Efficacy and safety of cerebrolysin in neurorecovery after moderate-severe traumatic brain injury: results from the CAPTAIN II trial

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Abstract

Introduction

The objective of this trial was to evaluate the efficacy and safety of Cerebrolysin in treating patients after moderate to severe traumatic brain injury (TBI) as an adjunct to standard care protocols. The trial was designed to investigate the clinical effects of Cerebrolysin in the acute (neuroprotective) stage and during early and long-term recovery as part of a neurorestorative strategy.

Materials and methods

The study was a phase IIIb/IV single-center, prospective, randomized, double-blind, placebo-controlled clinical trial. Eligible patients with a Glasgow Coma Score (GCS) between 7 and 12 received study medication (50 ml of Cerebrolysin or physiological saline solution per day for 10 days, followed by two additional treatment cycles with 10 ml per day for 10 days) in addition to standard care. We tested ensembles of efficacy criteria for 90, 30, and 10 days after TBI with a priori ordered hypotheses using a multivariate, directional test, to reflect the global status of patients after TBI.

Results

The study enrolled 142 patients, of which 139 underwent formal analysis (mean age = 47.4, mean admission GCS = 10.4, and mean Baseline Prognostic Risk Score = 2.6). The primary endpoint, a multidimensional ensemble of 13 outcome scales, indicated a "small-to-medium"–sized effect in favor of Cerebrolysin, statistically significant at day 90 ($MW_{combined}$ = 0.59, 95% CI 0.52 to 0.66, P = 0.0119). Safety and tolerability observations were comparable between treatment groups.

Conclusion

Our trial confirms previous beneficial effects of the multimodal, biological agent Cerebrolysin for overall outcome after moderate to severe TBI, as measured by a multidimensional approach. Study findings must be appraised and aggregated in conjunction with existing literature, as to improve the overall level of insight regarding therapeutic options for TBI patients. The widely used pharmacologic intervention may benefit from a large-scale observational study to map its use and to establish comparative effectiveness in real-world clinical settings.

Keywords

Traumatic brain injury Cerebrolysin Multidimensional approach Wei-Lachin pooling

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s10072-019-04181-y (https://doi.org/10.1007/s10072-019-04181-y)) contains supplementary material, which is available to authorized users.

Notes

Compliance with ethical standards

CAPTAIN II, a single-center, prospective, randomized, double-blind, placebo-controlled clinical trial, was approved by the Ethics Committee of the University of Medicine and Pharmacy in Cluj-Napoca, Romania (No. 714/07.03.2013). A full study protocol is available in the ISRCTN registry (No. 17097163).

Conflict of interest

Authors of the manuscript report being members in Advisory Board of the CAPTAIN I trial.

Publisher's note

Supplementary material

10072_2019_4181_MOESM1_ESM.docx (29 kb)
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