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 Letter of information for next of kin on participation in medical scientific research

You are receiving this letter because your partner/relative has been affected by an acute ischemic stroke and has sadly passed away. First of all, we offer you our heartfelt condolences for your loss. Through this way, we would like to provide you with additional information about your relative's participation in a medical scientific trial during the hospitalisation.

This study on the effect of placing a stent in the carotid artery was set up by the University Medical Centre 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.

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. At the moment, this is still uncertain.

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.

An ischemic stroke occurs when a blood vessel in the brain is obstructed by a clot, causing part of the brain to not receive blood and become 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 are treated with 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. A severe narrowing in the carotid artery presents a high risk of another ischemic stroke. Therefore, people with a narrowed carotid artery often have surgery within 2 weeks of the initial stroke to prevent a recurrent stroke. 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.

The advantages of direct stenting during catheterisation are that a patient only has to undergo surgery once and the risk of another stroke is immediately reduced. A possible disadvantage is that after stenting, people take two blood thinners for a longer period of time than when not stenting. Therefore,

with this study, we want to investigate whether immediate stenting of a carotid stenosis at the time of catheter treatment of the stroke works at least as well as delayed treatment of the carotid stenosis.

In this study, we want to determine 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.

For this study, all participants will be randomly assigned to one of the following two treatment groups:

- Group 1: patients will undergo immediate stenting of the carotid artery at the time of catheter treatment for acute stroke.

- Group 2: patients will not undergo stenting of the carotid artery at the time of catheter treatment for acute stroke (control group, standard treatment)

The assignment to treatment groups and the treatment itself occurred before you provided fully-informed, written consent to participate in the scientific study. It was our intention not to seek consent to participate in the study at the acute stage, but to postpone it until a calmer time. The reasons for this were the severity of your loved one's symptoms on admission to hospital and the importance of removing the clot and treating the cause as soon as possible. Furthermore, previous research shows that this treatment has a limited risk.

In these exceptional circumstances 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 can, by way of exception, 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 dd-mm-yyyy.

In your relative’s case, the treatment did not prevent his/her death. During hospitalisation, we were unable to inform your relative or you about the study earlier and obtain written consent for further participation in the study. Therefore, we would like to inform you about this study now.

The use of your relative’s data is of great importance for future stroke patients. We will therefore use the data when analysing the study results of the entire group of participants.

This study does not involve any additional costs.

An insurance policy has been taken out in case any damage is incurred due to participation in this study.

More information regarding insurance, the use and retention of your relative’s data and the funding/cost of this study can be found in Appendix 2.

Should you still need further information after reading this letter, we are of course happy to respond to your questions. You can contact the local researcher or one of his staff by telephone. The contact details can be found in appendix 1, page 3

ANNEX 1 – 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 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 favourable opinion after consulting the Ethics Committees of each centre 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 favourable 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.

Funding/costs

For the Belgian centers participating, funding was applied for and obtained from the Belgian Health Care Knowledge Center (KCE). This 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.

This study involves no additional costs. Only costs related to routine medical treatment of your relative may be charged.

Confidentiality guarantee

The data of your relative 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 your relative and what it is used for in the study. This data relates to your relative's current clinical situation, medical history, and the results of examinations carried out for treating your relative's health according to the applicable standard of care.

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 relative's name, e.g. in the context of a publication or a conference, and that he/she will encrypt your relative's 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 relative's code.

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 relative's medical records.
The personal data transferred does not contain any combination of elements that would make it possible to identify your relative.
The administrator of the research data appointed by the client cannot identify your relative 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.

To check the quality of the study, your relative's 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.

The sponsor will use the data collected in the context of this study but also wants to use it in other studies on the same condition. Outside the context described in this document, your relative's data can only be used if an ethics committee has given its approval.

Your relative's 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 relative's national registry number to the eHealth platform as a third trusted party, for pseudonymization. This means replacing your relative's 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 relative's identity will always be known only to your healthcare provider or healthcare institution. For the pseudonymization, the eHealth platform temporarily has your relative's 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 relative's 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 relative's 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.

All KCE researchers are legally bound by their professional duty of confidentiality.

If you have any questions or comments about the processing of your relative's 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).

You can always contact your relative's doctor-researcher if you have any questions about how we use your relative's data. The Data Protection Officer of the Research Centre is also available to you. The contact details are given in Annex 1, page 3.

Finally, if you have a complaint about the processing of 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 1, page 3.

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.

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 the condition or due to known side effects of the 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 the 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 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 1, page 3.