Supplement for the Impulse application of CVON2015-01 CONTRAST

This document is an addendum to the general Impulse brochure. It describes why the Collaboration for New treatments of Acute Stroke (CONTRAST) consortium is invited to apply for an Impulse Grant, the goals and scope for their Impulse Program application, and specific points of attention.

Stroke / Background

A cerebrovascular accident (CVA) is also known as a stroke. A stroke is when blood flow to a part of the brain is stopped either by a blockage or rupture of a blood vessel. The two main types of strokes are an ischemic stroke, caused by a blockage, and a hemorrhagic stroke, caused by the rupture of a blood vessel. An ischemic stroke prevents blood and oxygen from reaching a part of the brain. A hemorrhagic stroke disrupts the blood flow to a part of the brain, but also causes damage when blood leaks into the brain or surrounding tissues. Whether a stroke is caused by a blockage or a rupture cannot be diagnosed on sight, but normally requires a CT- or MRI-scan.

Strokes occur with a high frequency and have a large impact on the lives of patients, their family and surroundings, and society. Even for stroke survivors, the consequences of a stroke can be severe due to damage to parts of the brain and the associated loss of function. Every second counts when treating a stroke. If blood supply to the affected brain region is restored within the first hours after a stroke, the patient has a good chance of surviving with minimal permanent damage to the brain.

Neurologists and neurointerventionists are increasingly capable of reopening blocked vessels through medication or endovascular intervention. However, treatment options for the different types of strokes are limited and it has yet to be determined which groups of patients benefit most from the specific treatments. Rehabilitation, training and long-term support for stroke survivors therefore remains an import part of treatment to regain as much of their brain function and quality of life as possible.

CONTRAST

CONTRAST is a collaboration between academic researchers, private and public partners. The overarching aim of CONTRAST is to improve outcome for patients with stroke by merging translational research and pragmatic randomized clinical trials, with firm goals for the future of Dutch stroke research and treatment.

In 2014, the DHF-funded MR CLEAN-study (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) was the first study to demonstrate the effectiveness of intra-arterial therapy with the use of a retrievable stent for the treatment of acute ischemic stroke. This success was followed by the creation of the CONTRAST consortium (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) in 2015. This consortium was born out of the success of the MR CLEAN study and based on the collaborative aims formulated in the national cardiovascular research agenda theme: acute treatment of stroke. With CONTRAST, a close collaboration was created between neurologists, (neuro)radiologists, neurosurgeons and other medical specialists in the Netherlands with representatives from nearly all university hospitals and connected with large non-academic hospitals. Collaboration on a national level has strengthened Dutch neurovascular research, while the joint knowledge, experience, and expertise facilitates research into less frequently occurring types of strokes.

From 2015 up to February 2022, the CONTRAST consortium has already finished four multi-center clinical trials that assess potential improvements of acute ischemic stroke treatment and one pilot study in hemorrhagic stroke. The results of these trials will improve treatment protocols and improve outcome for patients with stroke. Furthermore, the CONTRAST consortium uses advanced imaging to identify groups of patients who will benefit from these interventions. Basic scientific projects that are carried out within the CONTRAST consortium aim to support the capacity building of preclinical stroke research in the Netherlands and elucidate mechanisms of incomplete microvascular reperfusion with the goal to develop novel stroke treatments. The Netherlands Experimental Stroke Alliance (NESA) was formed by members of CONTRAST. NESA aims to provide an environment of continuing successful experimental stroke research in the Netherlands. This includes basic science studies, which play a fundamental role in the elucidation of pathophysiological mechanisms, the identification of novel diagnostic markers, and the development of new treatments for cerebral ischemia or hemorrhage. Finally, data obtained during the multi-center clinical trials is being used to improve stroke care by creating a model for efficient distribution of advanced imaging and treatment modalities for stroke in western countries, such as the Netherlands.

Position of Stroke within the DHF, BFN, and DCVA

The high prevalence of stroke and its severe impact on patients, their families and surroundings put solutions for the disease burden caused by stroke high on the agenda for the Dutch Heart Foundation (DHF), the Brain Foundation Netherlands (BFN), and the Dutch CardioVascular Alliance (DCVA). The acute treatment of stroke is the third theme on a national research agenda for cardiovascular disease as initiated by the DHF and co-created by, amongst others, patients, researchers, and health care professionals.

The DHF aims that all patients suffering from a stroke get the best possible treatment as soon as possible, adjusted to their specific situation. By striving for this goal, we prevent or limit brain damage caused by stroke. More patients survive a stroke and are capable of picking up their daily lives again in an independent manner. For more information about the challenges and objectives in coming years, read the evaluation of theme 4 of the research agenda: Acute treatment of stroke.

The BFN wants to minimize disease burden caused by stroke for all stroke survivors, also on the long run (chronic phase), and maximize quality of life for these patients. After the acute and subacute phase, some problems occur only in the chronic phase when people are picking up their lives again, such as fatigue, concentration problems or overstimulation. The BFN aims for attention and solutions for these so called ‘invisible consequences’ of stroke.

The DCVA has the ambition to lower the cardiovascular disease burden by 25% in 2030 by earlier recognition of disease and rapid translation of excellent science into health improvement. DCVA (and CVON) consortia and projects work on earlier detection of persons at risk of developing a stroke, improved diagnosis of different types of strokes, and improved treatment of different types of strokes. The FIRST-fund, co-founded by the DCVA, has provided start-up funding for a company developing a blood clot dissolving drug that could be used to treat ischemic stroke patients.

Continuation of the successful activities of the CONTRAST consortium is therefore fully in line with the missions and research agendas of the DHF, BFN and DCVA.

Impulse Program and CONTRAST

The Dutch neurovascular research community is internationally renowned for its clinical studies into treatment options for acute stroke. The existing neurovascular healthcare infrastructure is compact and built on strong collaborations between neurologists, (neuro)radiologists, neurosurgeons and other medical specialists. This offers unique opportunities for research into healthcare problems that require a swift response and strong organization, as is the case for research into acute stroke treatment. The Dutch neurovascular research community has the potential to develop into a testing ground for innovation in ambulatory diagnostics and rapid and effective treatment of acute stroke. Combined with attention for rehabilitation of stroke survivors, we can truly make a difference for patients and their surroundings.

Goal of the Impulse Program and a task of a national thematic consortium is to:

- Strengthen and/or establish thematic networks;
- Initiate innovative research;
- Implement research findings into daily clinical practice.

The Impulse Program provides CONTRAST the opportunity to not only accelerate reaching its ambitions but also to expand their national collaboration and to develop a consortium that is positioned centrally within the Dutch cardio- and neurovascular research and healthcare landscape. The DHF and BFN invite CONTRAST to submit an application because of its progress in the past five years, the promising results, and the expressed ambition to continue and expand their impactful collaborations with other stroke initiatives. The new consortium should at least contribute to the ambitions of the DHF as described in the Dutch national cardiovascular research agenda and to the ambitions of the BFN regarding the chronic phase of stroke survivors. Taking steps towards the implementation of findings in clinical practice is one of the main objectives of this program.

Scope

The scope of the Impulse consortium should be on lowering the disease burden for patients suffering from stroke. The project ideally consists of three parts that are intertwined:

a. Earlier diagnosis of stroke
b. Rapid and effective treatment of acute stroke
c. Improved rehabilitation for stroke survivors in the (sub)acute and chronic phase

Tasks for the initiators

In addition to the tasks of the initiators as set out in the Impulse Program brochure (Chapter 2) specific tasks apply:

- Broad support for the Impulse Program is for a large part created by the inclusivity during the initiating phase. We expect initiators and future research leaders of a national thematic consortium on stroke to consult with relevant Dutch research groups working on stroke. The goal of these consultations is to explore whether these groups can become part of the new consortium. If groups have research plans that strongly contribute to the main goal of the Impulse consortium and no funding is available, this plan should be fully incorporated in the program and a joint plan for attracting additional funding should become part of the project plan.
- Initiators are expected to discuss with the current consortium leaders of the CONTRAST consortium, with other respected experts in the field of (pre)-clinical stroke research and with stroke care professionals on how to maintain and further strengthen the national network around stroke.

The CONTRAST consortium has suggested two initiators for the Impulse application, namely Prof. Aad van der Lugt (Erasmus MC) and Prof. Yvo Roos (Amsterdam UMC). The DHF and BFN have agreed with the appointment of these two initiators. If this proofs desirable during the application phase, it is possible to appoint a third initiator in consultation between the current initiators and both funding agencies.

Directives for the application

- Focus on the continuation of the most successful and promising research lines and results from the CONTRAST consortium. Critically evaluate which projects within the CONTRAST consortium should not be continued.
- Facilitate a smooth transition from the CONTRAST consortium to the new consortium, ensuring that data and samples generated in the context of CONTRAST are stored in a durable way and remain available for reuse.
- Provide opportunities for research talents from CONTRAST to develop into a leadership role in the new consortium, while taking diversity aspects into account in the leadership team.
- Strengthen interaction with the DCVA and other DCVA consortia to allow mutual beneficial exchange of knowledge and expertise.
- While CONTRAST is focused on treatments for acute ischemic stroke, the new consortium expands its focus to a broader range of strokes, including hemorrhagic stroke.
- Create an efficient and durable infrastructure for neurovascular clinical trials in the Netherlands. Such a clinical trial infrastructure should make it possible to readily include new treatment centers; include specific stroke patients; and share relevant data with researchers and centers participating in the study.
- Create a sustainable national registry for specific types of stroke in the Netherlands. This registry contains data including, but not limited to, the type of stroke; patient delay and system delay; mode of transport and routing; patient characteristics; stroke severity; interventions and medical treatment, outcome (morbidity, mortality, modified Ranking scale); destination following treatment; rehabilitation; and patient reported outcome measures (PROMs). The registry should be able to accommodate observational studies and embedded intervention studies on early

rehabilitation and early secondary prevention. Aggregated data obtained with this registration will become available for the website www.hartenvaatcijfers.nl.

- Develop and execute research projects and initiatives that further improve the early diagnosis and care for stroke patients.
- Develop and execute research projects and initiatives that improve quality of life of stroke survivors in the subacute and chronic phase. This includes secondary prevention, treatments, and interventions in patients who had been treated for large vessel occlusion. For this purpose, it is desirable to include relevant expertise regarding stroke rehabilitation and support for reintegration in society in the newly formed consortium. Furthermore, we expect the consortium to collaborate with patients and/or patient groups to develop key goals for improved quality of life.
- Explore improvements in the chain of care for stroke patients, facilitating a smooth transition from acute healthcare to stroke rehabilitation and reintegration into society.
- Continue and strengthen fundamental and pre-clinical research into the causes and/or pathophysiology of strokes within the Netherlands Experimental Stroke Alliance (NESA). And strengthen the collaboration with the Dutch CardioVascular Alliance, her partners and consortia. The ultimate goal is to develop improved methods for diagnosis, therapeutic options, or rehabilitation methods that reduce the burden of stroke.
- Collaborate with medium and large enterprises in preclinical and clinical research. Large randomized controlled trials should preferably be co-funded by industrial partners.

Planning

Beginning of March 2022	Invitational call launched
26th of July 2022	**Submission of proposal**
Beginning of Aug 2022	Eligibility check, start evaluation by external reviewers
Medio of Sept 2022	Deadline external reviews
Medio of Sept 2022	Compilation of the reviews sent to consortium
Beginning of Oct 2022	**Assessment meeting**
End of Oct 2022	Decision by boards of DHF and BFN

More information

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Please reach out to discuss any questions, unclarities or matters during the application process.