

## CZECH STROKE RESEARCH NETWORK – STROCZECH

### 1<sup>st</sup> YEAR REPORT

#### A. INTRO

The **purpose** of this document is to provide an overview and update on the Czech Stroke Research Network (STROCZECH), the first Disease Oriented Network within CZECRIN. This report is for stakeholders, namely to CZECRIN Boards and Committees, Ministry of Education, Youth and Sports, involved hospitals, employees and partners.

#### Introduction of the Network

The goal of the Czech Stroke Research Network (STROCZECH) is to take advantage of both the existing and effectively working network of stroke centres in the Czech Republic and CZECRIN research infrastructure to build an environment, human structure and know-how for development of academic clinical trials in stroke in the Czech Republic.

The ambition is to conduct large multi-centre clinical trials, which will be initiated by investigators from the Czech Republic, or conducted in cooperation with international partners. Aims are to achieve medicine-changing research results to stroke care, to build know-how in conducting randomized clinical trials in the Czech Republic, and to promote Czech Republic as a country with strong scientific potential.

The STROCZECH Network was planned to start within the CZECRIN research infrastructure in 2020.

#### B. REPORT

##### 1) PROCESS OF BUILDING NETWORK OF HOSPITALS

In the Czech Republic, there are 45 stroke centres authorized by the Ministry of Health to provide stroke care based on Ministry of Health Journal (Věstník) No. 2015/issue 11. From 45 stroke centres, there are 32 Primary stroke centres ready to administer intravenous/thrombolytic treatment, and 13 Comprehensive stroke centres providing both intravenous and endovascular treatment.

In 2019, before the STROCZECH officially started, all 45 stroke centres were addressed and were offered to be involved in the Network. Twenty centres expressed their interest and met criteria needed for conducting academy clinical trials at the same time. Initiating online meetings of the Network Coordinator (St. Anne's University Hospital) with each hospital/stroke centre are conducted to discuss mutual cooperation in detail. Nine online meetings were held by the end of November 2020.

The list and map of involved stroke centres are in Table 1 and Figure 1 below.

1. General University Hospital in Prague	11. University Hospital Olomouc
2. University Hospital Motol	12. Tomas Bata Regional Hospital Zlin
3. Military University Hospital Prague	13. University Hospital Ostrava
4. Na Homolce Hospital	14. Vítkovice Hospital Ostrava
5. Královské Vinohrady University Hospital	15. Karviná Hospital
6. Thomayer Hospital	16. University Hospital Hradec Králové
7. Jihlava Hospital	17. Pardubice Hospital
8. St. Anne's University Hospital Brno	18. Liberec Regional Hospital
9. University Hospital Brno	19. České Budějovice Hospital
10. Vyškov Hospital	20. Písek Hospital

Tab. 1 List of hospitals participating in the Czech Stroke Research Network

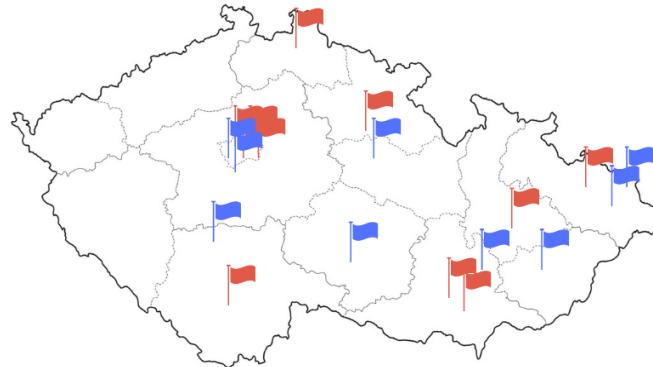


Fig. 1 Map of stroke centres involved in the STROCZECH. Red flags represent Comprehensive cerebrovascular centres and blue flags represent Primary stroke centres.

### **Contracting centres, nurses and research projects**

In this, initial phase of the STROCZECH, there was a need to develop specific agreements, which have been prepared in cooperation with lawyers from CZECRIN, St. Anne's University Hospital and Masaryk University.

- a) General agreement between the STROCZECH Coordinator (St. Anne's University Hospital) and a partner hospital as member of the STROCZECH. This contract defines conditions of STROCZECH trials implementation and responsibilities of both CZECRIN Coordinator and partner hospital, as well as defining conditions of work for CZECRIN Study Nurse/Coordinator.
- b) Employment contracts for CZECRIN Study Nurse/Coordinator reflecting working in more than one hospital in the Network.
- c) Specific agreement/exhibition on conducting particular clinical trials in the centre.

Development of all agreements was a big part of the initiation phase of the stroke network.

## **2) BUILDING HUMAN-RESOURCE INFRASTRUCTURE**

In the first year of STROCZECH, the human infrastructure and its know-how started to be built. There are 1) STROCZECH Scientific Committee for covering scientific management, 2) Executive management team, and 3) team of Study Nurses/Coordinators.

### **2.1 Scientific Management**

STROCZECH Scientific Committee was established from the representatives of the Cerebrovascular Division Board of Czech Neurology Society, which was elected via official voting system organized by Czech Neurology Society. The STROCZECH is proud to have following professionals on board:

1. Prof. Robert Mikulík, MD, PhD, FESO (St. Anne's University Hospital Brno) – Chair
2. Assoc. prof. Aleš Tomek, MD, PhD, FESO (University Hospital Motol)
3. Assoc. prof. Michal Bar, MD, PhD, FESO (University Hospital Ostrava)
4. Prof. Roman Herzig, MD, PhD, FESO, FEAN (University Hospital Hradec Králové)
5. Martin Kovář, MD (Na Homolce Hospital)
6. Jiří Neumann, MD (Chomutov Hospital)
7. Petra Reková, MD (General University Hospital in Prague)
8. Dagmar Součková, MD (Na Homolce Hospital)
9. Assoc. prof. MUDr. Daniel Šaňák, MD, PhD, FESO (University Hospital Olomouc)
10. Ondřej Škoda, MD, PhD (Jihlava Hospital)
11. Prof. David Školoudík, MD, PhD, FESO (University Hospital Ostrava)
12. Martin Šrámek, MD (Military University Hospital Prague)
13. Daniel Václavík, MD, PhD (Vítkovice Hospital Ostrava)

STROCZECH Scientific Committee meets quarterly (in person, now online). In 2020, three meetings took place (March 3, June 16 and September 14). The next one will be held on December 10. The Committee defines STROCZECH scientific objectives, plans and chooses appropriate proposals for clinical trials, and plans projects with respect to the optimal capacity allocation of research nurses within the Network. Meeting minutes are taken regularly.

## **2.2 Executive Management**

The Network is managed and coordinated by STROCZECH Director, prof. Robert Mikulík, STROCZECH Manager, Veronika Svobodová, and STROCZECH Coordinator, Martina Sittová, PhD, who succeeded in open selection procedure on the coordinating position. All are the members of the Stroke Research Program of International Clinical Research Center (ICRC), St. Anne's University Hospital in Brno. The executive management team is responsible for overall concept of the network, development of communication channels with network members, development of network of study nurses/coordinators, and for coordination of development and implementing clinical trials. The executive team is strongly supported by CZECRIN core team, other Stroke Research Program colleagues and by administrative teams of International Clinical Research Center.

The STROCZECH Coordinator conducts a team of study nurses/coordinators (described below), who are essential for running trials in the Network.

## **2.3 Network of Study Nurses/Coordinators**

Based on selection procedure and interviews, the nurses were hired to conduct trials in hospitals, which are members of the network. At present, there are 5 core nurses each covering 1-3 hospitals in their region, and several nurses on short-term contracts. In 2020 there is a strong focus on training of the new STROCZECH staff.

- a) In September, the first workshop for research nurses was organized in St. Anne's University Hospital in Brno by both STROCZECH Executive management team and CZECRIN core team. In two days and approximately 15 lectures, the nurses learned basics on stroke and on the work of a research nurse. They learned about the Czech Stroke Research Network and the CZECRIN infrastructure. Several lectures offered them a deep insight into running clinical trials, with focus on pharmacovigilance, monitoring, data management and project management. Planned research projects were introduced and nurses had opportunity to deal with Stroke Riskometer application for risk factor management, which is a tool for a planned clinical trial. Nurses also passed a simulation training aimed at obtaining informed consent from a patient to participate in clinical trial.
- b) The CZECRIN Coordinator, dr. Sittová, and several nurses attended a short study stay at Masaryk Memorial Cancer Institute, Brno, where they learned more about running academy clinical trials in practice.
- c) In November, Study Nurses/Coordinators were planned to pass a Study Coordinator certified course organized by NCO-NZO (National Centre for Nursing and Non-Medical Health Professions). Due to COVID-19 pandemic, the course was postponed to February 2021.
- d) ANGELS Initiative provided an interesting webinar for research nurses, attended by STROCZECH Nurses as well, where the self-education tool for stroke nurses was introduced.
- e) There are regular weekly meetings of the STROCZECH Coordinator with the network Study Nurses/Coordinators. At the meeting actual issues are discussed, and educational lectures are kept, such as Stroke care organization in the Czech Republic; Cooperation with professional stroke organisations and stroke support organisations; Animal models in stroke research etc. Minutes of each meeting are recorded.



Fig. 2 Research nurses kick off meeting, September 2020

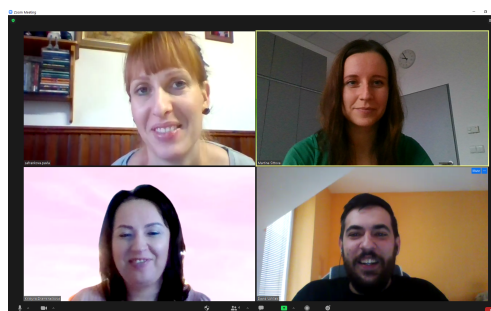


Fig. 3 Online STROCZECH regular weekly meeting with Research Nurses/Coordinators

### Standard operating procedures (SOP)

Directives, SOPs and internal guidelines are being prepared for the STROCZECH. The first directive describing the adaptation process of new research nurses entered into force in Q1 2020. The internal Manual for conducting clinical trials is under review nowadays.

### 4) TRIALS AND PROJECTS IN PROGRESS

There are several clinical trials and research projects in different level of preparation:

#### Alteplase vs Tenecteplase in patients with acute ischaemic stroke (AcT) – under preparation

In collaboration with University Hospital Calgary, we are preparing the new clinical trial AcT, which compares two different thrombolytic treatment alteplase which is a standard treatment for acute ischemic stroke patients with Tenecteplase which is standardly used for myocardial infarctions. The use of Tenecteplase holds promise to have additional benefits. In total 500 patients will be enrolled within up to 14 centres in the Czech Republic. AcT is a registry-based pragmatic randomized controlled trial. The results will be published together with the data from Canadian partners. Currently, we have the approval from the State Institute for Drug Control and from 13 Ethics committees of involved hospitals.

#### CHIP – running

The aim of this academic research is to obtain knowledge on the biology mechanisms of CHIP and atherosclerosis. CHIP = clonal haematopoiesis of indeterminate potential. The data imply that somatic mutations in hematopoietic cells may contribute to the development of human atherosclerosis. The relationship between CHIP and risk of ischemic stroke has not been explored in details but is highly clinically relevant for several reasons. To demonstrate this theory, we are collecting tissue samples obtained during vascular surgeries. The samples are tested for presence of CHIP positive macrophages/monocytes within atherosclerotic plaques. Till now, we have been able to obtain 60 samples of the tissue in our hospital, plus 63 blood samples were collected from St. Anne's University Hospital and Regional Hospital Liberec.

#### PROOF – running

The PROOF (Penumbral rescue by normobaric O<sub>2</sub> administration in patients with acute ischaemic stroke) is an academy trial funded by Horizon 2020 EU Research program. The main objective of the PROOF trial is to investigate efficacy and safety of normobaric hyperoxygenation as a neuroprotective treatment in patients receiving endovascular mechanical thrombectomy. The trial is already running in one centre; the implementation in other STROCZECH centres is in progress.

#### CONVINCE – running

This clinical study evaluates effect of low dose colchicin for secondary prevention after stroke. The trial has been initiated by University College Dublin. The Principal Investigator is Prof Peter Kelly from Mater Misericordiae University Hospital. The trial is running III phase and the duration of follow up of patients is 5 years. In the Czech Republic the trial is conducted in 3 STROCZECH sites: St. Anne's University Hospital, University Hospital in Motol, and Jihlava Hospital.

#### **Stroke care changes in COVID-19 pandemic – running**

Monitoring quality of stroke care is being organized by Stroke Division of Czech Neurology Society. Stroke care quality data are collected in Registry of Stroke Care Quality, RES-Q. To reflect the changes in number of stroke patients and status of provided care the RES-Q team prepared a COVID-related form. The retrospective study is now being performed by STROCZECH Study Nurses.

#### **Riskometer as an effective tool for reducing stroke risk factors? – under preparation**

Stroke Riskometer is a unique mobile application that is used to calculate personal risk of stroke and to manage risk factors. The application was developed by stroke epidemiologists in Auckland Technical University, New Zealand. Based on this application the global RIBURST study is running to monitor health of population and effectivity of reducing stroke risk factors using the application. The RIBURS study, focused on low-risk population, will start to be implemented within STROCZECH in December 2020.

#### **Stroke Book as a comprehensive information material for improving life after stroke – under preparation**

The Stroke Book is an informational and educational publication designed for stroke patients and their families. This was issued and used in Brno only. The plan is to develop regional-adapted versions, and to monitor added value of this way of patients'/caregivers' education on the quality of their life after stroke.

#### **Papers**

The first two papers are under preparation, as results of the STROCZECH.

- 1) A systematic review is currently being prepared as a basis for future clinical trial. Aminophylline is a drug used for multiple purposes e.g., asthma or sleep apnoea syndrome. According to the literature it may be a suitable candidate for neuroprotective treatment in patients with acute ischemic stroke.
- 2) A methodology paper on building disease-oriented network documenting the STROCZECH experience is in progress.

#### **5) PR, internal and external communication**

The STROCZECH aims at building both internal and external PR and communication channels to keep all members updated, to bring new opportunities and new cooperation, and to spread a positive knowledge on clinical trials among lay public.

For external communication, we have built:

- 1) The STROCZECH title and logo was developed (see Figure 4). It is used together with CZECRIN logo.
- 2) The STROCZECH website is in progress. Information on the STROCZECH is available at CZECRIN website.
- 3) The current plans are: a) to arrange a press conference launching the STROCZECH, b) introducing the network to international stroke community (e.g., through cooperation with European Stroke Organisation), and c) PR articles in hospital- and topic-related magazines focused on Czech stroke community and lay public.



Fig. 4 STROCZECH logo

For internal communication, we have ensured:

- 1) Regular weekly meetings with nurses.
- 2) Regular quarterly meeting of Scientific Committee.
- 3) Newsletter as a communication tool with hospitals will be issued on monthly bases. The first newsletter was issued in November 2020.

#### **6) INTERNATIONAL COOPERATION**

Within the first year of its existence, the STROCZECH started to cooperate with several international partners:

STROCZECH became the part of Global Alliance of Independent Networks focused on Stroke trials (GAINS) that was initiated to improve outcomes of stroke patients and their caregivers by facilitating, strengthening, and nurturing stroke trial networks and stroke trials worldwide (<https://www.globalstroketrials.org/>).

STROCZECH became a partner for conducting international clinical trials: 1) The trial AcT in which two thrombolytics are being compared is in collaboration with the University Hospital Calgary, Canada. 2) The other one is focused on the administration of high flow oxygen to the patients with endovascular thrombectomy (PROOF). The partner of this trial is the Tübingen University Hospital.

## 7) NATIONAL COOPERATION

Within the first year of its existence, the STROCZECH has built partnership on national level:

STROCZECH cooperates with Angels Initiative, the worldwide initiative aiming at optimizing stroke care and building a global community of stroke professionals. The Angels Initiative offers STROCZECH members certified e-learning courses, and established also the first Stroke Nurse Steering Committee in the Czech Republic. STROCZECH has its representative in this Committee.

STROCZECH is one of the founding members of new Czech “Coalition against Stroke”, which was established in October 2020 as an association of professional organizations, hospitals, patient organizations and other stroke support initiatives. The coalition aims to create a nationwide stroke awareness activity for the general public and to join the separated efforts in further improving stroke care and life after stroke.

The STROCZECH is supported by the Board of the Stroke Division of the Czech Neurology Society.

## 8) COVID-19 pandemic and STROCZECH

COVID-19 pandemic has had a big impact on operations within STROCZECH. Hospitals involved in the STROCZECH had to face to COVID-19 pandemic organizational issues, clinical trials were stopped for some time, and starting new projects, incl. process of involvement into STROCZECH was postponed.

The pandemic has had an impact on specific trials in preparation as well. AcT trial has been delayed because of the lack of study medication Tenecteplase during the pandemic and very likely even in near future.

Some educational events were cancelled (e.g. certification course for clinical trials coordinators or the Czech Congress for stroke nurses). The STROCZECH research nurses have been helping in COVID departments (Figure 4) and members of the STROCZECH have been contributing to publishing evidence based COVID-19 data (summaries from published papers in most prestige scientific journals) to lay public (<https://covid.fnusa.cz>). The articles contributed to fight against fake news on COVID-19. The STROCZECH members and other professionals published together 90 articles/summaries, the most successful article prepared by the STROCZECH Coordinator, Dr Sittová, has >26.000 post views so far (<https://iweb3.fnusa.cz/ztrata-cichu-priciny-diagnoza-lecba/>).



Fig. 5 Research nurses helping patients with COVID-19

## C. PLANS

In the current period of 2021 – 2022 we are planning to hire nurses for another STROCZECH centres (Northern Moravian region) and we will keep focusing on the education of research nurses in advanced stroke care and clinical trial management. In 2021, the Study Nurses will participate in the certified course for Study



coordinators provided by NCO-NZO (National Center for Nursing and Non-Medical Health Professions). We will support all Study Coordinators to pass the certification.

We expect to complete and stabilize the network of hospitals incl. establishing regular contacts with principal investigator of each centre. We will develop a Network Committee, following the structure of CZECRIN, as a platform for representatives of all involved hospitals to discuss implementation issues of particular trials.

It is planned to initiate AcT trial and develop two new clinical trial protocols for testing aminophylline as a potential neuroprotective drug. Further retrospective clinical studies will be applied to the STROCZECH Network. We expect that all trials which are under preparation nowadays, will start during 2021 and 2022. At this period, the new Horizon Europe EU funding program will be opened, this we will put our effort in participating in proposals for new academy driven clinical trials.

**In the new period of 2023 – 2029**, we expect that STROCZECH will be a stable network with well performing members. Thus, we will be able to focus on development and implementation of high-profile, large clinical trials, which will be competitive and respectful on a global scale and will provide breakthrough results affecting stroke care. To be able to achieve this, we can see at least two fields specific for STROCZECH, we would like to focus on: a) a development of **knowledge in designing large clinical trials** in cooperation with CZECRIN core team, and b) **completing and implementing imaging database platform** for collecting imaging data of stroke patients (in process), as this component is and will be crucial for all stroke trials. This platform will enable us to design more ambitious trials.

Additional to enhancing the network we would like to support intensive enrolment of patients into trials in existing STROCZECH centres, thus we expect an increase of FTE (full-time equivalent) of research nurses in particular centres.

Summarizing scientific results and their publishing in most prestige stroke journals based on running trials in STROCZECH will be the priority as well.

The STROCZECH will put its effort to obtain funding from Horizon Europe Program for international clinical trials with other European partners.

The STROCZECH would be a proud partner of the STROKE BRNO Cluster ([www.strokebrno.com](http://www.strokebrno.com)), which is oriented on pre-clinical research in stroke aiming at development of new methods of stroke imaging and stroke treatment. The STROCZECH could be a good platform for translating new discoveries from pre-clinical phase to clinical testing.

#### **D. SUMMARY**

The Czech Stroke Research Network (STROCZECH) officially started its activity in 1/2020. The Scientific Committee was established and chaired by Prof. Robert Mikulík, the initiator and PI of this Network. All stroke centres in the Czech Republic were offered to participate in the network. Nowadays 20 of them are members of the network based on their interest to participate in academy clinical trials and based on meeting requirements for conducting such trials. The team of Study Nurses/Coordinators for involved hospitals was built, the Nurses/Coordinators are being trained and participate in research projects.

Despite COVID-19 pandemic, which has been affecting STROCZECH activities, the first trials already started in several stroke centres, and new trials are under preparation. STROCZECH became a proud member of the GAINS international alliance of stroke research networks for academy clinical trials, which enables the STROCZECH to participate in international clinical trials developed within this global alliance.

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