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Webinar EVER Pharma

Opening the Vessel Is Not Enough – Is Cerebrolysin the Answer for Improved Long-Term Outcomes After Recanalization Therapy?

November 19, 2024

Cerebrolysin®

Reconnecting Neurons.
Empowering for Life.

Webinar EVER Pharma (November 19, 2024)

Opening the Vessel Is Not Enough – Is Cerebrolysin the Answer for Improved Long-Term Outcomes After Recanalization Therapy?

MODERATOR

Epifania Collantes
Philippines

EXPERTS

Manuel Martinez
Mexico

Jacek Staszewski
Poland

Marina Roje-Bedeković
Croatia

Minwoo Lee
South Korea

INTRODUCTION

The ongoing CERECAP (CErebrolysinRECanalizationAnd-Perfusion) pilot trial series investigates whether adding a cytoprotective agent, like Cerebrolysin, to recanalization therapy can improve long-term outcomes in stroke patients, and whether certain patient groups benefit more than others. The panel, consisting of leading stroke experts, shared their clinical experiences using Cerebrolysin as an adjunct to standard treatment.

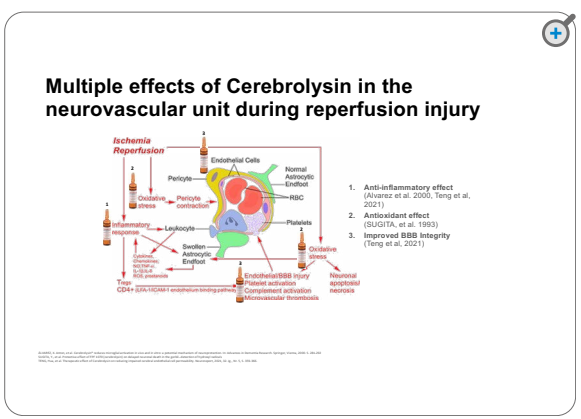
Introduction by Dr. Epifania Collantes

Dr. Collantes began by outlining the current state of thrombolysis and thrombectomy treatments. Using data from the HERMES collaboration and a post-marketing registry of Penumbra systems, she highlighted that many patients fail to achieve good functional outcomes (mRS 0-2) despite successful recanalization. She cited several reasons for this phenomenon, including reperfusion injuries, inflammation, endothelial swelling, bleeding, distal emboli, and microvascular spasms. These factors can lead to ischemia and cell death even after the blocked blood vessel is reopened.

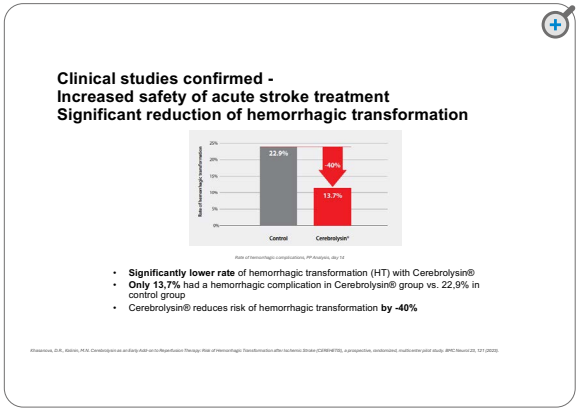
To address these challenges, Dr. Collantes introduced the **CERECAP Project (CErebrolysin RECanalisation And Perfusion).** This initiative currently includes 20 studies with over 1,500 patients investigating the efficacy of Cerebrolysin as an adjunctive therapy to recanalization for various stroke subtypes. The studies share common endpoints, including mRS (modified Rankin Scale) at day 90, NIHSS (National Institutes of Health Stroke Scale), MoCA (Montreal Cognition Assessment), and the occurrence of hemorrhagic transformations. A meta-analysis of all CERECAP studies is planned once these are completed, approximately in 3-4 years.

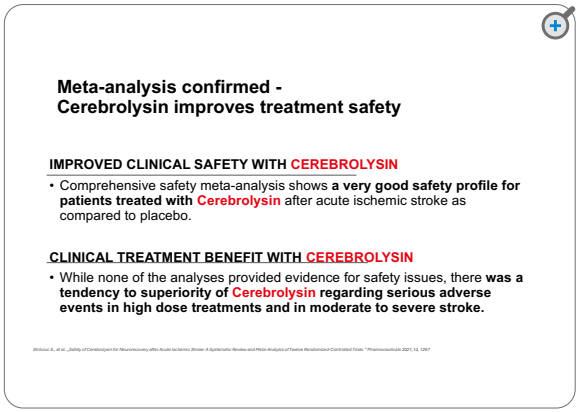
Presentation by Dr. Manuel Martinez

Dr. Manuel Martinez discussed the mechanism of action of Cerebrolysin, a compound composed of neuropeptides and free amino acids, which mimics and modulates neurotrophic factor activities. He emphasized its anti-inflammatory and antioxidant properties and its ability to restore the integrity of the blood-brain barrier.

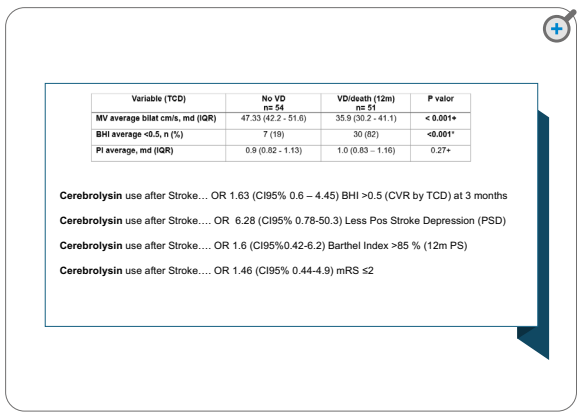


Additionally, he presented data from the CEREHETIS-trial, a prospective, randomized study involving 126 patients receiving tPA and Cerebrolysin and compared to the control group receiving only tPA. The results show that Cerebrolysin significantly reduced the rate of hemorrhagic transformations compared to the control group. He also discussed the comprehensive safety meta-analysis by Strilciuc *et al.* (2021) which shows a very good safety profile for patients treated with Cerebrolysin. It demonstrated that Cerebrolysin offers superior safety regarding serious adverse events, particularly in high-dose treatments and in cases of moderate to severe stroke.





Dr. Martinez concluded by presenting the results of a recently analyzed multi-center, longitudinal study from Mexico in which 30% of patients received Cerebrolysin. The hypothesis was that post-stroke hemorrhagic features detected by TCD (Transcranial Doppler sonography) are associated with post-stroke cognitive impairment. After the stroke, TCD and MRI was performed, and patients were followed up for 12 months at 3, 6, and 12-months intervals. The results show that Cerebrolysin is associated with reduced post-stroke depression after 12 months, a higher Barthel Index score, and less dependence. Overall, Cerebrolysin was linked to better outcomes and reduced disability.



Variable (TCD)	No VD n= 54	VD/death (12m) n= 51	P valor
MV average bilat cm/s, md (IQR)	47.33 (42.2 - 51.6)	35.9 (30.2 - 41.1)	< 0.001+
BHI average <0.5, n (%)	7 (19)	30 (82)	<0.001*
PI average, md (IQR)	0.9 (0.82 - 1.13)	1.0 (0.83 – 1.16)	0.27+

Cerebrolysin use after Stroke… OR 1.63 (CI95% 0.6 – 4.45) BHI >0.5 (CVR by TCD) at 3 months

Cerebrolysin use after Stroke…. OR 6.28 (CI95% 0.78-50.3) Less Pos Stroke Depression (PSD)

Cerebrolysin use after Stroke…. OR 1.6 (CI95%0.42-6.2) Barthel Index >85 % (12m PS)

Cerebrolysin use after Stroke…. OR 1.46 (CI95% 0.44-4.9) mRS ≤2

The take-home message emphasized that anti-inflammatory and antioxidant effects of Cerebrolysin could help repair stroke-related injuries. Pharmacological care, including rehabilitation, is crucial. Cerebrolysin may complement acute treatment, reduce complications, and improve prognosis when used immediately after or during acute stroke.

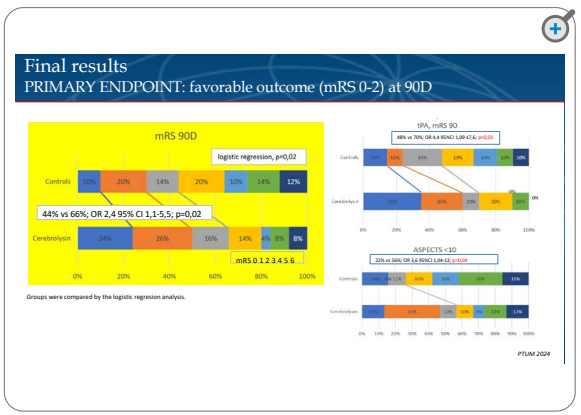
Presentation by Dr. Jacek Staszewski

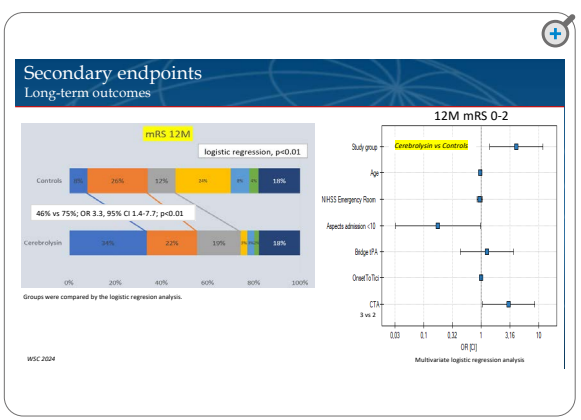
Dr. Jacek Staszewski focused on the importance of protecting the blood-brain barrier in stroke, emphasizing the need for a multimodal approach with pleiotropic agents to ensure effective cerebral protection.

He presented the CERECAP-WIM (Wojskowy Instytut Medyczny) study, which investigated Cerebrolysin as an adjunct therapy to endovascular therapy (EVT) in patients with acute ischemic stroke. These patients had baseline imaging showing a small ischemic core, good collaterals, effective recanalization after mechanical thrombectomy, but persistent significant deficits.

The study results showed that the Cerebrolysin group had a significantly higher rate of favorable functional outcomes after 90 days and 12 months compared to the control group. Additionally, Cerebrolysin reduced the risk of both symptomatic and asymptomatic intracerebral hemorrhages by over 60%.

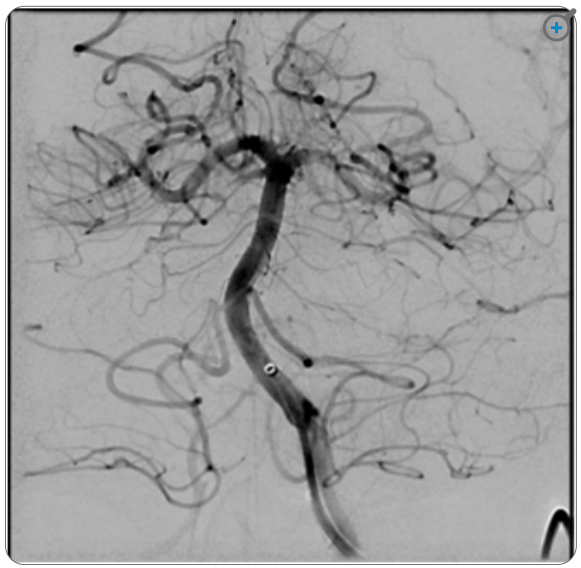
Dr. Staszewski also shared his recent experiences with Cerebrolysin in patients with various neurological conditions, including stroke, traumatic brain injury, vascular dementia, Alzheimer's disease, retinal infarction, and spinal cord infarction. He highlighted the potential benefits of Cerebrolysin in these conditions and stressed the need for further research.



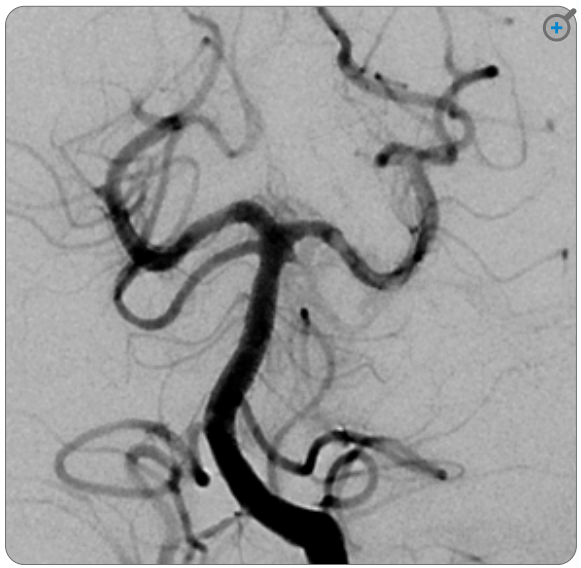


Presentation by Dr. Marina Roje-Bedeković

Dr. Marina Roje-Bedeković started her presentation with a case report of a 52-year-old man with basilar artery occlusion (BAO). Despite repeated mechanical thrombectomy and rescue intra-arterial tPA, the patient experienced re-occlusion of the basilar artery within 75 hours. However, after another bridging IV-tPA and mechanical thrombectomy, the patient fully recovered and was discharged on day 18 with an NIHSS of 0 and a Rankin Score of 0.



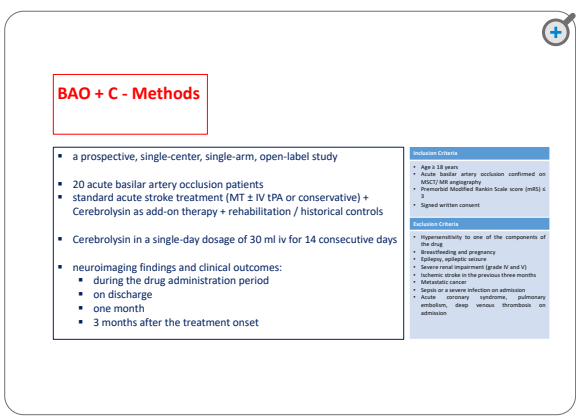
After the first MT with rescue IA tPA - reestablished flow in the BA and partial recanalization of the right SCA (TICI 2b)

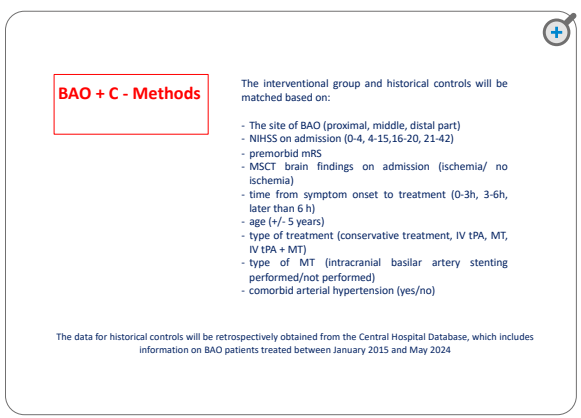


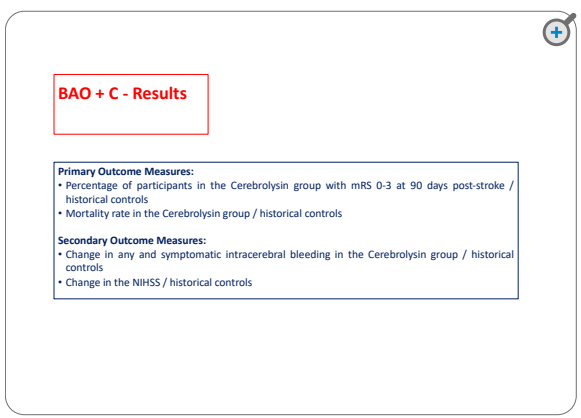
After the second MT - complete BA and right SCA recanalization (TICI 2c)

Dr. Roje-Bedeković emphasized that this was a fortunate exception, as most BAO patients have significantly worse outcomes. She discussed the challenges in diagnosing and treating BAO, its high mortality rate, and limited treatment options, stressing the urgent need for new therapies to improve outcomes.

She then presented her ongoing prospective, single-arm, open-label study evaluating the efficacy and safety of Cerebrolysin in 20 patients with acute basilar artery occlusion (BAO). Patients receive 30 ml of Cerebrolysin IV daily for 14 days in addition to standard therapy. The study's primary endpoints are the proportion of patients with a Rankin Score of 0-3 at 90 days and the mortality rate compared to historical controls. Initial results are very promising.

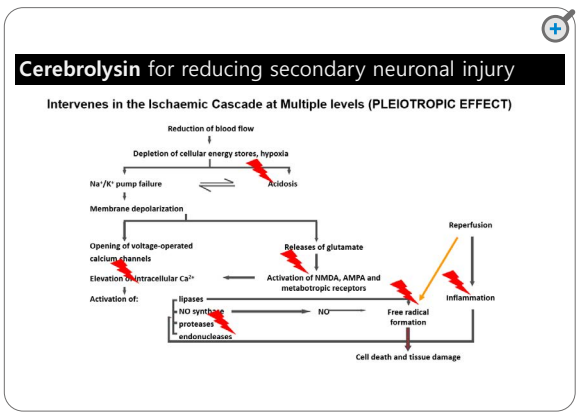






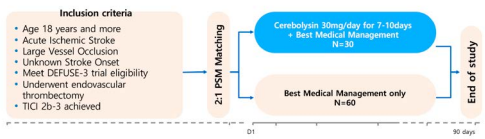
Presentation by Dr. Minwoo Lee

Dr. Minwoo Lee discussed the challenges in treating wake-up stroke patients, where the exact time of symptom onset is unknown, complicating decisions on thrombolysis and EVT. He presented recent findings suggesting that symptom onset in wake-up strokes often occurs shortly before the patient wakes up, enabling targeted acute interventions. Despite progress, outcomes for wake-up stroke patients remain worse than those with known onset, mainly due to less frequent use of acute therapies. Dr. Lee emphasized extending treatment windows for IVT and EVT in wake-up strokes, supported by studies like WAKE-UP, DEFUSE 3, and DAWN. He highlighted the importance of cerebral protection in wake-up stroke patients, presenting Cerebrolysin as a promising option with pleiotropic effects targeting multiple ischemic cascade mechanisms, including excitotoxicity, inflammation, oxidative stress, and blood-brain barrier dysfunction.



Dr. Lee also gave an outlook on a Korean CERECAP study, a retrospective, multicenter observational study evaluating the efficacy and safety of Cerebrolysin in wake-up stroke patients undergoing EVT. He introduced the study structure as well as presenting primary and secondary outcome parameters.

Study Design



Primary Outcome: good functional outcome (mRs 0-2)
Secondary Outcomes: NIHSS, MoCA, ICH and etc

Secondary Outcomes

- **Secondary outcomes**
  - Stroke Severity
    - National Institutes of Health Stroke Scale **(NIHSS)**: This will be assessed at two time points, specifically **on discharge and again at day 90**, to gauge the overall neurological status of the patients.
  - Mortality Rates
    - The study will track **mortality rates over the 90-day period** to determine if there is a significant reduction in deaths among the participants receiving Cerebrolysin compared to those who do not.
  - Hemorrhagic Transformation Rates
    - Both **symptomatic and asymptomatic hemorrhagic transformation rates** will be monitored over the 90 days, providing insight into the safety profile of Cerebrolysin in this patient population.
  - Cognitive outcomes
    - This cognitive assessment will be conducted at day 90 post-stroke to evaluate any changes in cognitive function following treatment using **MoCA**

Primary Outcomes

- **Primary outcome**
  - The primary outcome of the study will be the **good functional outcome** using **modified Rankin Scale (MRS) score**, which ranges from 0 to 2, measured at 90 days following the onset of the stroke.
  - This scale assesses the degree of disability or dependence in daily activities, thereby providing a critical measure of functional outcome.

Summary

The webinar highlighted the limitations of stand-alone recanalization therapy to improve long-term outcomes for acute ischemic stroke patients. All four webinar speakers emphasized the need for adjunctive treatments to address post-recanalization challenges such as inflammation, blood-brain barrier dysfunction, and ischemic injury. Cerebrolysin was mentioned by all speakers as a promising option with pleiotropic effects, supported by multiple studies showing its potential to enhance recovery, reduce complications, and improve functional outcomes in various stroke scenarios. Continued research through the CERECAP initiative aims to further validate its role in stroke care.

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.

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

www.cerebrolysin.com

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