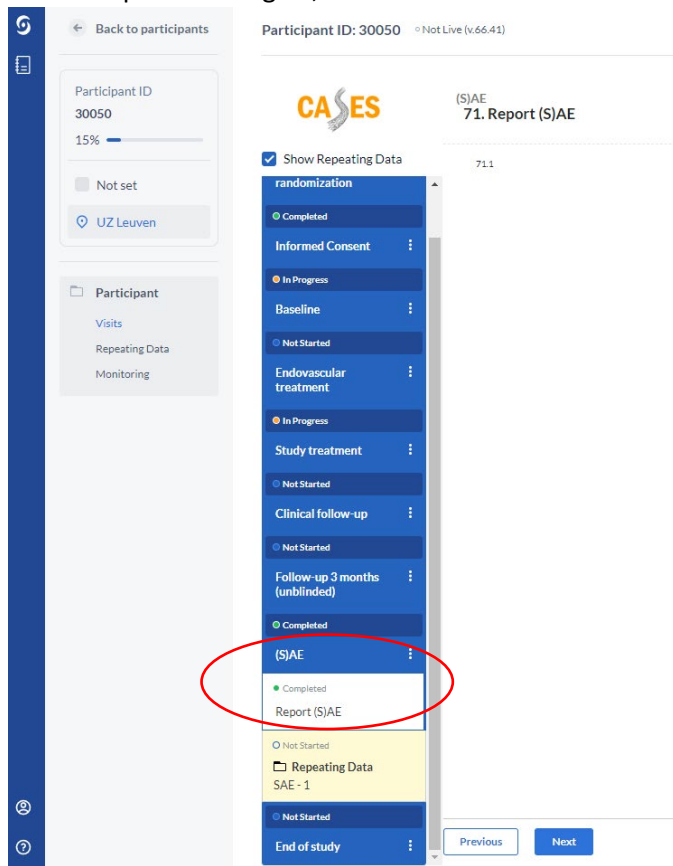
- To return to the rest of that participant's eCRFs, click on 'visits' on the far left of the screen.



- To see a list of all SAEs of one participant, click on 'Repeating Data' on the far left of the screen. The list of all SAEs is displayed under the heading 'All repeating data'. By clicking on the appropriate SAE, you can open the participant's SAE CRF to view/complete.



The SAEs can also be viewed individually (and adjusted if necessary) via the left-hand menu under 'Report SAE'. Again, the relevant SAE CRF can be opened by clicking on it.



## 6.9. Follow-up

The clinical outcome assessment by telephone at 3 months (with a margin of +/- 2 weeks) of patients included in the CAS ES trial is centrally organized by the national coordinating centers (UMC Groningen for the Netherlands and UZ Leuven for Belgium).

For more information about the (blinded) 90 day clinical follow-up, we refer to the SOP 'clinical follow-up by telephone at 3 months in the CAS ES trial': [CAS ES - trial protocol and trial documents](#)

## 6. Related documents

- Checklist CAS ES trial
- CRF CAS ES on paper (all combined)
- CRF CAS ES SAE form
- Study Protocol CAS ES
- Informed Consent Forms CAS ES
  - Belgium
  - The Netherlands
- SOP deferred consent
- SOP clinical follow-up by telephone at 3 months in the CAS ES trial

All important documents can be found on the CAS ES website: [CAS ES - trial protocol and trial documents](#)

## 8. Contact Information Study team

### CASES study team

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## 9. Appendices

### 9.1 Appendix 1: NIHSS

NIHSS Scoring			
Scale Item	Coma	Difficult or Confused	Tips
<b>1a LOC Responsiveness</b>	2 - for some movement 3 - Flaccid or no movement	0 - if awake, alert	Can usually tell score by greeting
<b>1b LOC Questions</b>	2	1 - ET tube, trauma, severe dysarthria; 2 - Aphasia, stupor, confusion	Score initial response; pt may write answers.
<b>1c LOC Commands</b>	2	2 - if unable to understand or follow the commands	You are not testing grip strength. May pantomime if pt doesn't respond to command; ok if impaired by weakness
<b>2 Best Gaze</b>	0 if normal eye movement noted	0 if patient able to track your movements	Coma - hold eyes open and turn head side-to-side. Confused - Make eye contact and move to other side of bed
<b>3 Visual</b>	0 if blinks to visual threat 3 if no blink in any field 3 if blind due to any cause	0 if blinks to visual threat 3 if no blink in any field 3 if blind due to any cause	Three ways to test - finger counting, finger movement or threat; test in 4 quads of each eye separately
<b>4 Facial Palsy</b>	3	If patient is verbal, observe for facial droop. If confused and nonverbal, use noxious stimulation to elicit grimace	Check NLF in advance; score 1 for minor asymmetry on smiling; score 2 major for asymmetry of smile; score 3 for absence of movement in upper <b>and</b> lower face
<b>5a, 5b Motor arm</b>	3 for no effort against gravity 4 for no movement at all	If unable to follow directions, use observation to score. Is the patient using the arm?	UNtestable only with amputation or fusion.
<b>6a, 6b Motor leg</b>	3 for no effort against gravity 4 for no movement at all	If unable to follow directions, use observation to score. Is the patient moving the leg?	UNtestable only with amputation or fusion.
<b>7 Limb ataxia</b>	0	0 if unable to follow directions	Absent if paralyzed or unable to understand. UNtestable only with amputation or fusion
<b>8 Sensory</b>	2	Use pinprick and observe patient's reactions if patient unable to cooperate	Ask pt, "can you feel this, can you feel this, and does it feel the same on each side"; (do not ask if sharper/duller)
<b>9 Best Language</b>	3	Choose score for stupor/limited cooperation: 2 - listener carries burden of communication; 3 - garbled or mute AND not following commands	Best language and COMPREHENSION; describe scene, name objects and read phrases. If blind, place object in hand and have patient describe
<b>10 Dysarthria</b>	2	1 - Difficult to understand (regardless of cause), 2 - speech not understandable, garbled	Listen to their words; if they can't read - have them repeat words or listen to the words they do say UNtestable only with physical barrier
<b>11 Extinction and Inattention</b>	0	Score only if present	Looking for lack of awareness with double tactile/visual stimulation

Reminders: a. Perform and score in numerical order. b. Accept first response. c. Do not coach.

For a detailed manual, please see: [NIH Stroke Scale](#)