## 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<br>2-4 cycles per year |
| **Alzheimer's disease** | 10-30 ml | as soon as possible | 1 cycle: 5 days weekly/4 weeks<br>2-4 cycles per year |



EVER PHARMA

### 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., Mihăescu 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




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

CERE/INT/05/2016.69

EVER PHARMA

STROKE

TBI

DEMENTIA

# 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

**Cerebrolysin®**
**Reconnecting Neurons.**
**Empowering for Life.**

## 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

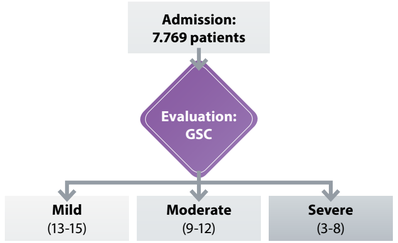
- A total of 7,769 adult patients with TBI who were admitted to 10 Romanian neurosurgery departments between 2005-2010 were included
- 1,618 received Cerebrolysin as an adjuvant therapy
- Two different treatment regimens in the Cerebrolysin group:
  - 1,142 received 20ml/day and
  - 476 were treated 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 | 1618 | **7769** |
| **Cerebrolysin 30 ml/day + standard care** | 476 | | |
| **Standard care (control group)** | 6151 | | |

## Baseline characteristics

Levels of concsiousness 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.



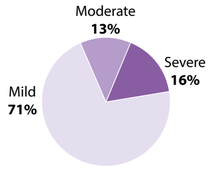




*Figure 1: Patient classification*

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

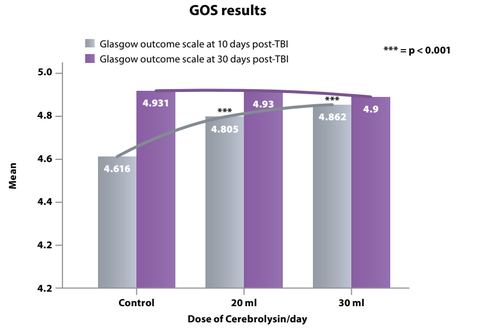



*Figure 2: GOS scores at 10 and 30 days post-TBI in the treatment groups of mild TBI patients*

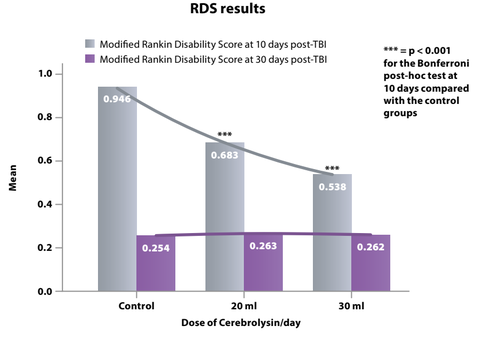



*Figure 3: RDS scores at 10 and 30 days post-TBI in the treatment groups of mild TBI patients*

### 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

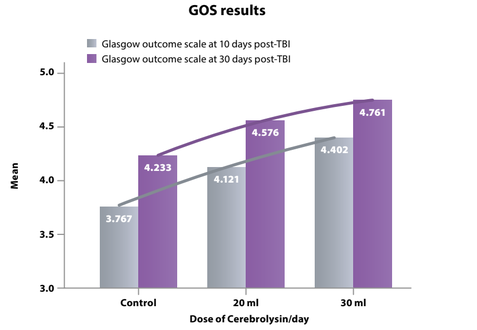



*Figure 4: GOS scores at 10 and 30 days post-TBI in the treatment groups of moderate TBI patients*

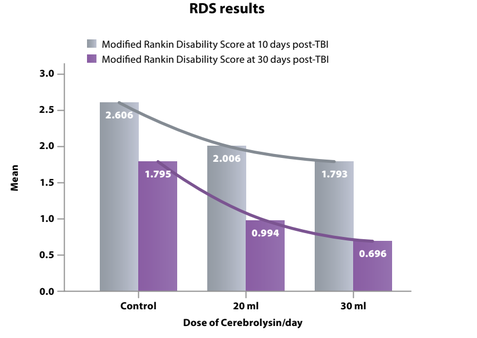



*Figure 5: RDS scores at 10 and 30 days post-TBI in the treatment groups of moderate TBI patients*

### 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 1.1points (RDS) improvement versus control
- **Less need for assistance** in everyday life with Cerebrolysin



## Severe TBI – Significantly **higher effectiveness** with Cerebrolysin

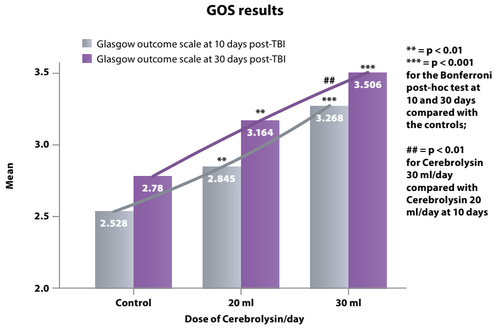



*Figure 6: GOS scores at 10 and 30 days post-TBI in the treatment groups of severe TBI patients*

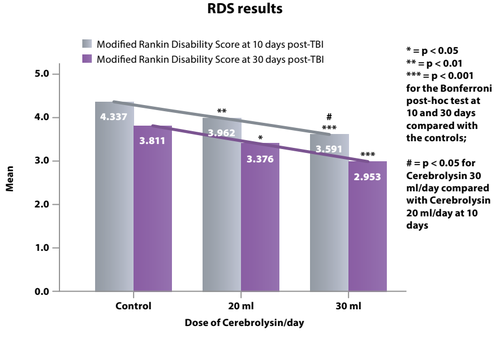



*Figure 7: RDS scores at 10 and 30 days post-TBI in the treatment groups of severe TBI patients*

### 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**