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# **Cerebroprotective strategies in acute ischemic stroke** – fiction or reality?



#### SPEAKERS



### **Marc Ribo**

Professor of Neurology, Department of Neurology at University Hospital Vall d'Hebron, Barcelona, Spain



**Roni Eichel** 

Chair of Department of Neurology , Shaare Zedek Medical Center, Jerusalem, Israel



**Slaven Pikija** 

Neurologist, Christian-Doppler-Klinik, Salzburg, Austria

#### INTRODUCTION

The use of cerebroprotective (formerly neuroprotective) strategies in the treatment of acute ischemic stroke, especially within the time window of thrombolysis and thrombectomy, has become a hot topic in recent years.

The moderator of the webinar was Dr. Marc Ribo from Barcelona, Spain. Together with two well-known stroke clinicians, Dr. Roni Eichel from Jerusalem, Isreal and Dr. Slaven Pikija from Salzburg, Austria, he gave the audience an overview of the scientific rationale for such a treatment concept.

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## Introduction

## Marc Ribo

When discussing the future of stroke treatment, one of the most important topics is the discussion of whether neuroprotection or – to use the more appropriate term – cerebroprotection can show benefits in clinical medicine.

In his introduction to the webinar entitled 'Cerebroprotective strategies in acute ischemic stroke – fiction or reality?' Dr. Marc Ribo presented first a short history of neuroprotection research. It turned out that the previous failures with neuroprotective agents led to a temporary halt of research in clinical stroke medicine.

However, the main part of his lecture was devoted to highlighting recent research articles that predict that neuroprotection could occupy an important place in AIS-treatment concepts when used in conjunction with recanalization therapies.

Finally, Dr. Ribo highlighted the consensus statement of the STAIR conference 2019, which not only introduced the new terms *cerebral cytoprotection* or *cerebroprotection*, but also mentioned how these agents can be a successful therapy option in acute stroke medicine.

Dr. Ribo's last slide convincingly showed that a successful implementation of cerebroprotective drugs is possible if the entire neurovascular unit becomes a therapeutic target. This will only be possible if agents with multimodal and pleiotropic properties, such as Cerebrolysin, become the focus of research in cerebroprotective treatment strategies.

# Post-Endovascular Cerebrolysin treatment for Acute Ischemic Stroke Roni Eichel

Dr. Roni Eichel began his presentation by discussing the need for additional treatment options, since recanalization treatments alone do not lead to an improved long-term outcome in about half of the treated patient population.

He also explained the most likely reason why endovascular treatment after acute ischemic stroke is often unsuccessful or only partially successful. The so-called EVT (EndoVascular Treatment) -no-flow phenomenon, widely accepted as a main cause of an unsatisfactory outcome, increases the need for evidencebased treatments in addition to thrombolysis and thrombectomy. Consequently, in an excellent visualization,

Dr. Eichel addressed the treatment goal of cerebroprotective drugs in stroke care, namely the reduction of mortality and disability.

In the last part of his presentation, Dr. Eichel briefly presented the recently started CERECAP study (CErebrolysin RECanalization And Perfusion), which assesses the safety and efficacy of the neuroprotective drug Cerebrolysin as an add-on therapy in patients with AIS after EVT with or without prior IV-tPA treatment.

# Cerebrolysin – an essential medication in stroke unit management – guidelines, trials and new research

## Slaven Pikija

Dr. Pikija began his lecture by pointing out that Cerebrolysin is already considered a standard add-on therapy for acute ischemic stroke in his hospital – for patients within and outside the time window for recanalization therapy, which also explains the title of his lecture.

After a brief overview of the clinical development history of Cerebrolysin, Dr. Pikija presented some cases that were treated in his stroke unit and showed a specific brain stem stroke with an unexpectedly positive outcome. He hypothesized that immediate treatment with Cerebrolysin could be one of the most important factors for a good outcome in a patient with AIS in the brain stem region. In the last part of Dr. Pikija's lecture, he shared his current research projects, which are based on this extensive treatment experience with Cerebrolysin, his clinical observations, and professional interests as a stroke physician.

Dr. Pikija's first proposal is an MRI-based longitudinal assessment of leukoaraiosis (LA) and the influence of Cerebrolysin.

The medical problem: After the first-ever stroke (FES), LA, also known as white matter disease, small vessel disease or leukoencephalopathy, may be a modifiable white matter disease. The LA is a poor predictor of recovery after the FES, as the LA progresses and may even accelerate after an FES. The reasons for this course are speculative, but it is hypothesized that a disruption of the blood-brain-barrier and a so-called neuroinflammatory penumbra after an FES plays a significant role. LA progression could be quantified using automatic MRI tools as shown. Given the abnormal exposure of brain antigens to the immune system after a stroke, one might assume that LA progresses locally but also distal from the stroke area and regardless of the vascular territory affected.

Dr. Pikija hypothesized that Cerebrolysin<sup>®</sup> with its known cerebroprotective, blood-brain-barrier stabilizing, and anti-inflammatory properties could have a positive effect on LA after an FES.

Finally, he described the cooperation project with the Johns-Hopkins University Hospital, which is in the final planning stage – see brief description below.

## Summary

Marc Ribot, Roni Eichel and Slaven Pikija presented convincing cases of successfully treated patients as well as promising new clinical research projects to the audience. Studies with the cerebroprotective drug Cerebrolysin showed improved long-term outcome of all stroke patients when treatment was started in the acute phase. These results have been acknowledged in numerous guidelines. The strong message to the audience is:

> Cerebroprotective treatment strategies in AIS are not fiction, but recommended and evidence-based reality.



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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