

Cerebrolysin is **safe and well tolerated**

No significant treatment-related differences were observed in the safety analyses, except for diarrhea, which was reported more frequently in Cerebrolysin-treated patients ($p < 0.01$ vs. Control).

Summary

- Cerebrolysin **significantly improved GOS and RDS** at day 10 in patients suffering from mild TBI and at days 10 and 30 in patients with moderate and severe patients
- Add-on treatment with Cerebrolysin improved the **clinical recovery and therefore also the activities of daily living of TBI patients**
- **Less need for assistance** in everyday life with Cerebrolysin
- **Higher dosage** treatment regimens with 30 ml are **more effective**
- **No safety concerns** reported and no specific events of intolerance to Cerebrolysin

Product information

Dosage regime:			
Disorder	Daily dosage	Initiation of treatment	Duration of treatment
Stroke	20-50 ml	as soon as possible	10-21 days
Traumatic brain injury	20-50 ml	as soon as possible	7-30 days
Vascular dementia	10-30 ml	as soon as possible	1 cycle: 5 days weekly/4 weeks 2-4 cycles per year
Alzheimer's disease	10-30 ml	as soon as possible	1 cycle: 5 days weekly/4 weeks 2-4 cycles per year



LITERATURE

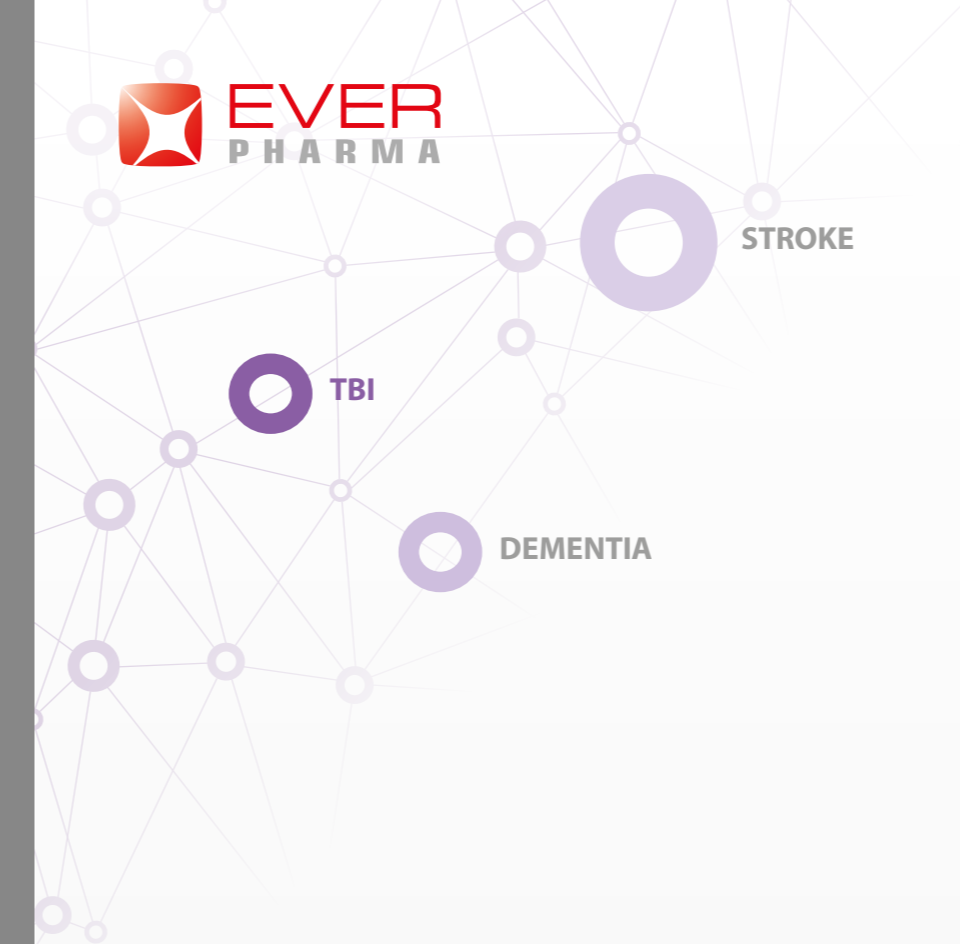
1. Muresanu D. F., Ciurea A. V., Gorgan R. M., Gheorghita E., Florian S., Stan H., Blaga A., Ianovici N., Iencean S. M., Turliuc D., Davidescu H. B., Mihalache C., Brehar F. M., Mihaescu A. S., Mardare D. C., Anghelescu A., Chiparus C., Lapadat M., Pruna V., Mohan D., Costea C., Costea D., Palade C., Bucur N., Figueroa J., Alvarez A., A Retrospective, Multi-center Cohort Study Evaluating the Severity-Related Effects of Cerebrolysin Treatment on Clinical Outcomes in Traumatic Brain Injury. *CNS Neurol Disord Drug Targets*. 2015 Apr 30. [Epub ahead of print]
2. Zhang C., Chopp M., Cui Y., Wang L., Zhang R., Zhang L., Lu M., Szalad A., Doppler E., Hitzl M. and Zhang Z. G., Cerebrolysin Enhances Neurogenesis in the Ischemic Brain and Improves Functional Outcome After Stroke, *Journal of Neuroscience Research* 2010;88:3275-3281
3. Ubhi K., Rockenstein E., Vazquez-Roque R., Mante M., Inglis C., Patrick C., Adame A., Fahnestock M., Doppler E., Novak P., Moessler H. and Masliah E., Cerebrolysin modulates Pronerve Growth Factor/ Nerve Growth Factor Ratio and Ameliorates the Cholinergic Deficit in a Transgenic Model of Alzheimer's Disease, *Journal of Neuroscience Research* 2013;91:167-177
4. Zhang L., Chopp M., Meier D. H., Winter S., Wang L., Szalad A., Lu M., Wei M., Cui Y., Zhang Z. G., Sonic Hedgehog Signaling Pathway mediates Cerebrolysin-Improved Neurological Function After Stroke, 2013;44:1965-1972

ABBREVIATED PRESCRIBING INFORMATION. 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 Authorisation 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.

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CERE/INT/05/2016/69



Improvement of clinical outcome and functional recovery after TBI

A retrospective, multi-center cohort study, Muresanu D.F. et al., *Neurol Disord Drug Targets*. 2015;14(5):587-99

Objective and design of the study

OBJECTIVE

This retrospective study investigated the effects of add-on Cerebrolysin treatment compared with standard medical care alone in TBI.

DESIGN

- A total of 7,769 adult patients with TBI who were admitted to 10 Romanian neurosurgery departments between 2005-2010 were included
- 1,618 received Cerebrolysin as an adjuvant therapy
- Two different treatment regimens in the Cerebrolysin group:
 - 1,142 received 20ml/day and
 - 476 were treated with a 30ml/day dose
- The duration of the Cerebrolysin treatment varied from 1 to 30 days, and the median treatment duration was 10 days
- Start within 48 hours after TBI
- Mode of administration: IV infusion

Treatment Regimen:

	N
Cerebrolysin 20 ml/day + standard care	1142
Cerebrolysin 30 ml/day + standard care	476
Standard care (control group)	6151
	1618
	7769

Baseline characteristics

Levels of consciousness as determined by Glasgow Coma Scale (GCS) at hospital admission were presented below. Analyses of efficacy were performed separately for the **subgroups of mild, moderate and severe** TBI patients.

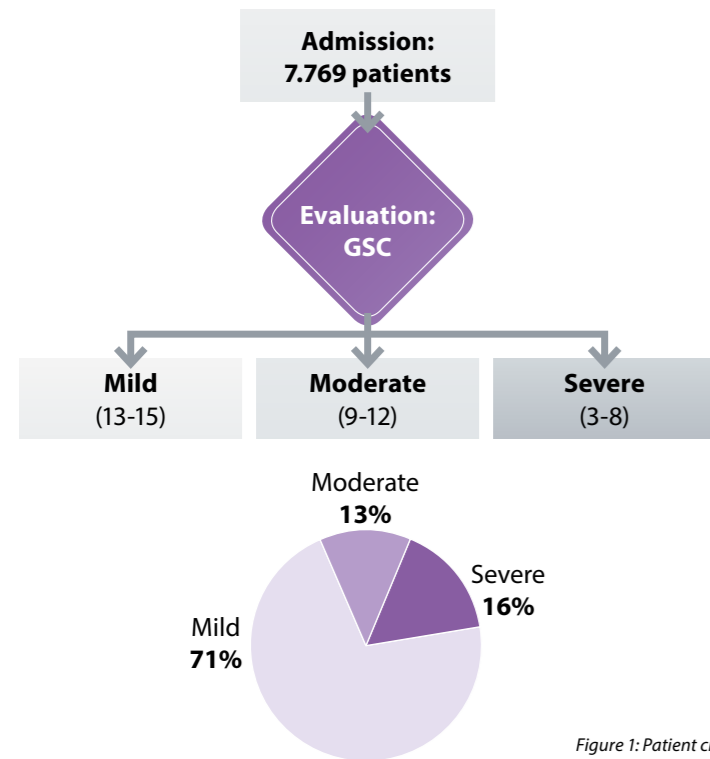


Figure 1: Patient classification

Cerebrolysin has been used more frequently in **moderate (40%)** and **severe (38%)** TBI cases as compared to patients with **mild injury (13.5%)**. Dosages increase with severity.

GCS-related severity:	Control N (%)	Cerebrolysin N (%)	Sum N (%)
3-8 (severe)	760 (12.4)	467 (28.9)	1,227 (15.8)
9-12 (moderate)	604 (9.8)	406 (25.1)	1,010 (13.0)
13-15 (mild)	4,787 (77.8)	745 (46.0)	5,532 (71.2)
Total number of cases	6,151 (100)	1,618 (100)	7,769 (100)

Efficacy Criteria

The patients were ranked by Glasgow Outcome Scale (GOS) and Modified Rankin Disability Score (RDS) 10 and 30 days post-TBI based on medical records.

Mild TBI – Early recovery with Cerebrolysin

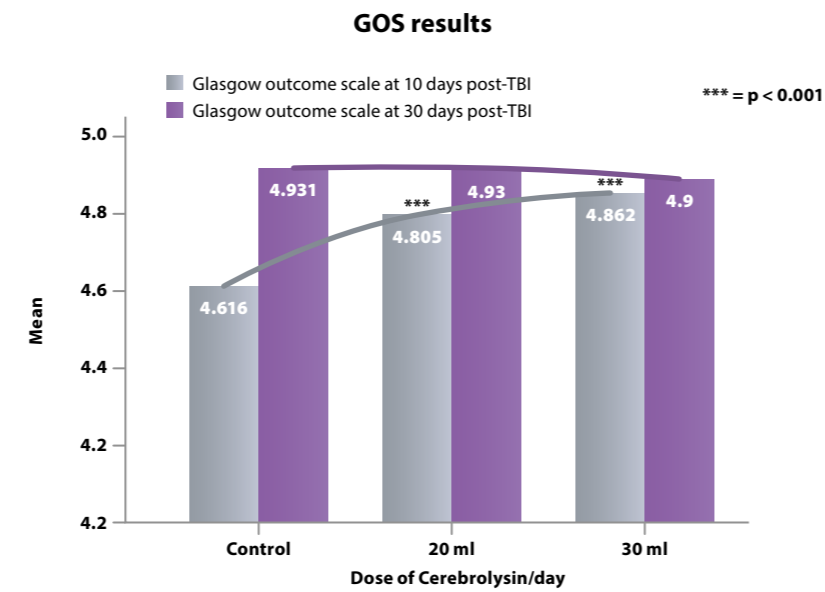


Figure 2: GOS scores at 10 and 30 days post-TBI in the treatment groups of mild TBI patients

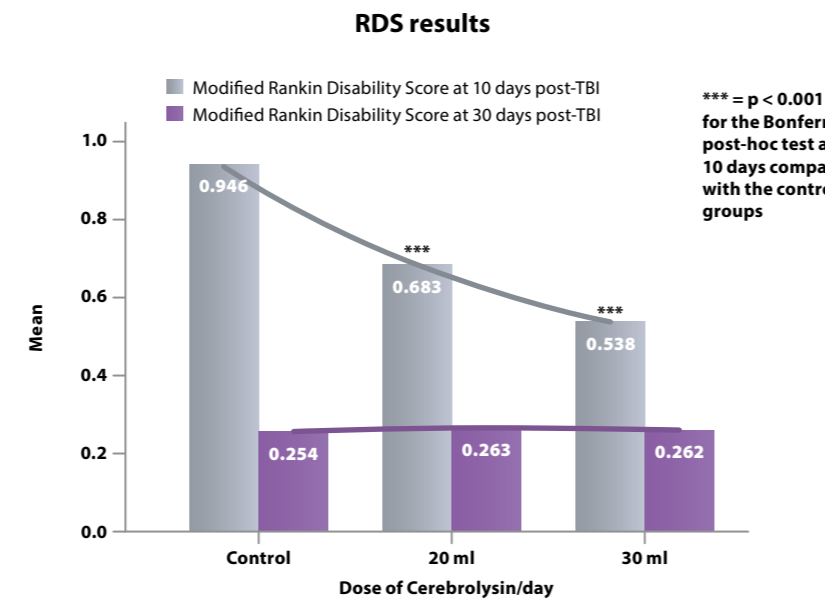


Figure 3: RDS scores at 10 and 30 days post-TBI in the treatment groups of mild TBI patients

CONCLUSIONS

- Significantly **better recovery** with Cerebrolysin was observed at day 10 in both scores
- Treatment of Cerebrolysin leads to an **earlier recovery and better rehabilitation results**
- No significant improvement on day 30 because of a ceiling effect

Moderate TBI – Significantly better recovery with Cerebrolysin

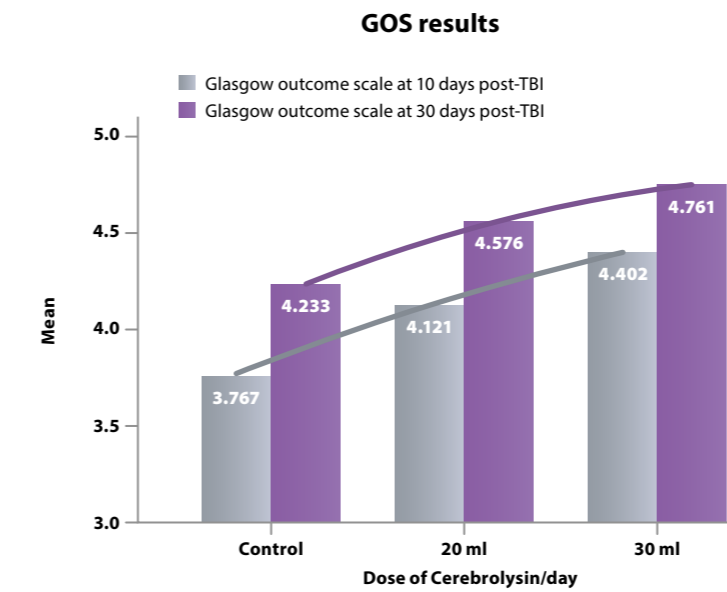


Figure 4: GOS scores at 10 and 30 days post-TBI in the treatment groups of moderate TBI patients

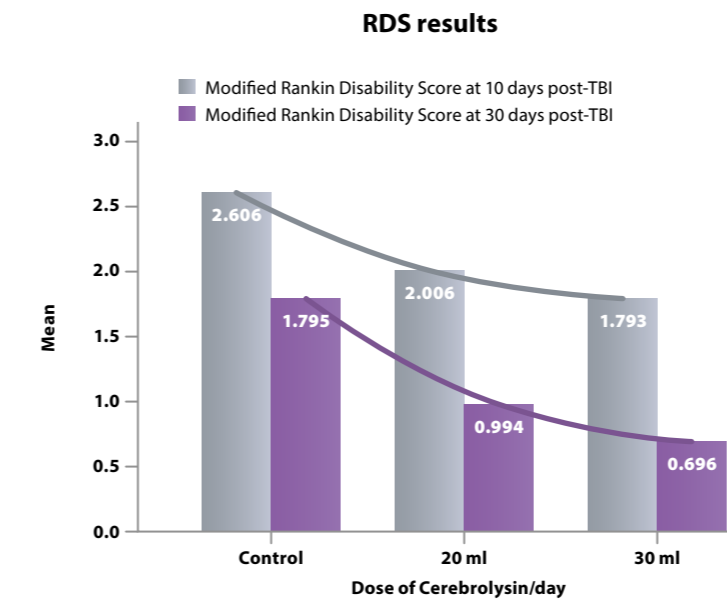


Figure 5: RDS scores at 10 and 30 days post-TBI in the treatment groups of moderate TBI patients

CONCLUSIONS

- Significantly **better recovery** with Cerebrolysin was observed at day 10 & day 30 in both scores
- 30 ml dosage of Cerebrolysin shows a better result and leads to over 0.5 points (GOS) and over 1.1 points (RDS) improvement versus control
- Less need for assistance** in everyday life with Cerebrolysin

Severe TBI – Significantly higher effectiveness with Cerebrolysin

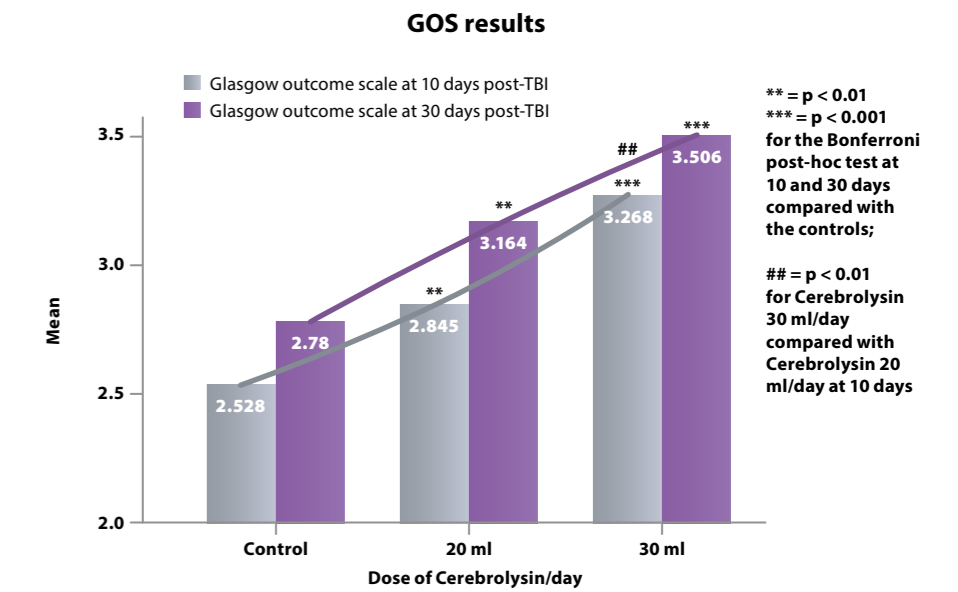


Figure 6: GOS scores at 10 and 30 days post-TBI in the treatment groups of severe TBI patients

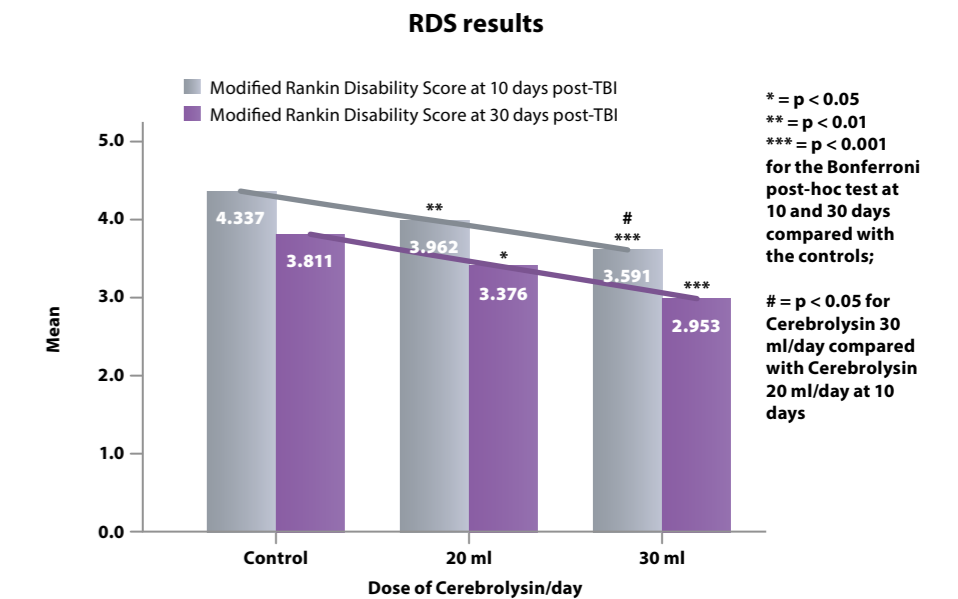


Figure 7: RDS scores at 10 and 30 days post-TBI in the treatment groups of severe TBI patients

CONCLUSIONS

- Cerebrolysin shows a significantly **higher effectiveness** at day 10 & day 30 in both scores
- 30 ml dosage of Cerebrolysin leads to over 0.75 points (GOS) and over 0.86 points (RDS) improvement over control
- Treatment with Cerebrolysin leads to an **improvement of activities of daily living**