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A registry study to observe clinical practices, safety and effectiveness of routine use of Cerebrolysin in the treatment of patients with moderate to severe neurological deficits after acute ischaemic stroke

Submission date	**Recruitment status**	[_] Prospectively registered
06/04/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
27/04/2021	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
12/09/2024	Circulatory System	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Stroke is a devastating disease and one of the primary causes for death and long-term morbidity imposing a heavy burden on patients, relatives and the health care system. Except for fibrinolytic therapy, which is only possible in a minor fraction of patients, there is no widely approved medication for the treatment of acute stroke.

Cerebrolysin has been approved for the treatment of stroke in over 45 countries worldwide. Since the approval of Cerebrolysin, stroke therapy has evolved, namely, with improved overall care, stroke units, more targeted rehabilitation, and the increasing availability of fibrinolytic therapy (rtPA, Actilyse) in specialized centers throughout the world. More recently, interventional therapies with various thrombus retrievers have emerged.

In addition, the Cerebrolysin treatment in stroke has evolved with different time windows, dosages and lengths of therapy being given in a pragmatic way by physicians within the specification of Product Characteristics for Cerebrolysin (SPC).

The main aim of this study is to systematically record Cerebrolysin treatment modalities and concomitant medication, according to local standards, in patients with moderate to severe neurological deficits after acute ischemic stroke and to assess the impact of these parameters on therapy outcome during early rehabilitation (day 21) and on day 90.

Besides this, the effectiveness and safety of Cerebrolysin therapy are monitored against the background of the now established and evolving stroke therapies (rtPA, thrombectomy). Furthermore, the effectiveness and safety of Cerebrolysin will be evaluated according to pre-existing diseases, concomitant medication and to applied rehabilitative actions. In the concomitant control group, these therapies alone or in combination will be compared to the addition of Cerebrolysin in these patients. Of interest is also the treatment in stroke units, with rtPA and systematic rehabilitation until day 21 and day 90.

An open observational treatment design has been chosen to collect data to capture the therapies as applied in real clinical practice. The pre-specified strategy follows the recommendations of the Principles for Good Research on Comparative Effectiveness (GRACE). A two-stage procedure is planned (Stage I: about 670 patients, Stage II: about 1400 patients).

Who can participate?
Patients aged 18 years or older, with clinical diagnosis of acute ischemic stroke, confirmed by imaging, no prior stroke, no prior disability.

What does the study involve?
All patients receive acute stroke care according to local treatment standards, which will not be amended or influenced by the study in any way. To evaluate the safety and effectiveness of Cerebrolysin in routine practice the outcome of Cerebrolysin-treated patients are compared with control group patients, who do not receive Cerebrolysin.

What are the possible benefits and risks of participating?
As this is a non-interventional study there are no additional treatments or evaluations. All patients receive acute stroke care according to local treatment standards, which will not be amended or influenced by the study. Patients are invited for two follow-up visits (day 21 and day 90) to evaluate and discuss the current status or their well-being. It is possible that a patient will receive Cerebrolysin according to treating physician’s choice. Cerebrolysin might help to limit neurological deficits after stroke and enhance recovery.
The information obtained from this study will be helpful for the optimization and further research in the treatment of patients suffering from stroke.
There is no potential risk by participation in the study, the routine treatment will not be changed in any way.

Where is the study run from?
EVER Neuro Pharma (Austria)

When is the study starting and how long is it expected to run for?
February 2017 to May 2024

Who is funding the study?
EVER Neuro Pharma (Austria)

Who is the main contact?
Dr Marion Jech, marion.jech@everpharma.com

Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT03480698

Secondary identifying numbers
EVER-AT-0717

Study information

Scientific Title
Cerebrolysin REGistry Study in Stroke- a High-quality Observational Study of Comparative Effectiveness

Acronym
C-REGS2

Study objectives
This study investigates the clinical practices, safety and effectiveness of Cerebrolysin in routine treatment of patients with moderate to severe neurological deficits after acute ischemic stroke. The study takes place because real-world data for the use of Cerebrolysin is needed.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 23/01/2018, Ethikkommission des Landes Oberösterreich (Ethics Committee of Upper Austria, Wagner Jauregg Weg15 , Linz, 4021, Austria; +42 (0)5 768087 Ext: 28631; ethikkommission.ooe@kepleruniklinikum.at), ref: 1026/2017

Study design
Prospective non-interventional registry study

Primary study design
Observational

Secondary study design
Registry study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Acute stroke

Interventions
Standard stroke care is compared to standard stroke care and Cerebrolysin as add-on.

All patients receive acute stroke care according to local treatment standards, which will not be amended or influenced by the study in any way. To evaluate the safety and effectiveness of Cerebrolysin in routine practice the outcome of Cerebrolysin-treated patients are compared with control group patients, who do not receive Cerebrolysin.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Neurologic disability measured using the modified Rankin Scale (mRS) at 3 months after stroke onset

Secondary outcome measures
1. Stroke severity measured using NIH Stroke Scale (NIHSS) at 21 days and 3 months after stroke onset
2. Neurologic disability measured using modified Rankin Scale (mRS) at 21 days after stroke onset
3. Cognitive impairment measured using Montreal - Cognitive Assessment (MoCA) at 3 months after stroke

Overall study start date
01/02/2017

Completion date
15/05/2024

Eligibility

Key inclusion criteria
1. Signed informed consent
2. Clinical diagnosis of acute ischemic stroke confirmed by imaging

3. Moderate to severe neurological deficits with NIH Stroke Scale (NIHSS) 8 to 15, both inclusive
4. No prior stroke
5. No prior disability
6. Patient's independence prior to stroke onset (pre-morbid mRS of 0 or 1)
7. Reasonable expectation of successful follow-up (max. 100 days)

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
2,000

Total final enrolment
1851

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
25/04/2018

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
Austria

Korea, South

Mexico

Philippines

Poland

Romania

Russian Federation

Ukraine

Viet Nam

Study participating centre
Kepler University Hospital Linz (KUK)
Klinik für Neurologie 2, Med Campus III, Kepler Universitätsklinikum
Krankenhausstraße 9
Linz
Austria
4020

Study participating centre
University Hospital Tulln
Abteilung für Neurologie
Alter Ziegelweg 10
Tulln
Austria
3430

Study participating centre
Hospital Amstetten
Abteilung für Neurologie
Krankenhausstraße 21
Amstetten
Austria
3300

Study participating centre
University Hospital Innsbruck
Universitätsklinik für Neurologie
Anichstraße 35
Innsbruck
Austria
6020

Study participating centre
University Hospital Salzburg
Christian-Doppler-Klinik
Ignaz-Harrer-Straße 79
Salzburg
Austria
5020

Study participating centre
Chungnam National University Sejong Hospital
20 Bodeum 7-ro
Sejong
Korea, South
30099

Study participating centre
Daegu Catholic University Medical Center
33, Duryugongwon-ro 17-gil, Nam-gu
Daegu
Korea, South
42472

Study participating centre
Southern Medical Hospital
Calle de Puente de Piedra No. 150
Toriello Guerra
Tlalpan
Ciudad de Mexico
Mexico
14140

Study participating centre
Spitalul Clinic Judetean de Urgenta „Pius Brînzeu” Timisoara
Bulevardul Liviu Rebreanu 156
Timișoara
Romania
300723

Study participating centre
Central District Hospital of Mozhaisk
Mozhaisk
Russian Federation
143200

Study participating centre
Region Clinical Hospital of Stavropol
Stavropol
Russian Federation
355029

Study participating centre
Kyiv Regional Clinical Hospital Stroke Unit
Kyiv
Ukraine
04107

Study participating centre
Vinnytsia Regional Psycho-Neurological Hospital
Vinnytsia
Ukraine
21037

Study participating centre
Thái Nguyên National Hospital
479 Lương Ngc Quyn, Phan Đình Phùng, Thành ph
Thái Nguyên
Viet Nam
unkn.

Study participating centre
107 Szpital Wojskowy z Przychodnią Samodzielny Publiczny Zakład Opieki Zdrowotnej
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Poland
78-600

Study participating centre
Instytut Psychiatrii i Neurologii w Warszawie
ul. Jana Sobieskiego 9
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Poland
02-957

Study participating centre
Perpetual Succour Hospital, Cebu City
Rm 412 Perpetual Succor Hospital SPC Medical Specialty Center, Gorodo Avenue

Cebu City
Philippines
6000

Study participating centre
St. Luke's Medical Center - Quezon City
279 E. Rodriguez Sr. Blvd.
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Sponsor information

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EVER Neuro Pharma (Austria)

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Sponsor type
Industry

Website
http://www.everpharma.com/

ROR
https://ror.org/032900178

Funder(s)

Funder type
Industry

Funder Name
EVER Neuro Pharma

Alternative Name(s)

EVER Pharma, EVER Neuro Pharma GmbH

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Austria

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
30/06/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
Name and email: Marion Jech marion.jech@everpharma.com
Type of data: hardlocked patient level analysis data
When and how long available: at time of publication, for 5 years
Access: password protected link
Shared with whom: academic or governmental institutions
For what type of analyses: re-analysis based on preplanned SAP methodology
Consent of participants obtained: Any patient identifiers as well as country- and site-specific information will be removed for full data anonymisation

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v3.3	01/03/2021	04/05/2021	No	No
Statistical Analysis Plan	version v1	24/10/2017	04/05/2021	No	No
Statistical Analysis Plan	version 1.1	22/07/2024	12/09/2024	No	No