ISRCTN88122184 https://doi.org/10.1186/ISRCTN88122184

# Can treatment with Cerebrolysin improve recovery after acute ischemic stroke?

| | | |
|---|---|---|
| **Submission date**<br>10/04/2020 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[X] Protocol<br>[_] Statistical analysis plan<br>[_] Results<br>[_] Individual participant data<br>[_] Record updated in last year |
| **Registration date**<br>29/04/2020 | **Overall study status**<br>Completed | |
| **Last Edited**<br>02/07/2024 | **Condition category**<br>Circulatory System | |

## Plain English summary of protocol

Current plain English summary as of 15/07/2021:
Background and study aims
Post-stroke cognitive impairment is a particularly serious consequence of cerebral ischemia and often inhibits or retards patient rehabilitation. The prevalence of post-stroke cognitive impairment ranges between 20-80%.
This is a study to investigate the effects of Cerebrolysin treatment on the recovery of patients with post-stroke cognitive impairment. The rationale of the study is based on the previously documented neuroprotective characteristics of Cerebrolysin with potential of preventive effects for cognitive decline after stroke.

Who can participate?
Adults between 40 and 80 years with acute ischemic stroke with onset 72 hours prior to screening.

What does the study involve?
Participants are invited to join this study at 72 hours after stroke onset. After informing patients about study procedures, benefits and potential risks, they sign a consent form. All participants included in the study must pass the screening criteria and baseline evaluations. Individuals are then allocated to one of two groups. The first group is administered Cerebrolysin 30 ml/day in four treatment cycles of ten days, while the second group receives a placebo, following the same schedule.

What are the possible benefits and risks of participating?
The potential benefit of Cerebrolysin administration is improved cognitive function and brain recovery in patients with stroke. The main risk for patients is developing adverse events (AE). Their severity and the causality to study medication are carefully assessed in order to establish a detailed safety profile of the intervention.

Where is the study run from?
CODEC is a multicenter trial, run from Cluj-Napoca, Timisoara, and Targu Mures (Romania).

When has the study started and how long is it expected to run for?
May 2020 to March 2026

Who is funding the study?
The Society for the Study of Neuroprotection and Neuroplasticity (SSNN) (Romania)

Who is the main contact?
Dr Olivia Verisezan Rosu
olivia.rosu@ssnn.ro

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# Contact information

**Type(s)**
Scientific

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**Type(s)**
Public

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**Contact details**
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olivia.rosu@ssnn.ro

# Additional identifiers

**Clinical Trials Information System (CTIS)**
Nil known

**Protocol serial number**
FSNANO100220

# Study information

**Scientific Title**
A randomized, placebo-controlled, double-blind trial to asses the effficacy and safety of CEREBROLYSIN in the treatment of Post-Stroke Cognitive Decline

**Acronym**
CODEC

## Study objectives
Patients randomized to Cerebrolysin will show improved cognitive outcome measured with a battery of co-primary neuropsychological tests as compared to patients randomized to placebo.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 27/03/2020, Ethics Committee of the Iuliu Hatieganu University of Medicine and Pharmacy (8 Babeş Street, 400012 Cluj-Napoca, Romania; +40-264-597-256; contact@umfcluj.ro), ref: 121/24.03.2020

## Study design
Randomized, placebo-controlled, double-blind, phase IV study

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Radiologically confirmed acute ischemic stroke with onset within 72 hours prior to screening

## Interventions
Current interventions as of 15/07/2021:
The synopsis of the study is organised in 4 visits:
1. Visit 1: Screening Part 1, Study Day -30 (within 72 h after stroke onset)
2. Visit 2: Screening Part 2 & Baseline, Study Day 1
3. Visit 3: Study Day 180
4. Visit 4: Study Day 360
All treatment cycles and efficacy evaluations will be performed within a window of ±3 working days.

No follow-up will be performed after the 360-day evaluation. The study arms will be administered the following treatment courses:
1. Treatment Group: Cerebrolysin Solution 30 ml diluted with 0.9% saline solution to 250 ml, administered by IV infusion
2. Placebo Group: 250 ml 0.9% saline solution administered by IV infusion

Treatment Cycle 1: Study day 1 – 10; 10 Infusions, once daily
Treatment Cycle 2: Study day 61-70; 10 Infusions, once daily
Treatment Cycle 3: Study day 121-130; 10 Infusions, once daily
Treatment Cycle 4: Study day 241-250; 10 Infusions, once daily

Randomisation and Blinding:
This study will be performed under double-blind conditions to keep investigators, other study personnel and patients blinded to treatment allocation. Cerebrolysin is an amber-colored solution. Therefore, colored infusion lines will be used for drug administration.

Patients meeting in- and exclusion criteria will obtain a random number corresponding to the random list generated in advance by a biometrician selected by the coordinator. Patients will be randomly allocated to the study groups in a 1:1 ratio.

A balanced random code list is prepared using the random permuted block scheme. In accordance with the ICH Biostatistics Guideline, the block size is intentionally not given in the study protocol.

The sealed random code list and the sets of sealed envelopes are prepared using the validated program RANCODE in a validated working environment at idv Data Analysis and Study Planning, Gauting, Germany. Sealed emergency envelopes will be provided to the Study Safety Officer (SSO) as well as to the Principle Investigator and the Study Nurse responsible for the preparation of the study medication.

The person who prepares the infusion at the study center will be independent of all other study specific procedures, in particular any safety or efficacy assessments and the study nurse is not allowed to disclose any information about treatment allocation.

The randomization envelope will be opened by the nurse at the time when the patient's first ready-to-use-infusion is being prepared. The double-blind study medication labels of the ready-to-use-infusion will identify only the unique randomization number which is the same as the patient number.

The whole study will be unblinded after closure of the database and determination of the analysis populations.

Previous interventions:
The synopsis of the study is organised in 4 visits:
1. Visit 1: Screening Part 1 - Study Day -30 (within 72 hours after stroke onset)
2. Visit 2: Screening Part 2 & Baseline - Study Day 0
3. Visit 3 - Study Day 180
4. Visit 4 - Study Day 360

No follow-up will be performed after the 360-day evaluation. The study arms will be administered the following treatment courses:
1. Treatment Group: Cerebrolysin Solution 30 ml diluted with 0.9% saline solution to 250 ml, administered by IV infusion
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## Intervention Type
Drug

## Phase
Phase IV

## Drug/device/biological/vaccine name(s)
Cerebrolysin

## Primary outcome(s)
1. Cognitive function assessed using Stroop Color-Word Test (Stroop, 1935) at 0, 180, 360 days
2. Cognitive function assessed using Trail Making Test Part A (Reitan, 1958) at 0, 180, 360 days
3. Cognitive function assessed using Digit Span Backwards Task (Wechsler adult intelligence scale – third edition) (Wechsler, 1997) at 0, 180, 360 days
4. Cognitive function assessed using Verbal Fluency Test – CFL Version (Benton & Hamsher, 1976) at 0, 180, 360 days
5. Cognitive function assessed using Digit Symbol (Wechsler adult intelligence scale – third edition) (Wechsler, 1997) at 0, 180, 360 days
6. Cognitive function assessed using Rey Auditory Verbal Learning Test (Rey, 1964) at 0, 180, 360 days

## Key secondary outcome(s))
1. Cognitive function assessed using Montreal Cognitive Assessment (MoCA) (Nasreddine, 2005) at 0, 180, 360 days
2. Stroke severity assessed by NIH Stroke Scale (http://www.nihstrokescale.org/) at 0, 180, 360 days
3. Functional outcome assessed by Modified Rankin Score (van Swieten J et al., 1988) at 0, 180, 360 days
4. Emotional status assessed using Hospital Anxiety and Depression Scale (Zigmond, 1983) at 0,

180, 360 days
5. Functional outcome assessed using EQ-5D-5L (Herdman, 2011)at 0, 180, 360 days

### Completion date
31/03/2026

## Eligibility

### Key inclusion criteria
Current participant inclusion criteria as of 15/07/2021:
1. Diagnosis of stroke, ischemic in origin (TACS or PACS), confirmed by MRI
2. Onset of Stroke within 72 h prior to screening
3. NIH Stroke Scale score between 5-15 at inpatient admission
4. Pre-stroke mRS of 0 or 1
5. No cognitive impairment prior to stroke with an IQ code score ≤3
6. Aged between 40 and 80 years, inclusive
7. Patient is willing and able to comply with the protocol for the duration of the study

Previous participant inclusion criteria:
1. Acute Ischemic Stroke confirmed by CT
2. Stroke is ischemic in origin - TACS or PACS
3. Onset of Stroke within 72 hours prior to screening
4. NIH Stroke Scale score between 5 and 15
5. Pre-stroke mRS of 0 or 1
6. No cognitive impairment prior to stroke with an IQ code score < 3
7. Age between 40 and 80 years, inclusive
8. Diagnosis of stroke ischemic in origin confirmed by MRI

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
40 years

### Upper age limit
80 years

### Sex
All

### Key exclusion criteria
Current participant exclusion criteria as of 15/07/2021:
1. Previous symptomatic ischaemic stroke or intracranial hemorrhage not related to the index stroke

2. Severe visual or hearing impairment interfering with psychometric test procedures
3. Pre-existing and active major neurological disease (eg. Parkinson’s Disease, Epilepsy)
4. Pre-existing and active major psychiatric disease, such as major depression, schizophrenia, bipolar disease, or dementia
5. History of significant alcohol or drug abuse
6. Advanced liver, kidney, cardiac, or pulmonary disease
7. A terminal medical diagnosis with survival <1 year
8. Pregnancy or lactating
9. Any contraindications to Cerebrolysin
10. Current enrolment in another therapeutic study
11. Dementia due to strategic index stroke
12. Major communication deficits with a Goodglass & Kaplan Score >2
13. Aphasia with an NIHSS Item 9 score of ≥2
14. Treatment with Cerebrolysin or Neuroprotectants in the last 30 days
15. Severe dementia with MMSE Score <12

Previous participant exclusion criteria:
1. Previous ischemic stroke or intracranial hemorrhage not related to the index stroke or previous TIA
2. Severe visual or hearing impairment interfering with psychometric test procedures
3. Pre-existing and active major neurological disease (eg. Parkinson’s Disease, Epilepsy)
4. Pre-existing and active major psychiatric disease, such as major depression, schizophrenia, bipolar disease, or dementia
5. History of significant alcohol or drug abuse
6. Advanced liver, kidney, cardiac, or pulmonary disease
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13. Aphasia with an NIHSS Item 9 score of > 2
14. Treatment with Cerebrolysin or Neuroprotectants in the last 30 days
15. Severe dementia with MMSE Score < 12

### Date of first enrolment
01/06/2020

### Date of final enrolment
31/03/2025

## Locations

### Countries of recruitment
Romania

### Study participating centre
**Timiş County Emergency Clinical Hospital**
156 Liviu Rebreanu Avenue

Timisoara
Romania
300723

**Study participating centre**
**County Emergency Hospital Cluj Napoca**
3-5 Clinicilor Street
Cluj Napoca
Romania
400000

# Sponsor information

**Organisation**
The foundation for the study of neuroscience and neuroregeneration

# Funder(s)

**Funder type**
Research organisation

**Funder Name**
The foundation for the study of neuroscience and neuroregeneration

# Results and Publications

**Individual participant data (IPD) sharing plan**
The data sharing plans for the current study are unknown and will be made available at a later date.

**IPD sharing plan summary**
Data sharing statement to be made available at a later date

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol file | version 2.1 | 28/05/2020 | 02/07/2024 | No | No |