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Webinar EVER Pharma

New horizons improving gold standard therapy in acute stroke –

Case discussions

June 22, 2022

Cerebrolysin®

Reconnecting Neurons.
Empowering for Life.

Webinar EVER Pharma (June 22, 2022)

New horizons improving gold standard therapy in acute stroke – Case discussions

EXPERTS

Maksim Domashenko

Chief Medical Director, Magnitogorsk Iron&Steel Clinical, Russia

Zdravka Poljakovic

Head of the Neurological Intensive care Unit, Medical School Zagreb, University Hospital Zagreb, Croatia

MODERATOR

Dimitre Staykov

Head of Neurology Department, Barmherzige Brüder Eisenstadt, Austria

INTRODUCTION

On June 22nd a webinar focusing on neurological emergencies – the treatment of ruptured SAH by intraventricular thrombolysis and acute ischemic stroke - was organized by EVER Pharma.

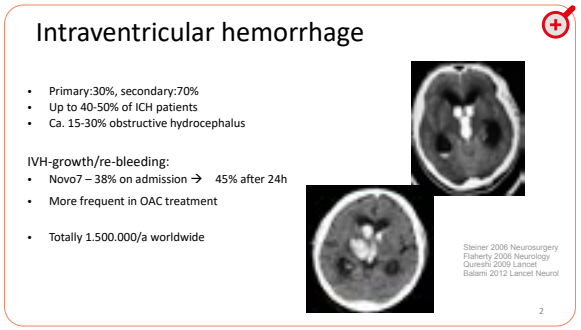
In the report you can find the summary of the 3 short presentations which focused on:

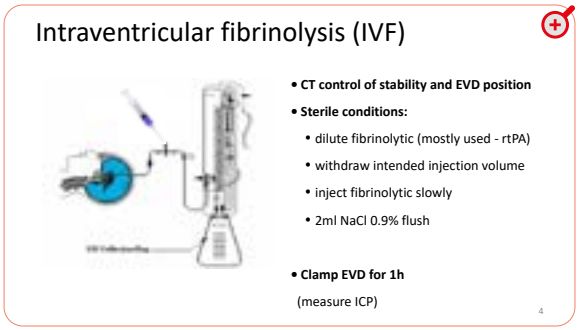
What is IVF and how does it work, current evidence

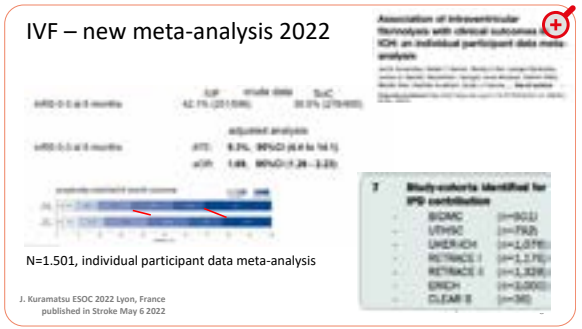
The moderator, Dimitre Staykov from Eisenstadt, Austria, presented a short overview about the epidemiology of intraventricular hemorrhage and also explained very clearly how this procedure is performed.

Staykov, who himself has been involved in the clinical development of intraventricular fibrinolysis (IVF), pointed out that the larger RCTs, e.g. the CLEAR-trial series did not yet demonstrate improved clinical outcomes but that a recent meta-analysis by Kuramatsu et al. on the association between IVF and clinical outcomes showed promising trends.

He closed his opening remarks that the research community focusing on this field of medicine remains confident that IVF will eventually demonstrate improvements in clinical outcome and reduce severe complications like hydrocephalus and mortality.





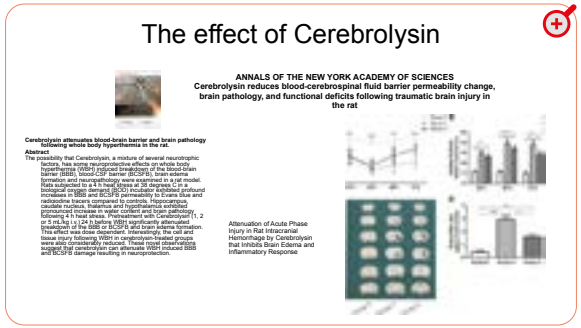


Cerebrolysin as add-on therapy after SAH coiling in severely affected patients

Zdravka Poljakovic presented her ongoing trial on hemorrhagic stroke after SAH in Hunt&Hess 4-5 patients. Poljakovic initially discussed the rationale why she hypothesizes that Cerebrolysin might improve safety and patient outcome when IVF is used in these severely affected patients.

Poljakovic explained that for these patients an effective agent with multimodal properties would be an additional benefit as maintaining the blood-brain barrier integrity as well as the promotion of anti-inflammatory effects could play a crucial role for these patients.

In this context she highlighted that published data confirmed that Cerebrolysin inhibits the effect of proinflammatory mediators, mimics the action of neurotrophic factors and inhibits free radical formation, all contributing to neuroprotective effects of this drug in SAH.

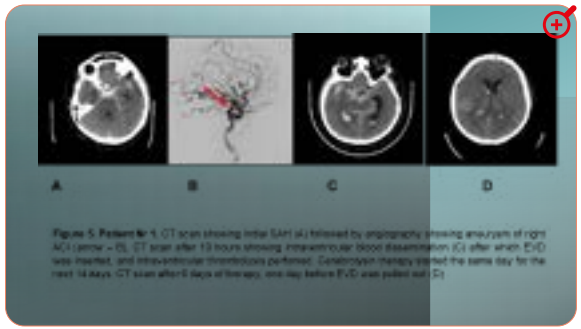


Next she shared the main aspects of her pilot study in acute aneurysmal subarachnoid hemorrhage and high initial Hunt& Hess grade (3-5) which are:

- Patients with HH III and higher with aneurysmal SAH
- Standard treatment protocol and Cerebrolysin systemic infusion as add-on therapy for minimum of 14 and maximum of 21 days in the dosage of 30 ml/day.
- Coiling
- EVD if needed /intraventricular trombolysis.
- Primary outcome of the study was measured with functional outcome (modified Rankin Scale, day 90) and secondary outcome was symptomatic vasospasm confirmed by neuroimaging

She continued her presentation showing some successfully treated patients and mentioned that the results, despite being only based on 10 treated patients, are confidence building, concluding:

"Our initial results confirmed safety of Cerebrolysin. Considering efficacy, our group of patients showed good outcome in 40% (4) of patients with mRS 0-3, 30% of patients had bad outcome and 30% died. We can conclude that our patients had slightly better outcome than expected, and although being far from a final conclusion, this results gives a promising impulse for the study continuation".



Cerebrolysin as add-on therapy in AIS after recanalization therapy

After these 2 presentations on SAH and the role Cerebrolysin can play in a medical field where very few drugs can be used safely, Staykov introduced Maxim Domashenko from Magnitogorsk in Russia.

His current interest is the role of Cerebrolysin as an add-on therapy to recanalization therapy due to the need of a treatment which reduces the hyperpermeability of the blood-brain-barrier (BBB) caused by the inflammatory effects rtPA exhibits and by the experimentally shown data that this agent can also increase the microcirculation in the penumbra.

Domashenko proceeded by introducing the study design of his pilot-study (n=50) which looks at the safety and efficacy of Cerebrolysin in patients with AIS after TICI 2b-3 thrombectomy.

As with the previous presentation of Poljakovic, also Domashenko's research project has not progressed very far at this moment but first results are encouraging, in his own study he saw no safety problems as well which also is in line with recently published data – preclinically and clinically:

Preclinical trial
Teng et al. 2021

Clinical trial
Poljakovic et al.2021

CERETHRE Study # Design

- **Group 1 (Cerebrolysin)**: 30 ml Cerebrolysin + 100,0 ml 0,9% NaCl immediately after TICI 2b-3 thrombectomy, basic treatment, early neurorehab
- **Group 2 (Control)**: 130,0 ml 0,9% NaCl immediately after TICI 2b-3 thrombectomy, basic treatment, early neurorehab

CERETHRE Study # primary endpoints

- Frequency of symptomatic HT (ECASS II classification) after 24 h and 14 day after stroke
- Frequency of non-symptomatic HT (ECASS II classification) after 24 h and 14 day after stroke

TAKE HOME MESSAGES OF THIS WEBINAR

Intraventricular Thrombolysis research shows first **promising results** in recent meta-analysis

In Hunt&Hess patients grade 3-5 mortality rates remain **high** - **reducing mortality** and complications while aiming for **better outcome** might be supported by Cerebrolysin

Neuroprotection with **Cerebrolysin** is a hot topic in acute stroke management – **improving safety** while potentially benefiting severely affected patients is a valuable research target showing already promising results

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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