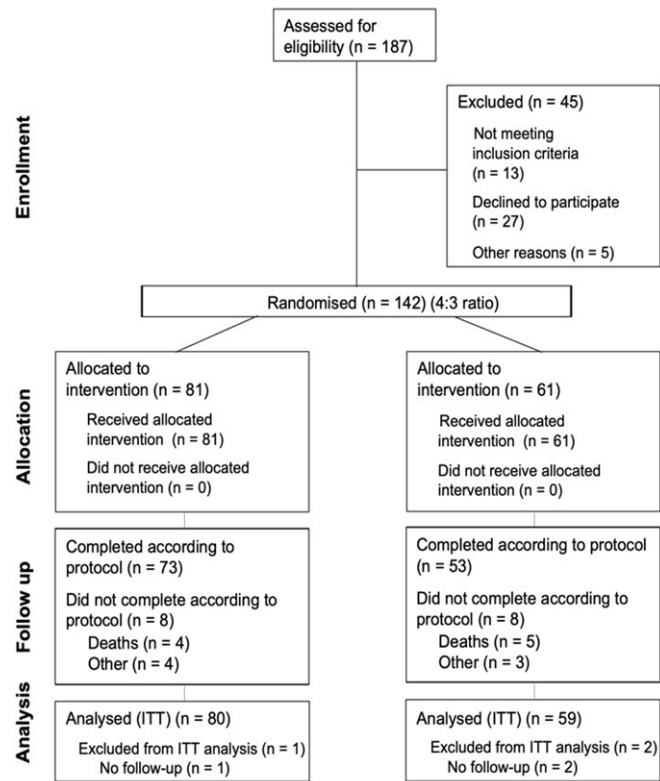


Participant flow

Flow diagram of patients in the CAPTAIN II trial



Baseline characteristics

Demographic baseline characteristics for the ITT study population

Indicator	Total, n=139	Cerebrolysin, n=80	Placebo, n=59
Male sex, number (%)	123 (88.5)	72 (90.0)	51 (86.4)
Mean age, years (SD)	47.4 (17.3)	46.4 (17.1)	48.8 (17.6)
Mean BPRS, (SD)	2.6 (1.8)	2.6 (1.8)	2.6 (1.8)
Mean AIS Face, (SD)	1.3 (0.5)	1.2 (0.4)	1.3 (0.5)
Mean AIS other regions (maximum score), (SD)	1.3 (0.4)	1.3 (0.5)	1.2 (0.4)
Mean GCS total score at admission, (SD)	10.4 (1.4)	10.2 (1.5)	10.6 (1.3)
Mean GCS motor score at admission, (SD)	4.6 (0.6)	4.6 (0.6)	4.7 (0.5)
Mean GCS total score pre-treatment, (SD)	10.9 (1.4)	10.8 (1.4)	11.0 (1.3)
Mean GCS motor score pre-treatment, (SD)	4.8 (0.4)	4.8 (0.6)	4.8 (0.4)
<i>BPRS - Baseline Prognostic Risk Score, GCS - Glasgow Coma Scale, AIS - Abbreviated Injury Scale, SD – standard deviation.</i>			

Primary outcome measures

The intention-to-treat (ITT) population, used for all efficacy analyses, included patients who had at least one dose of medication and at least one post-baseline observation of at least one primary efficacy criterion. A sensitivity analysis was performed for a per-protocol (PP) data set as an exploratory approach. The PP population included all patients who were eligible for ITT evaluation and who additionally did not show significant protocol deviations.

Multivariate Outcome Ensemble at Day 90 - Intention-To-Treat (ITT)

Day 90 (ITT)	MW	95% CI	N1/N2	P
GO4LPCF	0.5571	0.4682-0.6460	80/59	0.2083
ER4LPCF	0.5258	0.4805-0.5712	80/59	0.2640
MS4LPCF	0.5439	0.4557-0.6320	80/59	0.3295
PSC4LPCF	0.6225	0.5233-0.7217	80/59	0.0155
PSSC4LPCF	0.5579	0.4604-0.6555	80/59	0.2444
CWWD4LPCF	0.6662	0.5720-0.7604	80/59	0.0005
CWCD4LPCF	0.5877	0.4930-0.6824	80/59	0.0696
DGF4LPCF	0.6101	0.5107-0.7094	77/59	0.0300
DGB4LPCF	0.6520	0.5519-0.7521	77/59	0.0029
CL1-4LPCF	0.6106	0.5149-0.7063	77/59	0.0235
CL2-4LPCF	0.5747	0.4785-0.6709	77/59	0.1279
HAD-4 LPCF	0.5346	0.4373-0.6318	77/59	0.4860
HDD-4LPCF	0.6469	0.5515-0.7424	77/59	0.0026
Combined	0.5915	0.5202-0.6628	80/59	0.0119

MW: Mann-Whitney; CI: confidence interval; N1: valid number Active Treatment; N2: valid number Placebo; GO4LPCF: Glasgow Outcome Scale Extended (GOS-E); ER4LPCF: Early Rehabilitation Barthel Index; MS4LPCF: Mini-Mental State Examination; PSC4LPCF: Processing Speed Index (PSI); Digit Symbol Coding; PSSC4LPCF: Processing Speed (PSI) Symbol Search; CWWD4LPCF: Stroop (VST) Word/Dots Interference; CWCD4LPCF: Stroop (VST) Color-Word/Dots Interference; DGF4LPCF: Digit Span Digit Forward Test; DGB4LPCF: Digit Span Digit Backward Test; CL1-4LPCF: Color Trails Test 1; CL2-4LPCF: Color Trails Test 2; HDA-4LPCF: HADS: Anxiety Sumscore; HDD-4LPCF: HADS: Depression Sumscore; Visit No. 4 = Day 90

Multivariate Outcome Ensemble at Day 90 - Per-Protocol Sensitivity Analysis (PP)

Day 90 (PP)	MW	95% CI	N1/N2	P
GO4LPCF	0.5733	0.4816-0.6651	74/55	0.1172
ER4LPCF	0.5252	0.4810-0.5693	74/55	0.2634
MS4LPCF	0.5692	0.4777-0.6606	74/55	0.1381
PSC4LPCF	0.6430	0.5394-0.7466	74/55	0.0068
PSSC4LPCF	0.5609	0.4597-0.6621	74/55	0.238
CWWD4LPCF	0.6661	0.5682-0.7640	74/55	0.0009
CWCD4LPCF	0.5916	0.4934-0.6899	74/55	0.0675
DGF4LPCF	0.6264	0.5231-0.7296	71/55	0.0164
DGB4LPCF	0.6694	0.5654-0.7733	71/55	0.0014
CL1-4LPCF	0.6342	0.5350-0.7333	71/55	0.008
CL2-4LPCF	0.5965	0.4969-0.6962	71/55	0.0575
HAD-4 LPCF	0.5318	0.4309-0.6326	71/55	0.5371
HDD-4LPCF	0.6458	0.5465-0.7452	71/55	0.004
Combined	0.6026	0.5297-0.6755	74/55	0.0058

MW: Mann-Whitney; CI: confidence interval; N1: valid number Active Treatment; N2: valid number Placebo; GO4LPCF: Glasgow Outcome Scale Extended (GOS-E); ER4LPCF: Early Rehabilitation Barthel Index; MS4LPCF: Mini-Mental State Examination; PSC4LPCF: Processing Speed Index (PSI); Digit Symbol Coding; PSSC4LPCF: Processing Speed (PSI) Symbol Search; CWWD4LPCF: Stroop (VST) Word/Dots Interference; CWCD4LPCF: Stroop (VST) Color-Word/Dots Interference; DGF4LPCF: Digit Span Digit Forward Test; DGB4LPCF: Digit Span Digit Backward Test; CL1-4LPCF: Color Trails Test 1; CL2-4LPCF: Color Trails Test 2; HDA-4LPCF: HADS: Anxiety Sumscore; HDD-4LPCF: HADS: Depression Sumscore; Visit No. 4 = Day 90

Multivariate Outcome Ensemble at Day 30 - Intention-To-Treat (ITT)

Day 30 (ITT)	MW	95% CI	N1/N2	P
GO3LPCF	0.5898	0.4978-0.6819	80/59	0.0557
ER3LPCF	0.5264	0.4698-0.5829	80/59	0.3604
MS3LPCF	0.5373	0.4435-0.6310	80/59	0.4356
PSC3LPCF	0.5524	0.4547-0.6502	80/59	0.2930
PSSC3LPCF	0.5529	0.4555-0.6502	80/59	0.2871
CWWD3LPCF	0.6290	0.5347-0.7233	80/59	0.0073
CWCD3LPCF	0.5510	0.4551-0.6468	80/59	0.2973
DGF3LPCF	0.6101	0.5104-0.7097	77/59	0.0304
DGB3LPCF	0.6272	0.5277-0.7267	77/59	0.0122
CL1-3LPCF	0.5816	0.4855-0.6776	77/59	0.0962
CL2-3LPCF	0.5747	0.4786-0.6709	77/59	0.1277
HDA-3 LPCF	0.5464	0.4500-0.6429	77/59	0.3453
HDD-3LPCF	0.6086	0.5128-0.7045	77/59	0.0263
Combined	0.5760	0.4998-0.6522	80/59	0.0508

MW: Mann-Whitney; CI: confidence interval; N1: valid number Active Treatment; N2: valid number Placebo; GO3LPCF: Glasgow Outcome Scale Extended (GOS-E); ER3LPCF: Early Rehabilitation Barthel Index; MS3LPCF: Mini-Mental State Examination; PSC3LPCF: Processing Speed Index (PSI); Digit Symbol Coding; PSSC3LPCF: Processing Speed (PSI) Symbol Search; CWWD3LPCF: Stroop (VST) Word/Dots Interference; CWCD3LPCF: Stroop (VST) Color-Word/Dots Interference; DGF3LPCF: Digit Span Digit Forward Test; DGB3LPCF: Digit Span Digit Backward Test; CL1-3LPCF: Color Trails Test 1; CL2-3LPCF: Color Trails Test 2; HDA-3LPCF: HADS: Anxiety Sumscore; HDD-3LPCF: HADS: Depression Sumscore; Visit No. 3 = Day 30

Multivariate Outcome Ensemble at Day 30 - Per-Protocol Sensitivity Analysis (PP)

Day 30 (PP)	MW	95% CI	N1/N2	P
GO3LPCF	0.6041	0.5087-0.6994	74/55	0.0324
ER3LPCF	0.5254	0.4681-0.5828	74/55	0.3847
MS3LPCF	0.5576	0.4602-0.6551	74/55	0.2466
PSC3LPCF	0.5743	0.4724-0.6763	74/55	0.1531
PSSC3LPCF	0.5619	0.4607-0.6631	74/55	0.2306
CWWD3LPCF	0.6399	0.5422-0.7377	74/55	0.0050
CWCD3LPCF	0.5561	0.4568-0.6555	74/55	0.2682
DGF3LPCF	0.6382	0.5343-0.7420	71/55	0.0091
DGB3LPCF	0.6460	0.5426-0.7494	71/55	0.0057
CL1-3LPCF	0.6104	0.5108-0.7099	71/55	0.0298
CL2-3LPCF	0.5965	0.4970-0.6961	71/55	0.0574
HDA-3 LPCF	0.5460	0.4458-0.6462	71/55	0.3685
HDD-3LPCF	0.6151	0.5161-0.7142	71/55	0.0227
Combined	0.5901	0.5121-0.6681	74/55	0.0236

MW: Mann-Whitney; CI: confidence interval; N1: valid number Active Treatment; N2: valid number Placebo; GO3LPCF: Glasgow Outcome Scale Extended (GOS-E); ER3LPCF: Early Rehabilitation Barthel Index; MS3LPCF: Mini-Mental State Examination; PSC3LPCF: Processing Speed Index (PSI); Digit Symbol Coding; PSSC3LPCF: Processing Speed (PSI) Symbol Search; CWWD3LPCF: Stroop (VST) Word/Dots Interference; CWCD3LPCF: Stroop (VST) Color-Word/Dots Interference; DGF3LPCF: Digit Span Digit Forward Test; DGB3LPCF: Digit Span Digit Backward Test; CL1-3LPCF: Color Trails Test 1; CL2-3LPCF: Color Trails Test 2; HDA-3LPCF: HADS: Anxiety Sumscore; HDD-3LPCF: HADS: Depression Sumscore; Visit No. 3 = Day 30

Adverse Events

Serious adverse events

Serious adverse event	Number of patients	Causality	Outcome
Bronchopneumonia	3	Unlikely	Fatal
Cardiac arrest	1	Not related	Recovered
Coma	4	Unlikely	Fatal
Pulmonary embolism	1	Unlikely	Fatal
Sepsis	2	Unlikely	Not recovered/Fatal
Knee fistula infection	1	Not related	Recovered