EVER PHARMA

All about:
CAPTAIN Meta-Analysis

Benefits of Cerebrolysin as add-on therapy for moderate-severe traumatic brain injury.

Vester, Johannes C., et al. „Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series."
Neurological Sciences (2021): 1-11.

- The effective treatment after TBI
- Save lives
- Early recovery
- Better quality of life

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Empowering for Life.

Study Details

- Included **2 clinical trials** (phase IIIb/IV prospective, randomized, double-blind, placebo-controlled)
- Eligible patients with **GCS between 6-12**
- **Medication:**
  Treatment Cycle 1 = Day 1 - 10 : 50 ml/day
  Treatment Cycle 2 = Day 31 - 40 : 10 ml/day
  Treatment Cycle 3 = Day 61 - 70 : 10 ml/day
- **Add-on** to standard therapy of TBI
- Cerebrolysin effective in different ethnicities located in Asia and Europe

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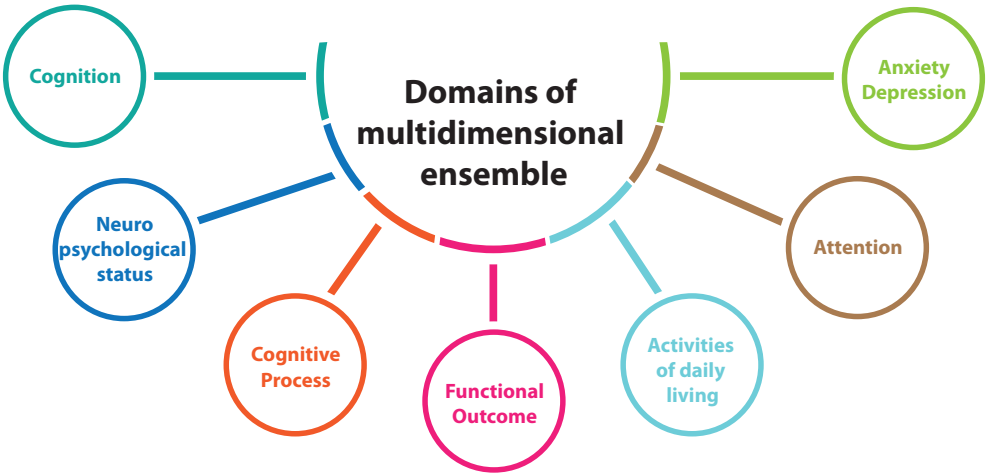
Strong statistical power

- Meta-Analysis = **Highest level of evidence**
- Primary endpoint = **Multidimensional ensemble** of functional and neuropsychological scales for 90, 30, and 10 days after TBI
- Combination of outcomes from a study = means of the multivariate **Mann-Whitney (MW)** effect size
- Effect size measurement tool = **Wei-Lachin-methode**



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TBI - A significant public health problem

Worldwide, TBI is a leading cause of injury-related death and disability, with a devastating impact on patients and their families.

70 million

TBI patients per year!

Treatment for TBI patients is essential!

Dewan, Michael C., et al. „Estimating the global incidence of traumatic brain injury." Journal of neurosurgery 130.4 (2018): 1080-1097.

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Effective treatment after TBI

- **Improved functional and cognitive outcomes**
- **Faster reintegration into work and social life**

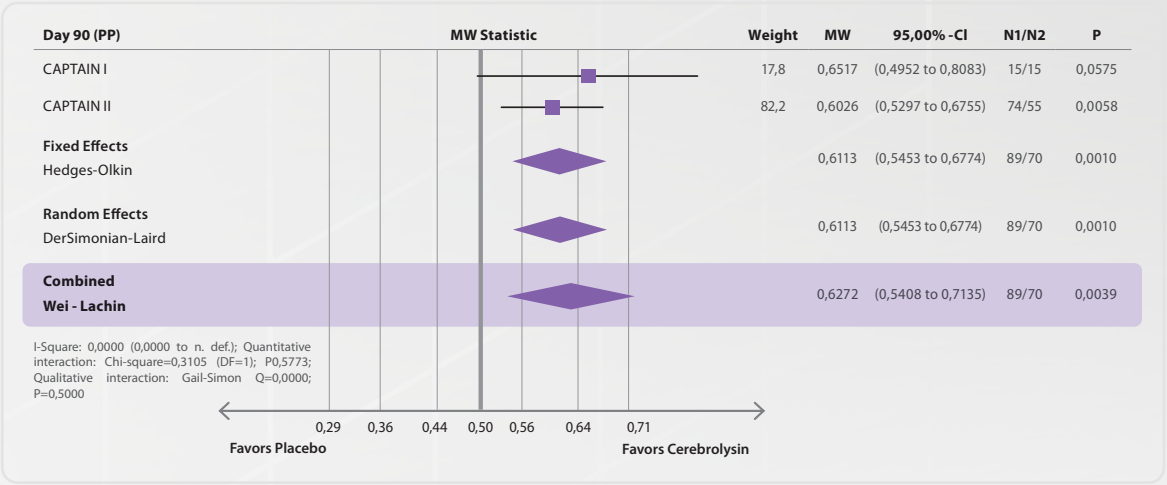

Figure: Confirmatory Multivariate Outcome Ensemble at Day 90, PP (Neurorecovery Phase)

- **Impressive** overall treatment effects
- **Medium superiority** with Cerebrolysin
- **Statistically significant**

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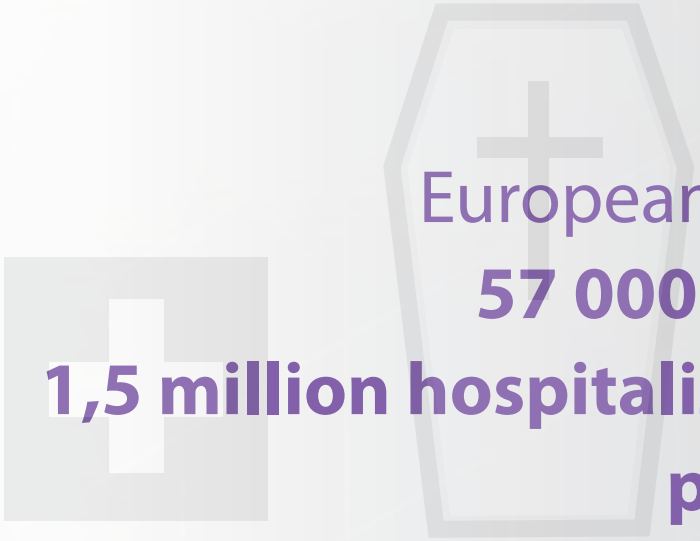
TBI - Major cause of death and disability

Severe TBI can result in mortality rates as high as 30-40%. Survivors experience a substantial burden of physical, psychiatric, emotional and cognitive disabilities which disrupt the lives of individuals and their families.



European Union:

57 000 deaths

1,5 million hospitalizations per year

Safe and effective treatment for TBI patients is essential!

https://www.center-tbi.eu/files/news/21571f81-20b8-4860-a3dd-1f6e27d02b3d.pdf

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Save lives after TBI

- **Higher chance of survival**
- **Lower rate of severe complications**

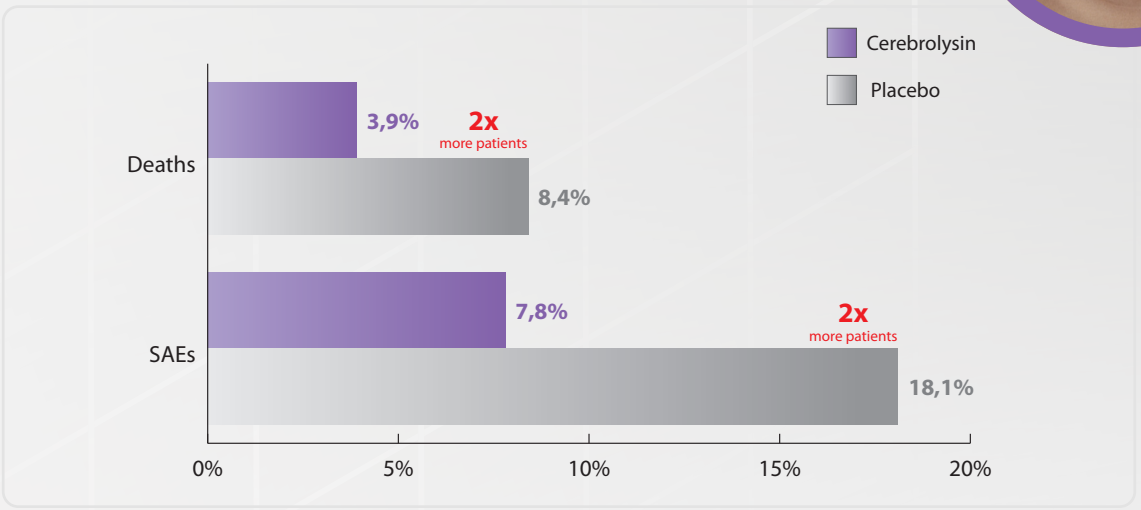

Figure: Safety Meta-Analyses

- **Mortality** in the Cerebrolysin group **reduced by 50%**
- 18,1% had SAEs in placebo group, **only 7,8% in Cerebrolysin group**

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TBI – Major costs for healthcare systems

TBI has a very high economic impact on individuals and families, and on society as a whole.

Annual global costs of care and consequences of TBI:

Annual costs:

USD 400 billion

Early treatment for TBI patients is essential!

https://www.center-tbi.eu/files/news/21571f81-20b8-4860-a3dd-1f6e27d02b3d.pdf

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Early Recovery with Cerebrolysin

- **Higher probability of earlier discharge from hospital**
- **Beneficial effects already on day 10**

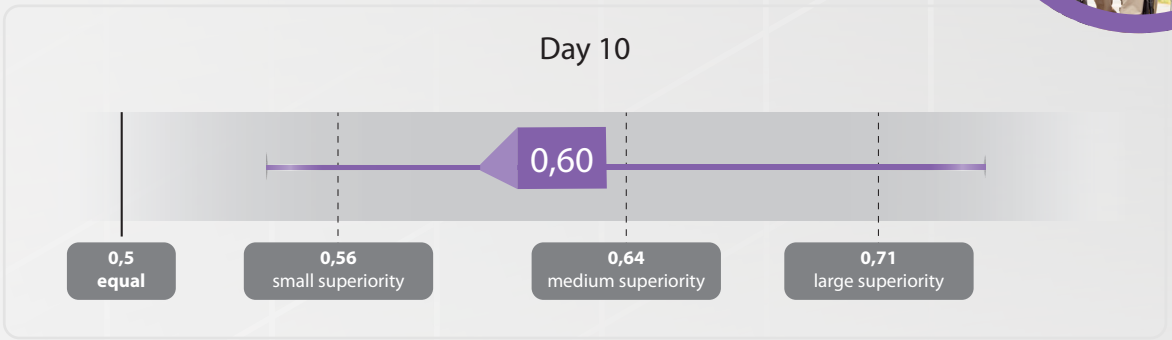

Figure: Confirmatory Multivariate Outcome Ensemble at Day 10, PP (Neuroprotection Phase) (Wert = 6,0)

- **Significant already on day 10**
- **Medium-sized superiority** for TBI patients on day 10
- **Already one early treatment cycle** brings significant medium superiority

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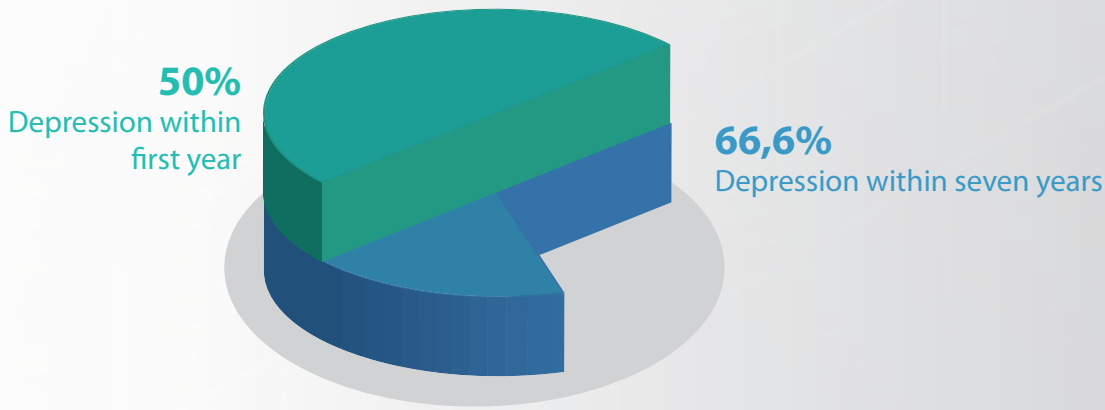
Depression - one of the most common comorbidities after TBI

About half of TBI patients are affected by depression within the first year after TBI and nearly 2/3 within seven years.



Treatment of post-TBI depression is essential!

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Better quality of life

- **Reduce the burden of depression after TBI**
- **Mentally fit again for daily life**
- **Superior quality of life**

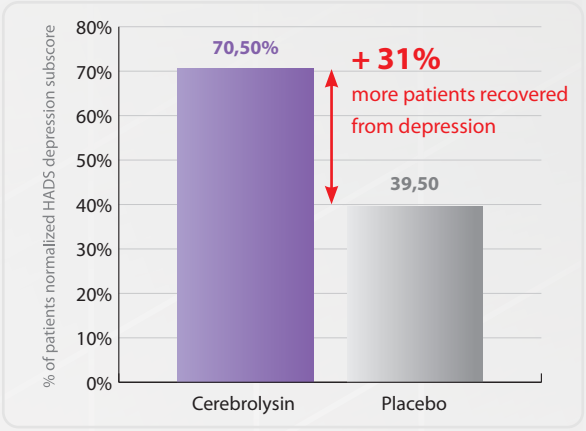

Figure: Normalization of the HADS score (Score 0-7) at Day 90

- **70,5%** of Cerebrolysin patients **recovered** from depression after TBI
- **+31% more Cerebrolysin patients** showed normalization in HADS depression score
- Cerebrolysin consistently shows **large-sized treatment effects**

After TBI - phenomenal results with a Cerebrolysin 10-day treatment regimen

- The effective treatment after TBI
- Save lives
- Early recovery
- Better quality of life

Disorder	Daily dosage	Initiation of treatment	Duration of treatment
Traumatic brain injury	20 - 50 ml	as soon as possible	7 - 30 days

Title: Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series.

Patients: CAPTAIN 1: 46 patients + CAPTAIN 2: 142 patients = **188 patients**

Treatment: Treatment Cycle 1 = Day 1 - 10 : 50 ml/day
Treatment Cycle 2 = Day 31 - 40 : 10 ml/day
Treatment Cycle 3 = Day 61 - 70 : 10 ml/day

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 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. (Reference SPC – CCDS Version 2.0/03.06.2016)

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CERE/INT/02/2021/3