Study title: **CASES** – **C**arotid **A**rtery **S**tenting during **E**ndovascular treatment of acute ischemic **S**troke (CASES) versus deferred treatment of carotid artery stenosis - A randomized multicenter clinical trial in patients with acute ischemic stroke and carotid artery stenosis undergoing endovascular treatment.

Sponsor of the study: University Medical Center Groningen

Belgium Coordinating Centre: University Hospitals Leuven

Central Medical Ethics Committee: Ethics Committee study UZ/KU Leuven, Herestraat 49, 3000 Leuven

Local Principial Researcher: << Name of Local Principal Investigator >>

I Essential information for your decision to participate

Introduction

For the attention of the patient: Because your clinical condition at the time of your admission to hospital, you were unable to make the decision whether or not to participate in the clinical study referred to above.

In cases such as this it is customary to appeal to a legal representative (usually a close relative). We ask that person to decide as closely as possible in the interest of the person he/she represents and taking into account this person's own will, whether this person may participate in the study. For some studies, experimental treatment should be started as soon as possible after admission.
Waiting to inform the legal representative about this study and obtain their consent for participation means that the usual treatment would be given, and the experimental treatment cannot be proposed in these circumstances.

For that reason, you were included in this study without having given your prior consent due to the critical situation you were in at the time, but possibly also without the consent of your legal representative because he/she was not able to give their consent in time.

For the attention of the legal representative: Because of the clinical condition of the person you represent at the time of his/her admission to hospital, he/she was unable to make the decision whether or not to participate in the clinical study referred to above.

Waiting to inform you about this study and obtain your consent to allow the participant you represent to take part means that the usual treatment would be given, and the experimental treatment cannot be proposed in these circumstances.

He/she is therefore included in this study without prior consent. Therefore, you are invited to decide whether he/she will continue to participate in this clinical trial, taking into account his/her wishes.

The sentences in the rest of this document are formulated as though we were addressing the person you represent directly.

In exceptional circumstances, when a prompt decision is necessary and it is highly probable that the participant will take part because of the benefits for the evolution of their clinical condition,the responsible ethics committee may exceptionally agree to the use of the experimental treatment without the consent of the participant or the legal representative, in accordance with the regulations of Chapter IV of the Act of May 2004 on experiments on the human person. This is called the emergency procedure.

Please note that the Ethics Committee approved the use of the emergency procedure for this study on 22-05-2023.

However, consent is needed from the patient and/or legal representative for further participation in the study and the collection and use of study data.

We invite you to read the attached document and confirm your participation. This document fully explains the objectives and procedures of the study, any risks and benefits of this study treatment and your rights as a clinical trial participant.
Please read this information carefully and put your questions to the researcher or his/her representative. This document consists of three parts: essential information for making your decision, additional information (annexes) and your written consent.

If you participate in this clinical trial, you should be aware that:

- This clinical trial is conducted after evaluation by the Research Ethics Committee UZ/KU Leuven (Central Committee) and the local Ethics Committees.
- Your participation is voluntary; there can be no coercion of any kind. Your signed consent is required for participation. After you have signed, you can inform the doctor leading the study that you wish to discontinue your participation. The decision on whether to participate will not have any negative impact on the quality of your care or your relationship with the doctors involved in the study.
- The data collected as part of your participation is confidential. Your anonymity is guaranteed when the results are published.
- You will not be charged for specific treatments, visits/consultations, examinations in the context of this study.
- Insurance has been taken out in case you incur any damages due to your participation in this clinical study.
- You can always contact your study doctor or a counsellor if you need additional information.
- This study will be conducted in accordance with the latest version of the Helsinki Declaration, the Belgian Act of 22 August 2002 on patients' rights, the Belgian Act of 7 May 2004 on experiments on the human person, European guidelines and the consensus of good clinical practice (ICH: International Conference on Harmonisation).

Additional information on your "Rights as a clinical trial participant" can be found in Annex 2, page 12.

Objective of the study

The aim of this study is to find out whether stenting of a severely narrowed carotid artery (carotid artery stenosis) during endovascular treatment of acute ischemic stroke is as effective as a deferred treatment approach of the carotid artery stenosis after catheter treatment.

If the study shows that this treatment is not less effective, the study data will then also be used to calculate cost-effectiveness of the immediate stenting approach.

Study background

This study was set up by the University Medical Center Groningen (UMCG) and is conducted by physicians at several hospitals in Belgium and the Netherlands. A total of 600 patients will participate in the study.

You have been hospitalized because you have suffered an acute ischemic stroke. An ischemic stroke occurs when a blood vessel in the brain is obstructed by a clot. Consequently, a part of the brain doesn't receive blood and becomes damaged. The symptoms that can result from this condition include paralysis, sensory impairment, language problems and/or partial blindness.

To increase the chances of recovery, patients receive a catheter treatment through the groin (endovascular treatment), if possible. Through this catheter treatment, the blood clot is mechanically removed from the blood vessel. For this treatment, the earlier the procedure, the greater the chance of recovery. About 1 in 3 treated people can function independently again after a 3-month recovery period.

In 1 in 5 people treated, the clot was caused by a severe narrowing in the carotid artery. This narrowing presents a high risk of another ischemic stroke. Therefore, current guidelines suggest that people with a narrowed carotid artery should undergo surgery within 2 weeks of the initial stroke to prevent a recurrent stroke. However, the narrowing in the carotid artery can also be corrected directly during the catheter treatment of the acute stroke by placing a stent in the carotid artery. A stent is a small tube with a mesh structure that can be placed in a blood vessel to correct a narrowing in the blood vessel

This study wants to investigate whether immediate stenting of the carotid artery stenosis during endovascular treatment of acute ischemic stroke is as effective as delayed treatment of the carotid artery stenosis.

Course of the study

You were included in this study via the emergency procedure. You were admitted to the hospital with an acute ischemic stroke and you also have a carotid artery stenosis. You required endovascular treatment for this.

Immediately after your hospital admission, you were randomly assigned to one of the two groups in this study.

If you were included in group 1, you underwent additional stenting of the carotid artery during the endovascular treatment of the acute stroke. This study treatment involves being transported to a treatment room almost immediately after the head scan. Once in the treatment room, a radiologist inserted a catheter into the artery in your groin under local anesthesia, mild sedation, or general anesthesia. Under medical imaging with X-rays, this catheter was advanced to the occluded blood vessel in your head. There, we attempted to remove the clot using catheter techniques (a removable stent and/or a small suction tube). The procedure took about 1 hour. During the procedure the carotid artery stenosis was treated with a permanent stent places in the carotid artery via catheters.

If you were assigned to group 2, you underwent the standard endovascular treatment without stenting of the carotid artery. However, the stenosis may have been treated by carefully inflating a balloon into the carotid artery in order to get past it to remove the blood clot in the brain. If you recover well over the next few weeks, additional surgery may follow to treat the stenosis.

The allocation to one of the two research groups and undergoing research treatment have already taken place without your prior consent.

We now ask you to consent to use the data already collected and continue to participate in this study.

The total duration of the study, from treatment to final check-up, is approximately 3 months.
During your hospitalization, the following tests/measurements have already taken place:

- Physical and neurological examination by the treating physician before and after the endovascular treatment
- Data regarding your medical history, medication and clinical situation are being collected and evaluated by the threating physician
- CT scan or MRI scan with and without contrast in the emergency department

During your continued hospitalization, the following tests/measurements will take place:

- about 24 hours after treatment, a CT scan of your neck and brain with and without contrast will be made and a physical and neurological examination will also be carried out
- the local research team will discuss with you which contact details will be shared with the central coordinating research team UZ Leuven
- 5-7 days after treatment or before discharge from the hospital (if discharge is earlier than 5-7 days), a physical and neurological examination will be carried out

After your discharge from the hospital, you will be contacted once by telephone by a staff member of the UZ Leuven central coordinating research team. This call takes place about 3 months after treatment and lasts about 15-30 minutes. During the interview you will be asked questions about your health status and quality of life (EQ-5D). Your level of functioning will be assessed using a scale (mRS = Modified Rankin Scale). The central coordinating research team will also send you two questionnaires (iMTA-PCQ and iMTA-MCQ) with questions about how you perceive your health status, whether you have been able to resume your activities, whether you have received treatment from other doctors, and whether you have relied on other health care providers. You will be asked to complete these questionnaires and return them to the central coordinating center with the enclosed addressed and stamped envelope. Completing the questionnaires takes about 30 minutes.

Contact details of the central coordinating center can be found in Annex 3, p 15.

Approximately 3 months after the stroke, a regular appointment will take place with your treating physician to follow up on your health condition, medication and any potential further treatment.
There will also be an ultrasound examination of the carotid artery after 3 months.

Some examinations are part of your normal care, while others are specific to the study. Examinations specific to this scientific study are:

- CT scan of your neck and brain with and without contrast, about 24 hours after treatment
- Telephone interview with an employee of the central coordinating research team UZ Leuven
- Questionnaires after 3 months
- Ultrasound examination of the carotid artery after 3 months at the local research center

In Annex 1, page 11, you will find a schematic overview of the course of the study.

Benefits

Participation in this study may or may not prove beneficial in treating your condition or reducing its symptoms. Immediate stenting may reduce the risk of recurrent stroke, but this is not certain.

No randomized clinical trial has been carried out yet to which clear conclusions about the effect of the two possible treatment strategies can be drawn. However, based on previous studies, patients who did undergo stenting of the carotid artery during catheterization seem to have a similar treatment effect as patients who did not undergo stenting.

The information obtained thanks to this study, may contribute to a better knowledge of the two treatment strategies in future patients with the same condition.

Risks and discomforts

During the stenting procedure, it is possible that a slowing of the heart rhythm or lowering of blood pressure may occur. To treat this temporary phenomenon, it could be that medication was administered during the procedure.

Treating the narrowing in the carotid artery leads to increased blood circulation in the brain. A possible complication of this is cerebral haemorrhage. The blood thinners required after stenting also could increase the risk of bleeding in stroke patients. So possibly there is a slightly higher risk of cerebral haemorrhage for patients in group 1.

Not stenting the carotid artery stenosis directly results in a higher risk of a recurrent stroke. Therefore, there may be a slightly higher risk of a new stroke for patients in group 2.

Possible adverse effects of the scans in this study:

- Radiation exposure: In a CT scan, we use X-rays. The total radiation exposure in this study is 5.6mSv in the CT scan with and without contrast and 1.2mSv in the CT scan without contrast. For comparison, the background radiation that each resident in the Netherlands/Belgium absorbs is ~2.5mSv per year. The radiation used during the examination may result in damage to your health. However, this risk is very small.
- Allergic reactions may occur if the CT scan is performed with contrast.

Alternatives

The acute treatment within the scope of the study was already carried out before your consent was obtained.

If you do not wish to participate in the study, this will not affect your further treatment. The researcher will advise you on all further treatment options.

For women of childbearing age

Pregnant women cannot participate in this study.
If you do become pregnant during the further follow-up period of this study, please inform the investigator.

Disclosure of new information

It is possible that important new information may become available during the course of this clinical trial. You will be notified of any new important information that may affect your decision to continue your participation in the study.

In that case, you will be asked either to sign a supplement to the consent statement or to sign a new information and consent document. If you decide to end your participation in the study in light of the new important information, your physician-investigator will ensure that you continue to be treated in the best possible way thereafter.

If you are participating in this clinical trial, we will ask you

- To fully cooperate with the proper conduct of this enquiry
- Not to withhold information about your health condition, the medications you are taking, or the symptoms you are experiencing
- Not to participate in another interventional clinical trial while taking part in this study
- To consent to the researcher informing your general practitioner and other doctors responsible for your health of your participation in this clinical trial
- To contact the investigator:
    - If you are admitted or treated in a hospital
    - If you experience sudden health problems
    - If you no longer wish to participate in the study
    - In your contact information changes

If you do not wish to participate or wish to stop the study

The decision to continue with the study is yours. Participation is voluntary.

If you no longer wish to take part, you will continue to be treated for your stroke in the usual way. The data available at that point will only be used if you do not object to their use in coded, non-traceable form. You can indicate this on Annex 4, page 16. "Use of clinical data in the absence of consent".

However, data on serious side effects, occurrence of brain haemorrhage and deathwill be used in a strictly anonymised form in the context of security analyses where it is important to have data from the entire patient group.

If you continue to participate, you can always change your mind and stop. You will then be treated in the usual way again. You do not have to say why you are stopping. However, you must tell the researcher immediately.

However, in case of withdrawal, the data collected until then will still be analyzed in coded form and the analyzed data will remain coded in the study documents. This is primarily for your medical safety. Please check that you agree to this before consenting to participate in the study.

End of the study

Your participation in the study stops if
- If the telephone interview with the research team, the questionnaire and the carotid ultrasound examination took place after 3 months
- You choose to stop
- The commissioner (UMC Groningen), the responsible public authority or the ethics committee decides to stop the study

The whole study is over when all participants have finished.

Use and collection of your data

This research project requires the collection and use of your medical and personal data, including the results of medical imaging.
All personal data collected as part of this research project, especially medical records, are subject to confidentiality and the provisions of the Data Protection Act.

If the study shows that one treatment works as well or better than another, the government agency funding the study, the KCE, may request a coded copy of some of the data from the study to assess whether a treatment, for example, should be reimbursed or recommended and whether its cost are justified. Your identity will never be disclosed to the KCE.
This data processing is necessary for the public interest to improve public health policy. The KCE is responsible for the data processed in the context of this additional research and must follow data protection rules.

More information on the use and collection of your data can be found in Annex 2, page 12.

Insurance for participants

Insurance has been arranged for everyone participating in the study. The insurance covers damage caused by the study. In Annex 2, page 12 you will find more information about the insurance. It also states to whom you can report damage.

Costs related to your participation

For the Belgian centres participating, funding was requested and obtained from the Federal Health Care Knowledge Centre (KCE) to reimburse the hospital for the time spent on the study by the researcher and his/her team. Therefore, if you decide to participate in this study, there will be no additional cost to you or your insurance company.

You can only be charged for costs related to routine medical treatment.
An overview of the studies and procedures belonging to this study can be found in the schematic overview on page 11 of Annex 1.

Contact

You can ask questions about the study at any time. Please contact your researcher or a member of the study team in case of ambiguities or if you have any kind of emergency during or after the study.

If you have any questions about your rights as a clinical trial participant, please contact your institution's Patients' Rights Ombudsman. If necessary, he/she can put you in touch with the Ethics Committee.

All contact details can be found in Annex 3, page 15.

Study title: **CASES** – Carotid Artery Stenting during Endovascular treatment of acute ischemic Stroke (CASES) versus deferred treatment of carotid artery stenosis - A randomized multicenter clinical trial in patients with acute ischemic stroke and carotid artery stenosis undergoing endovascular treatment.

Sponsor of the study: University Medical Center Groningen

Belgium Coordinating Centre: University Hospitals Leuven

Central Medical Ethics Committee: Ethics Committee study UZ/KU Leuven, Herestraat 49, 3000 Leuven

Local Principial Researcher: << Name of Local Principal Investigator >>

II Consent form – Participant

- I declare that I have been informed about the nature of the study, its purpose, duration, possible risks and benefits and what is expected of me. I have taken note of the information document and its annexes.
- I have had enough time to think about it and discuss it with a person of my choice, such as my GP or family member.
- I was given the opportunity to ask all the questions that occurred to me and received a satisfactory answer.
- I understand that my participation in this study is voluntary and that I am free to terminate it without affecting my relationship with the therapeutic team responsible for my health. The data collected up to the point of withdrawal will still be assessed as part of the study.
- I was informed about possible alternatives to the study, e.g. other treatment procedures.
- I agree that my general practitioner or other specialists in charge of my health will be informed of my participation in this clinical trial.
- In case of further treatment outside the study center, I authorize my treating physicians to pass on all data relevant to the study to the researcher.
- I understand that during my participation in this study data will be collected about me and that the researcher and the client will guarantee the confidentiality of this data.
- I consent to the processing of my personal data as described in the section on confidentiality guarantees (Annex 1). I also authorize the transfer and processing of this data to countries other than Belgium.
- I consent to my contact details being shared with the central coordinating research team UZ Leuven.
- I will be informed of results and/or incidental findings that directly affect my health. I will inform my researcher if I do not wish to be so informed.
- I am aware that the obligations set out in the information form must be fulfilled. In the interest of my health, the researcher can exclude me from the study at any time.
- I have received a copy of the information to the participant and the informed consent form.
- I consent that the research data from this study may be used by the funders of this study (BeNeFIT call, being KCE in Belgium and ZonMw in the Netherlands) or similar public health institutions in Europe for additional analyses such as determining which treatment is most cost-effective. The researchers conducting these analyses will not see your identifying data and are bound by professional confidentiality.

- I do □ **have**
  □ **not have** objection to the use of my research data already collected for the purpose of possible future scientific research on the same topic carried out in accordance with recognised ethical standards, even if the nature of the research is not known at this stage
- I do □ **have**
  □ **not have** objection to the submission of my coded data for review by manufacturers or regulatory agencies in Belgium , the Netherlands, Europe and/or the United States.
- I do □ **have**
  □ **not have** objection o being contacted for a follow-up research study after this study.

Participant

Name and first name of participant:

Date and time:

Signature of the participant:

Investigator

- I, the undersigned investigator, confirm that I have verbally provided the necessary information about the study and have given the participant a copy of the information document.
- I confirm that no pressure was brought to bear to persuade the patient to agree to participate in the study and that I am willing to answer additional questions if necessary.
- I confirm that I am acting according to the ethical principles set out in the latest version of the "Helsinki Declaration", "Sound Clinical Practice" and the Belgian Act of 7 May 2004 regarding human experiments.

Surname and first name of the investigator:

Date and time:

Signature of the investigator:

Study title: **CASES** – Carotid Artery Stenting during Endovascular treatment of acute ischemic Stroke (CASES) versus deferred treatment of carotid artery stenosis - A randomized multicenter clinical trial in patients with acute ischemic stroke and carotid artery stenosis undergoing endovascular treatment.

Sponsor of the study: University Medical Center Groningen

Belgium Coordinating Centre: University Hospitals Leuven

Central Medical Ethics Committee: Ethics Committee study UZ/KU Leuven, Herestraat 49, 3000 Leuven

Local Principial Researcher: << Name of Local Principal Investigator >>

II Consent form – Legal representative

- I declare that I have been informed about the nature of the study, its purpose, duration, possible risks and benefits and what is expected of me. I have taken note of the information document and its annexes.
- I have had enough time to think about it and discuss it with a person of my choice, such as my GP or family member.
- I was given the opportunity to ask all the questions that occurred to me and received a satisfactory answer.
- I understand that participation in this study is voluntary and that I am free to terminate it without affecting the relationship with the therapeutic team responsible for the health of the person I represent. The data collected up to the point of withdrawal will still be assessed as part of the study.
- I was informed about possible alternatives to the study, e.g. other treatment procedures.
- I agree that the general practitioner of the person I represent or other specialists in charge of his/her health will be informed of participation in this clinical trial.
- In case of further treatment outside the study center, I authorize the treating physicians to pass on all data relevant to the study to the researcher.
- I understand that during participation in this study data will be collected about the person I represent and that the researcher and the client will guarantee the confidentiality of this data.
- I consent to the processing of personal data of the person I represent as described in the section on confidentiality guarantees (Annex 1). I also authorize the transfer and processing of this data to countries other than Belgium.
- I consent to my contact details being shared with the central coordinating research team UZ Leuven.
- I will be informed of results and/or incidental findings that directly affect the health of the person I represent. I will inform the researcher if I do not wish to be so informed.
- I am aware that the obligations set out in the information form must be fulfilled. In the interest of the health of the person I represent, the researcher can exclude the participant from the study at any time.
- I have received a copy of the information to the legal representative and the informed consent form.
- I consent that the research data from this study may be used by the funders of this study (BeNeFIT call, being KCE in Belgium and ZonMw in the Netherlands) or similar public health institutions in Europe for additional analyses such as determining which treatment is most cost-effective. The researchers conducting these analyses will not see your identifying data and are bound by professional confidentiality.

- I do □ **have**
  □ **not have** objection to the use of research data of the person I represent already collected for the purpose of possible future scientific research on the same topic carried out in accordance with recognised ethical standards, even if the nature of the research is not known at this stage
- I do □ **have**
  □ **not have** objection to the submission of coded data for review by manufacturers or regulatory agencies in Belgium , the Netherlands, Europe and/or the United States.
- I do □ **have**
  □ **not have** objection o being contacted for a follow-up research study after this study.

Legal Representative

Name and first name of legal representative:

Relation to the person represented:

Date and time:

Signature of the legal representative:

Investigator

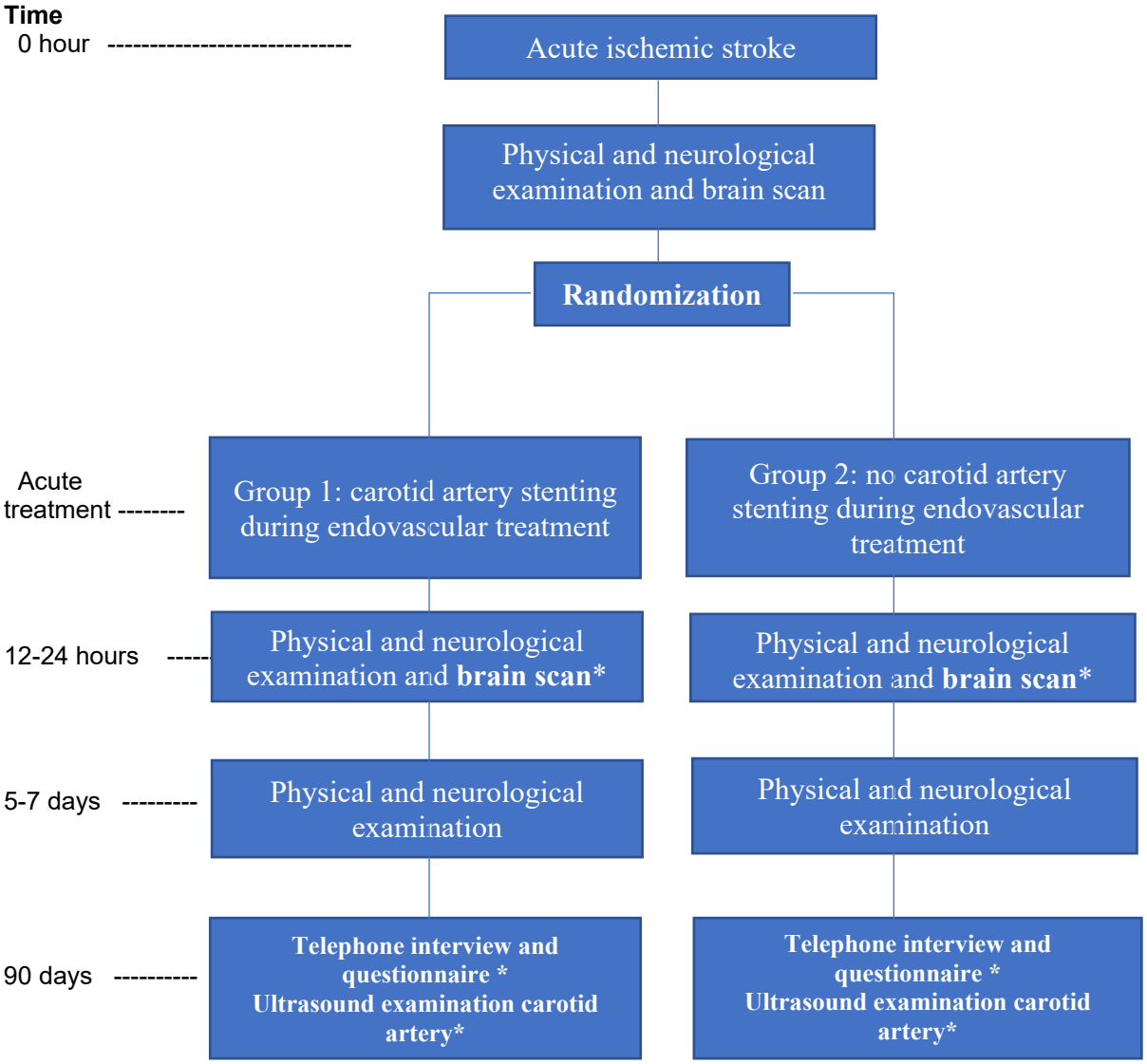
- I, the undersigned researcher, confirm that I have verbally provided the necessary information about the study and have given the legal representative a copy of the information document.
- I confirm that no pressure was brought to bear to persuade the patient to agree to participate in the study and that I am willing to answer additional questions if necessary.
- I confirm that I am acting according to the ethical principles set out in the latest version of the "Helsinki Declaration", "Sound Clinical Practice" and the Belgian Act of 7 May 2004 regarding human experiments.

Surname and first name of the investigator:

Date and time:

Signature of the investigator:

ANNEX 1 Schematic overview of the study



Nota : Investigations and tests as part of the study are marked with an asterix *

ANNEX 2 Additional information on the protection and rights of the participants in a clinical trial

Ethics committees
This study was evaluated by an independent ethical committee, the Research Ethics Committee UZ/KU Leuven, which issued a favorable opinion after consulting the ethics committees of each center in which this study will be conducted. The task of the ethics committees is to protect the individuals participating in clinical trials. They check whether your rights as a patient and as a participant in a study are respected, whether - based on current knowledge - the balance between risks and benefits is favorable for the participants, whether the study is scientifically relevant and ethically sound.

The ethics committees give an opinion on this in accordance with the Belgian Act of 7 May 2004.

You should in no way consider the positive advice of the ethics committees as an encouragement to participate in this study.

Voluntary participation
Do not hesitate to ask any questions that occur to you before you sign. Take the time to talk it over with a confidant if you wish.

You have the right not to participate or to stop participating in this study without having to provide a reason, even if you have previously agreed to participate in this study. Your decision will in no way affect your relationship with the doctor-researcher nor the quality of your subsequent care.

You will sign the consent form if you agree to participate in this study.
The doctor-researcher will also sign this form, confirming that he/she has given you the necessary information about this study. You will receive the copy intended for you.

For your safety, however, it is recommended that you inform the study doctor if you decide to discontinue your participation in the study.

Costs related to your participation
For the Belgian centers participating, funding was applied for and obtained from the Belgian Health Care Knowledge Center (KCE) to reimburse the hospital for the time spent on the study by the research doctor and his/her team, for consultations specifically in the context of the study, and for all examinations scheduled in the context of this study.

Therefore, if you decide to participate in this study, there will be no additional costs for you or for your insurance company. Only costs related to routine medical treatment may be charged to you.

Confidentiality guarantee
Your participation in the study means that the doctor-researcher collects data about you and the study sponsor uses them for research and for scientific and medical publications.

Your data will be processed in accordance with the European General Data Protection Regulation (GDPR) and the Belgian Data Protection Act. The University Medical Center Groningen is responsible for data processing.
You have the right to ask the doctor-researcher what data he/she has collected about you and what it is used for in the study. This data relates to your current clinical situation, your medical history, and the results of examinations carried out for treating your health according to the applicable standard of care. You have the right to inspect these data and to have them corrected if they are inaccurate.

All data collected will be kept for 25 years.

The doctor-researcher is obliged to treat these collected data as confidential

This means that he/she undertakes never to divulge your name, e.g. in the context of a publication or a conference, and that he/she will encrypt your data (an identification code in the study will replace your identity) before passing it on to the manager of the database, the CONTRAST Consortium, Erasmus MC.
The doctor-researcher and his/her research team know your code.
Your contact information will be collected and passed on to the central coordinating research team UZ Leuven to contact you by phone at 3 months as part of the study. These contact details are not part of the study analysis.

Throughout the clinical trial, the researcher and his/her team will be the only persons able to establish a link between the transferred data and your medical records.
The personal data transferred on your current clinical situation, medical history and on the results of examinations do not contain any combination of elements that would make it possible to identify you.
The administrator of the research data appointed by the client cannot identify you based on the transferred data. This person is responsible for collecting the data collected by all doctor-researchers participating in this study and for processing and protecting that data in accordance with the Belgian law on the protection of privacy (GDPR).

To check the quality of the study, your medical records may be inspected by persons bound by professional secrecy, such as representatives of the ethics committees, the sponsor of the study or an external auditing company. This can only be done under strict conditions, under the responsibility of the doctor-researcher and under his/her supervision (or that of his/her research assistants).
The (coded) research data can be passed on to Belgian or other regulatory authorities, the relevant ethics committees, and other doctors and/or institutions cooperating with the sponsor.

It may also be transferred to other sites of the client in Belgium and other countries where personal data protection standards may be different or less strict. This is always done in coded form, as explained above.

Therefore, your consent to participate in this study also means that you agree to your coded medical data being used for the purposes described in this information form and to its being transferred to the persons mentioned above and/or institutions.

The sponsor will use the data collected in the context of the study you are participating in but also wants to use it in other studies on the same condition as yours. Outside the context described in this document, your data can only be used if an ethics committee has given its approval and after your consent.

By agreeing to participate in this study, your study data may also be used by the funder (KCE) or by similar public health research institutes in Europe for further analyses, e.g., to determine which of the treatments studied is preferable. The KCE is an independent research center that provides scientific advice on public health topics. The objectives and tasks of the KCE are defined in Articles 262 to 268 of the Program Law (I) of December 24, 2002. As part of these missions, the KCE must have access to certain personal data relating to the health of Belgian citizens and has the task of conducting analyses based on coded (pseudonymized) data in the public interest.
For these future projects, KCE or similar public health research institutes in Europe, as data controllers, will seek approval from the Social Security and Health Chamber of the Information Security Committee (IVC) in accordance with relevant legislation. IVC decisions are public and can be consulted on the IVC website (https://www.ehealth.fgov.be/ehealthplatform/nl/sectoraal-comite/documenten). KCE reports are also publicly available https://kce.fgov.be/en/publications/all-reports-0). It is not possible for the KCE to inform you personally because the KCE does not have your contact information.
At the end of the study, the healthcare provider or healthcare facility of this study may be asked to transfer your national registry number to the eHealth platform as a third trusted party, for pseudonymization. This means replacing your national registry number with a meaningless code. The eHealth Platform has the legal mandate to do this (Article 5 of the Act of August 21, 2008 establishing and organizing the eHealth Platform and various provisions).
Your identity will always be known only to your healthcare provider or healthcare institution. For the pseudonymization, the eHealth platform temporarily has your national registration number at its disposal, but not your other data or the data from this study. The KCE has only pseudonymized personal data without identity information.

In this way, for the KCE, data from this study can be linked to data from other sources, such as healthcare billing data, without the KCE knowing your identity. However, linking the study data with other data for the KCE is only possible under strict conditions and after a positive opinion from an independent organization, the Information Security Committee (IVC). The IVC assesses whether the requested processing can be done correctly according to the applicable legislation. All decisions of the IVC are public and can be consulted on the website of the ICV (https://www.ehealth.fgov.be/ehealthplatform/nl/sectoraal-comite/documenten). KCE reports are also publicly available (https://kce.fgov.be/en/publications/all-reports-0) and contain only anonymous results.

Your data are processed in accordance with the Belgian Law of July 30, 2018 on the protection of natural persons with regard to the processing of personal data and the Regulation (EU) 2016/679 of April 27, 2016, which entered into force on May 25, 2018, on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (GDPR).
All KCE researchers are legally bound by their professional duty of confidentiality.
If you have any questions or comments about the processing of your data, you can easily contact the KCE as the data controller at info@kce.fgov.be or by letter to KCE, Boulevard du Jardin Botanique 55, 1000 Brussels. If you wish, the KCE Data Protection Officer can provide you with more information about the protection of your personal data. You can contact him via e-mail (kce_dpo@kce.fgov.be).

If you withdraw your consent to participate in the study, the collected coded data will be retained before your withdrawal. This secures the validity of the study. No new information will be passed on to the client.

You can always contact your doctor-researcher if you have any questions about how we use your data. The Data Protection Officer of the Research Centre is also available to you. The contact details are given in Annex 3, page 15.

Finally, if you have a complaint about the processing of your data, you can contact the Belgian supervisory authority that monitors compliance with the fundamental principles of personal data protection, the Data Protection Authority (DPA). The contact details are given in Annex 3, page 15.

Insurance for participants
Every participation in a study involves risk, however small. The client is liable - even if there is no fault - for the damage incurred by the participant or, in the event of his/her death, by his/her successors, which is directly or indirectly related to his/her participation in the study. You do not have to prove any fault for this. The client has taken out insurance for this liability.

We therefore ask you to report any new health problem to the medical examiner. He/she can give you additional information about possible treatments.
If the doctor-researcher considers that there may be a link with the study (there is no link with the study in case of damage due to the natural course of your condition or due to known side effects of your standard treatment), he/she will inform the sponsor of the study, which will initiate the declaration procedure with the insurance company. It will appoint an expert to assess the connection between your new health complaints and the study if it deems necessary.

In case of disagreement with the doctor-researcher or with the expert appointed by the insurance company, and whenever you deem it necessary, you or, in case of death, your beneficiaries can make a claim on the insurer directly in Belgium.
The law provides that the insurer may be subjected to the claim either in the courts of the place where the harmful events occurred, in the courts in your place of residence, or the courts in the location of the insurer's registered office.

Contact details and the insurer's policy number are given in Annex 3, page 15.

ANNEX 3 – Contact details

STUDY TEAM OF THE LOCAL STUDY CENTER	
Principal investigator	<< Insert local contact information >>
Study coordinator	<< Insert local contact information >>
Emergency contact	<< Insert local contact information >>

OMBUDSMAN SERVICE questions and remarks about your rights as a study participant
<< Insert local contact information >>

DATA PROTECTION OFFICER questions about data confidentiality
<< Insert local contact information >>

BELGIUM COORDINATION CENTER UZ LEUVEN	
Principal investigator:	Prof. Dr. Robin Lemmens UZ Leuven - Neurologie Herestraat 49 B-3000 Leuven
Studie coördinatoren	Dr. Louise Maes email : louise.maes@uzleuven.be
	Mw. Annemie Devroye email : annemie.devroye@uzleuven.be
	Mw. Evelyn Marcelis email : evelyn.marcelis@uzleuven.be

BELGIAN DATA PROTECTION AUTHORITY complaints relating to data confidentiality
Drukpersstraat 35, 1000 Brussel E-mail: contact@apd-gba.be Telefoon: +32 2 274 48 00 Website: www.gegevensbeschermingsautoriteit.be

INSURANCE COMPANY
MS Amlin Insurance SE Koning Albert II laan 37, B-1030 Brussel Policy number: 299.053.700

ANNEX 4 – Use of clinical data in the absence of consent - participant

- I have read the information letter. I also had the opportunity to ask questions. My questions were adequately answered. I had enough time to decide whether to take part in the study.

- I do **not** give my consent to participate in the study, there will be no surveys or interviews that are not necessary for my treatment.
- I do □ **have**
  □ **not** have objection to the use of my previously collected research data in coded (non-personally identifiable) form.

- I do □ **have**
  □ **not** have objection to the use of my research data already collected for the purpose of possible future scientific research on the same topic carried out in accordance with recognised ethical standards, even if the nature of the research is not known at this stage

Participant

Surname and first name of the participant :

Date and time:

Signature of participant:

Investigator

- I, the undersigned researcher, confirm that I have verbally provided the necessary information about the study and have given the participant a copy of the information document.
- I confirm that I am acting in accordance with the ethical principles set out in the latest version of the "Declaration of Helsinki", the "Good Clinical Practice" and the Belgian law of 7 May 2004 regarding experiments on humans.

Name and first name of the investigator :

Date and time:

Signature of the investigator:

ANNEX 4 – Use of clinical data in the absence of consent – legal representative

- I have read the information letter. I also had the opportunity to ask questions. My questions were adequately answered. I had enough time to decide whether to take part in the study.

- I do **not** give my consent to participate in the study, there will be no surveys or interviews that are not necessary for the treatment of the person I represent
- I do □ **have**
  □ **not** have objection to the use of previously collected research data of the person I represent in coded (non-personally identifiable) form.

- I do □ **have**
  □ **not** have objection to the use of research data of the person I represent already collected for the purpose of possible future scientific research on the same topic carried out in accordance with recognised ethical standards, even if the nature of the research is not known at this stage

Legal Representative

Name and first name of legal representative:

Relation to the person represented:

Date and time:

Signature of the legal representative:

Investigator

- I, the undersigned researcher, confirm that I have verbally provided the necessary information about the study and have given the legal representative a copy of the information document.
- I confirm that I am acting in accordance with the ethical principles set out in the latest version of the "Declaration of Helsinki", the "Good Clinical Practice" and the Belgian law of 7 May 2004 regarding experiments on humans.

Name and first name of the investigator :

Date and time:

Signature of the investigator: