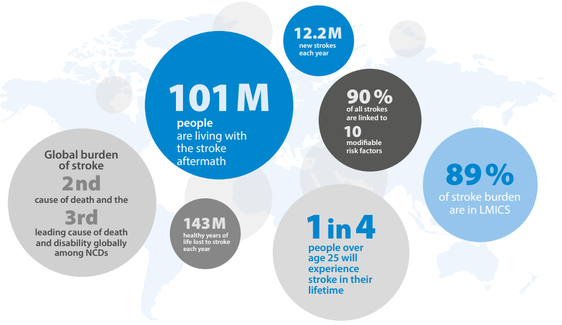
Stroke is a global burden!



Study Purpose

The main objective of the **C**erebrolysin **REG**istry Study in **S**troke **(CREGS)** was to systematically record the **routine clinical use of Cerebrolysin** in patients with **moderate ischemic stroke** following the principles of a **prospective** comparative **effectiveness study** (CES) to compare its effectiveness in terms of **functional recovery** to patients treated with standard therapy alone.

Treatment

- Treatment duration and dosing were NOT pre-defined in the protocol
- Administered according to local treatment standard
  → **Reflecting real-world treatment behaviour**
- Median Cerebrolysin dosage was 30 ml
- Median treatment duration was 10 days

Outcome criteria

Primary outcome

- mRS after 3 month

Secondary outcomes

- NIHSS at day 21 + after 3 months
- mRS at day 21
- MoCA after 3 months
- Patients with excellent recovery (mRS score 0-1) after 3 months
- Patients with functional independence (mRS score 0-2) after 3 months

Safety analysis

Treat stroke patients with Cerebrolysin as soon as possible

Disorder	Daily dosage	Initiation of treatment	Duration of treatment
Stroke	30 ml	as soon as possible ideally from day 1	21 days

Cerebrolysin is safe and well tolerated.

As recommended in different guidelines

Cerebrolysin - First and only pharmacological agent evidence-based for all acute ischemic stroke patients

- Early and sustained functional recovery
- Effective as stand-alone therapy
- Preserves cognitive functions
- Enhances the effects of recanalization therapy

Confirmed in a global HQCER study involving 1.865 patients

Titel: CREGS – A multinational, high-quality comparative effectiveness study of Cerebrolysin in moderate acute ischemic stroke

Cerebrolysin REGistry Study in Stroke Prospective, restricted cohort design

Patients: 1.865 enrolled patients
1.806 Intention to Include (ITI) patients
1.044 patients treated with Cerebrolysin puls standard treatment + 762 patients treated with only standard treatment

Treatment: 30 ml for 10 days (median)

Feigin, V. L., Brainin, M., Norrving, B., Martins, S. O., Pandian, J., Lindsay, P., F Grupper, M., & Rautalin, I. (2025). World Stroke Organization: Global Stroke Fact Sheet 2025. International journal of stroke : official journal of the International Stroke Society, 20(2), 132–144. https://doi.org/10.1177/17474930241308142 GBD 2021 Stroke Risk Factor Collaborators (2024). Global, regional, and national burden of stroke and its risk factors, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet. Neurology, 23(10), 973–1003. https://www.world-stroke.org/world-stroke-day-campaign/about-stroke/impact-of-stroke

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ABBREVIATED PRESCRIBING INFORMATION – Cerebrolysin. Name of the medicinal product: Cerebrolysin - Solution for injection. Qualitative and quantitative composition: One ml contains 215.2 mg of Cerebrolysin concentrate in aqueous solution. List of excipients: Sodium hydroxide and water for injection. Therapeutic indications: For treatment of cerebrovascular disorders. Especially in the following indications: Senile dementia of Alzheimer's type. Vascular dementia. Stroke. Craniocerebral trauma (commotio and contusio). Contraindications: Hypersensitivity to one of the components of the drug, epilepsy, severe renal impairment. Marketing Authorization Holder: EVER Neuro Pharma GmbH, A-4866 Unterach Only available on prescription and in pharmacies. More information about pharmaceutical form, posology and method of administration, special warnings and precautions for use, interaction with other medicinal products and other forms of interaction, fertility, pregnancy and lactation, effects on ability to drive and use machines, undesirable effects, overdose, pharmacodynamics properties, pharmacokinetic properties, preclinical safety data, incompatibilities, shelf life, special precautions for storage, nature and contents of the container and special precautions for disposal is available in the summary of product characteristics. (Reference SPC-CCDS Version 2.0/03.06.2016)

EVER Neuro Pharma GmbH, Oberburgau 3, 4866 Unterach, Austria, www.everpharma.com, www.cerebrolysin.com

CERE/INT/09/2025/24

EVER PHARMA

STROKE

TBI

COGNITIVE DISORDERS

CREGS

A multinational, high-quality comparative effectiveness study of Cerebrolysin in moderate acute ischemic stroke

Cerebrolysin **REG**istry Study in **S**troke
Prospective, restricted cohort design

Vosko et al., International Journal of Stroke (2025)
https://doi.org/10.1177/17474930251375439

Cerebrolysin - First and only pharmacological agent evidence-based for all acute ischemic stroke patients

- Early and sustained functional recovery
- Effective as stand-alone therapy
- Preserves cognitive functions
- Enhances the effects of recanalization therapy

Confirmed in a global real-world data study involving 1.865 patients

Cerebrolysin®

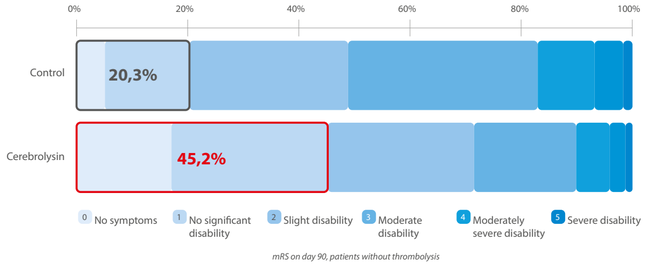
Reconnecting Neurons. Empowering for Life.

Early and sustained functional recovery

Model	Mann-Whitney Statistic (MW)	MW	95,00%-CI	N1/N2	P
Stochastic Ordering					
mRS Day 90 – primary endpoint Wei-Lachin		0,6157	(0,5910 to 0,6404)	969/726	0,0000
mRS day 21 Wei-Lachin		0,6065	(0,5811 to 0,6319)	998/738	0,0000
NIHSS Day 90 Wei-Lachin		0,5781	(0,5561 to 0,6002)	956/714	0,0000
NIHSS Day 21 Wei-Lachin		0,5792	(0,5576 to 0,6008)	998/736	0,0000

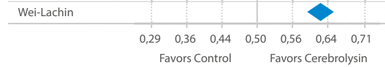
- **Statistically significance** in all outcome measures
- Cerebrolysin showed **superiority** in all functional outcomes (mRS, NIHSS)
- Detectable **already at day 21** and persisting through day 90

Effective as stand-alone therapy



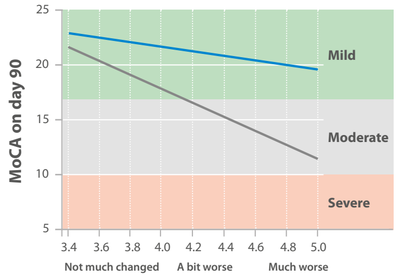
mRS on day 90, patients without thrombolysis

Model	Mann-Whitney Statistic (MW)	MW	95,00%-CI	N1/N2	P
Stochastic Ordering					
Wei-Lachin		0,6224	(0,5943 to 0,6505)	766 / 639	0,0000



- Cerebrolysin shows **statistically significant superiority** in patients without thrombolysis therapy
- Results are **consistent** with the primary outcome
- **45% of the patients** treated with Cerebrolysin gain mRS score 0-1
- Only 20% in the control group reached the same result

Preserves cognitive functions

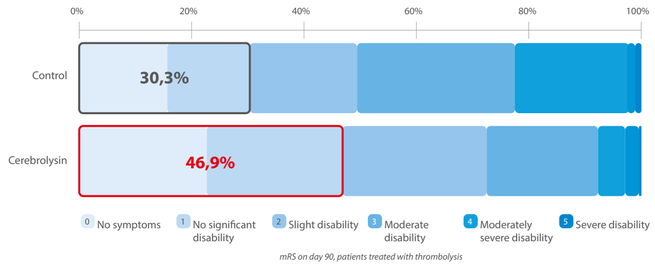


Model	Mann-Whitney Statistic (MW)	MW	95,00%-CI	N1/N2	P
Stochastic Ordering					
Wei-Lachin		0,5530	(0,5282 to 0,5778)	873/637	0,0000

- Cerebrolysin shows **statistically significant superiority**
- Cerebrolysin patients **remain very stable**
- Patients in the **control group show a marked decline**
- The difference between treatment and control is even **more pronounced in the high-risk group**
- Patients receiving Cerebrolysin demonstrate better MoCA outcomes
- **Cerebrolysin protects against cognitive decline**

Excellent safety profile confirmed (again)!

Enhances the effects of recanalization therapy



mRS on day 90, patients treated with thrombolysis

Model	Mann-Whitney Statistic (MW)	MW	95,00%-CI	N1/N2	P
Stochastic Ordering					
Wei-Lachin		0,5723	(0,5091 to 0,6354)	167/82	0,0248

- Cerebrolysin shows statistically **significant superiority**
- **47% of patients** treated with Cerebrolysin gain mRS score 0-1
- 30% ***only*** in the control group

Final overview