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Webinar EVER Pharma
**Get with the guidelines in
post-stroke motor recovery –
Expert panel discussion**

May 24, 2022

Cerebrolysin[®]

Reconnecting Neurons.
Empowering for Life.

Webinar EVER Pharma (May 24, 2022)

Get with the guidelines in post-stroke motor recovery – Expert panel discussion



EXPERTS

MODERATOR



Dr. Cornelia Brunner

Neurologist at University
Clinic Tulln, Austria



Dr. Robert Teasell

Medical Director of the
Stroke Rehabilitation
Program at Parkwood
Institute, Canada



Prof. Karin Diserens

Deputy Physician,
Department of
Neurology and Clinical
Neurosciences, Head of
the Transversal Unit of
Acute Neurorehabilitation
(NRA), University Hospital,
Lausanne, Switzerland



Dr. Ales Tomek

Neurologist at Motol
University Hospital at
Prague, Czech Republic



Dr. Steven Zeiler

Johns Hopkins University,
Baltimore, USA

Webinar EVER Pharma (May 24, 2022)

Get with the guidelines in post-stroke motor recovery – Expert panel discussion



INTRODUCTION

On May 24th EVER Pharma conducted its 2nd webinar in 2022 titled 'Get with the guidelines in post-stroke motor recovery – Expert panel discussion'. Four international stroke specialists formed an international panel, expertly moderated by Professor Steven Zeiler to discuss the evidence of Cerebrolysin in post-stroke rehabilitation and – as a consequence – the inclusion into various international treatment guidelines with high recommendation levels.

Only one positive trial in post-stroke motor recovery is CARS trial – Zeiler's Talk

Cerebrolysin recommended in Canadian Stroke Rehab Evidence-based Review – Teasell's Talk

EAN guidelines recommend Cerebrolysin for clinical use – Diserens's Talk

Cerebrolysin - A standard therapy in acute stroke medicine – Brunner's Talk

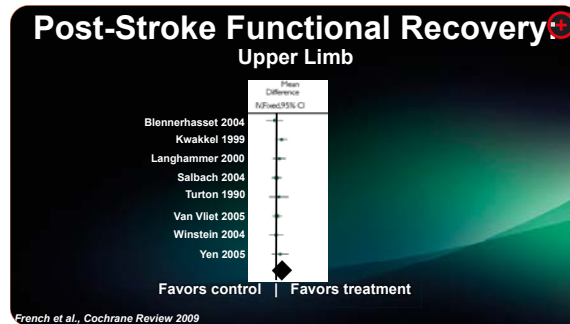
Stroke rehabilitation needs detailed and practical guidelines – Tomek's Talk

TAKE HOME MESSAGES

SUMMARY

Only one positive trial in post-stroke motor recovery is CARS trial – Zeiler’s Talk

Dr. Zeiler opened the session with some general remarks about the widely acknowledged understanding that the effects of post-stroke physiotherapy are limited and that additional treatments are needed to improve long-term outcome for stroke patients and also mentioned in this context that the only positive trial in post-stroke motor recovery, considering all treatment forms (robotics, physiotherapy, pharmacology, etc.) is the CARS-trial. This was prominently published in *Lancet Neurology* in 2019 and can be considered as the most important publication documenting Cerebrolysin as evidence-based medicine beyond any doubt.



A survey with the participants followed which aimed to demonstrate the importance of effective treatment methods for patients with motor complications. The majority of the audience correctly stated that around 80% of stroke patients suffer from upper motor complications, the most frequent of all stroke consequences.

Advances and challenges in stroke rehabilitation

Cathy M Stinear, Catherine E Lang, Steven Zeiler, Winston D Byblow | *Lancet Neurol* 2020; 19: 348-50

- 14 of 15 clinical trials negative 2016 – 2019
 - All trials of technology.....negative
 - All trials of PT/OT.....negative
 - Pharmacological.....positive
 - Cerebrolysin

Cerebrolysin recommended in Canadian Stroke Rehab Evidence-based Review – Teasell’s Talk

Prof. Robert Teasell, Research Director and Chair at Western University London, Ontario who is also the leading author of the Canadian Stroke Rehab Evidence-based Review, continued outlining the strengths of the review as the world’s leading and most comprehensive evidence-based review in stroke rehabilitation. Consequently, the review serves as an essential resource for different country guidelines. He presented the details about the Cerebrolysin recommendations within this review, highlighting the results in the three researched domains which are motor function, activities of daily living and stroke severity and summarizes that “Cerebrolysin may be beneficial for upper limb function following stroke”.

Stroke Rehab Evidence-Based Review

- SREBR designed to be **comprehensive, up-to-date, accessible review which would help guide a best-practice approach**
- **World’s leading most comprehensive evidence-based review of stroke rehab** (20th edition-underway) analyzing 3,500 RCTs and 3,500 other studies
- 2,300 RCTs are of Motor Interventions; 500 Cognitive Interventions
- **Critical resource for clinical guidelines** from different countries including the Canadian Stroke Best Practice Guidelines and Ontario QBP

EBRSR
www.ebrsr.com

Cerebrolysin in Upper Extremity Recovery Post Stroke

MOTOR FUNCTION			
LoE	Conclusion Statement	RCTs	References
1a	Cerebrolysin may produce greater improvements in motor function than placebo.	2	Chang et al. 2010; Moriwaki et al. 2016

ACTIVITIES OF DAILY LIVING			
LoE	Conclusion Statement	RCTs	References
1b	Cerebrolysin may produce greater improvements in activities of daily living than placebo.	1	Chang et al. 2010

STROKE SEVERITY			
LoE	Conclusion Statement	RCTs	References
1b	Cerebrolysin may produce greater improvements in measures of stroke severity than placebo.	1	Chang et al. 2010

Key points

Cerebrolysin may be beneficial for aspects of upper limb function following stroke.

EAN guidelines recommend Cerebrolysin for clinical use – Diserens’s Talk

Prof. Karin Diserens from University Hospital Lausanne, Switzerland serves as the Head of the Acute Neurorehabilitation Unit. She is a co-author of the EAN-Guidelines and emphasized the importance of this specific guidelines and the thorough methods to develop these guidelines.

What this guideline committee aimed to find out was if the addition of pharmacological agents to early motor rehabilitation is beneficial for patients in regards to early motor performance, neurological function and global functional outcome. The assessment, development and evaluation of the data was conducted within the GRADE framework, one of the most important and acknowledged methodologies globally to develop guidelines.

The results were published in July 2021 and recommended Cerebrolysin for clinical use, ideally with a 30ml daily dosage and for a minimum of 10 days. All other agents were either not recommended for clinical use at all or within a limited scope.

GUIDELINES

European Academy of Neurology and European Federation of Neurorehabilitation Societies guideline on pharmacological support in early motor rehabilitation after acute ischaemic stroke

Ettore Beghi¹ | Heinrich Binder² | Codruta Birle³ | Natan Bornstein⁴ | Karin Diserens⁵ | Stanislav Groppa⁶ | Volker Homberg⁷ | Vitalie Lisnic⁸ | Maura Puglatti⁹ | Gary Randall¹⁰ | Leopold Saltuari¹¹ | Stefan Strlicuc¹² | Johannes Vester¹³ | Dafin Muresanu^{3,11}

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Abstract
Background and purpose: Early pharmacological support for post-stroke neurorehabilitation has seen an abundance of mixed results from clinical trials, leaving practitioners at a loss regarding the best options to improve patient outcomes. The objective of this evidence-based guideline is to support clinical decision-making of healthcare professionals involved in the recovery of stroke survivors.
Methods: This guideline was developed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework. PubMed, Cochrane Library and Embase were searched (from database inception to June 2018, inclusive) to identify studies on pharmacological interventions for stroke rehabilitation initiated in the first 7 days (inclusive) after stroke, which were delivered together with neurorehabilitation. A sensitivity analysis was conducted on identified interventions to address results from breaking studies (from end of search to February 2020).

Approved by the EAN Scientific Committee and Guideline Production Group on 28 January 2021
 Eur J Neurol. 2021;001-15. www.ejnl.eu/article/view/1000001 | © 2021 European Academy of Neurology | 1

Cerebrolysin - A standard therapy in acute stroke medicine – Brunner's Talk

Dr. Cornelia Brunner from University Hospital Tulln in Austria highlighted that rehabilitation should start in the very early phase after brain damage caused by stroke. She then discussed the process which finally led to the decision of her hospital to develop a Standard Operating Procedure (SOP) regulating the inclusion of Cerebrolysin into the routine treatment of motor impaired patients.

This SOP was recently adapted after the EAN guidelines on post-stroke rehabilitation were published.

SOP 08/2020 Adapted in 2021 based on EAN recommendations

- Cerebrolysin*
 - should be given in patients with NIHSS ≥ 8 after ischemic stroke (without any „inclusion/exclusion criteria“)
 - within 24-72 hours post stroke onset
 - prescribed for at least 10 days
 - once daily
 - 30ml intravenously in addition to rehabilitative process
- In case of minor stroke, NIHSS ≤ 8 – SOP from 08/2020

Due to COVID Pandemic and closure of our rehabilitation unit, the SOP wasnt realizable as planned in clinical routine till now.

Dr. Brunner clearly pointed out that the various guideline recommendations not only help her and colleagues in the decision-making processes but that an SOP also makes sure that the standardization of treatment for stroke patients with motor complications is facilitated.

In her take home message Dr. Brunner sent out a very important message to stroke physicians – see below.

Outlook

- Cerebrolysin*:
 - should become a standard therapy in stroke
 - should be implemented in clinical practice in accordance to guidelines
 - can be defined as therapy in acute stroke medicine
- Goals:
 - improving long term outcome and disability of stroke patients
 - reducing caregiver burden
 - significant improvement: quality of life (QoL) and activities of daily living (ADL)

Stroke rehabilitation needs detailed and practical guidelines – Tomek’s Talk

As the final panelist Prof. Ales Tomek from 2nd Medical Faculty of Charles University Prague, Czech showed not only the main challenges in stroke care as perceived by the medical community but also how these challenges are managed through the help of existing and very detailed guidelines. Interestingly, rehabilitation guidelines are not yet formulated in his country.



Dr. Tomek then introduced plans of the government to increase the attention to identify and later to measure improvements of certain quality indicators for rehabilitation, something which is already routinely done in acute stroke. Currently a project is ongoing which aims to replicate monitoring and improving acute care indicators also in stroke rehabilitation.

In this context Dr. Tomek mentioned the EAN-Guideline as highly relevant for decision-making processes, pointing out that he himself was critical about the evidence of Cerebrolysin until recently but nowadays acknowledges the agent as a potent and relevant medication in stroke, reciting some passages from the German Society of Neurorehabilitation guideline recommending Cerebrolysin - even discussing a specific treatment regimen following the CARS-Trial.

In the end he concluded that stroke rehabilitation needs detailed and practical guidelines for every type of treatment and that pharmacological agents like Cerebrolysin play also an important role.

Conclusions

- Stroke rehabilitation needs **detailed and practical guidelines for every type of treatment** including pharmacological support
- Rehabilitation needs to be more** centrally organized, and alike in different centers
- Rehabilitation needs **quality of care monitoring** indicators with regular benchmarking

TAKE HOME MESSAGES

Teasell:

Early, intensive and task specific care has dramatically changed outcomes

Diserens:

We need pharmacological agents in rehab guidelines

Brunner:

Neurorecovery is a dynamic multi-factorial process and for which pharmacological and non pharmacological treatments need to be applied at the right time

Tomek:

I am happy that I can help early on and there is an evidence based drug which I can give to my patients

SUMMARY

The four panelists as well as the moderator provided essential information about the excellent evidence of Cerebrolysin in motor recovery which consequently led to the inclusion into important guidelines. All speakers support the idea to “Get with the Guidelines” encouraging clinicians globally to implement guideline recommendations into routine clinical practice.



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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