Clinical trial results:
Antibodies against Nogo-A to enhance plasticity, regeneration and functional recovery after acute spinal cord injury

Summary

EudraCT number	2016-001227-31
Trial protocol	DE CZ
Global end of trial date	31 January 2023

Results information

Result version number	v1 (current)
This version publication date	26 March 2025
First version publication date	26 March 2025

Trial information

Trial identification

Sponsor protocol code	NISCI

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03935321
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Zurich (UZH) University Hospital Balgrist
Sponsor organisation address	Forchstrasse 340, Zürich, Switzerland, 8008
Public contact	Spinal Cord Injury Center, Prof. Dr. Armin Curt Forchstrasse 3, CH-Zürich, +41 44 3863901, armin.curt@balgrist.ch
Scientific contact	Spinal Cord Injury Center, Prof. Dr. Armin Curt Forchstrasse 340, CH-Zürich, +41 44 3863901, armin.curt@balgrist.ch
Sponsor organisation name	University Hospital Heidelberg
Sponsor organisation address	Im Neuenheimer Fled 672, Heidelberg, Germany, 69120
Public contact	Sponsors legel representative in the EU, Prof. Dr. Norbert Weidner, +49 6221 5626321, norbert.weidner@med.uni-heidelberg.de
Scientific contact	Sponsors legel representative in the EU, Prof. Dr. Norbert Weidner, +49 6221 5626321, norbert.weidner@med.uni-heidelberg.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2023
Global end of trial reached?	Yes
Global end of trial date	31 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy of acute treatment (initiation of drug treatment within 4 - 28 days post-injury) with NG-101 by repeated intrathecal (i.t.) bolus injections on day 168.

Protection of trial subjects:

Extensive screening examination was undertaken.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	Germany: 90
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Switzerland: 33
Worldwide total number of subjects	129
EEA total number of subjects	96

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	110

From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study population consisted of tetraplegic patients ranging from 18 to 70 years of age, with an acute cervical SCI classified as AIS A-D at screening. The study was conducted in Europe and Switzerland in conjunction with the European multinational spinal cord injury trial network (EMSCI) network (www.emsci.org).

Pre-assignment

Screening details:

During the screeing period, the patient was assessed for study eligibility. The following assessment were conducted:
inclusion/exclusion criteria, Medical history, vital signs, height/weight, pregnancy test (for females), concomitant medication, ISNCSCI protocol, assessments of pain, bladder, neurophysiology, MRI, blood samples

Period 1

Period 1 title	All patients (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

All patients and study site staff (excluding staff receiving IMP shipments and preparing the injections) remained blinded to the treatment assignment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intrathecal use

Dosage and administration details:

6 doses of 3 mL Placebo intrathecal bolus injection

Arm title	NG-101

Arm description: -

Arm type	Experimental
Investigational medicinal product name	NG-101
Investigational medicinal product code	
Other name	ATI355, anti-Nogo-A antibody
Pharmaceutical forms	Injection
Routes of administration	Intrathecal use

Dosage and administration details:

repeated intrathecal bolus injections: 6 injections of 45 mg [in 3 mL] each

Number of subjects in period 1	Placebo	NG-101
Started	50	79
Completed	48	78
Not completed	2	1
never received treatment	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	NG-101
Reporting group description: -	

Reporting group values	Placebo	NG-101	Total
Number of subjects	50	79	129
Age categorical Units: Subjects			
Adults (18-64 years)	41	67	108
From 65-84 years	9	12	21
Age continuous			
Mean age was calculated from truncated date of birth (performed for data protection).			
Units: years arithmetic mean full range (min-max)	 46.83 19 to 70	 46.60 18 to 70	 -
Gender categorical Units: Subjects			
Female	9	11	20
Male	41	68	109

Subject analysis sets	
Subject analysis set title	Full analysis set, placebo arm
Subject analysis set type	Full analysis
Subject analysis set description: The full analysis set (FAS) comprises all patients, with a valid informed consent, who were randomized into the placebo arm and received the placebo at least once.	
Subject analysis set title	Full analysis set, NG-101 arm
Subject analysis set type	Full analysis
Subject analysis set description: All patients randomised to the treatment arm, receiving study treatment at least once	

Reporting group values	Full analysis set, placebo arm	Full analysis set, NG-101 arm	
Number of subjects	48	78	
Age categorical Units: Subjects			
Adults (18-64 years)	40	67	
From 65-84 years	8	11	
Age continuous			
Mean age was calculated from truncated date of birth (performed for data protection).			
Units: years arithmetic mean full range (min-max)	 46.25 19 to 70	 46,34 18 to 70	

Gender categorical Units: Subjects			
Female	19		
Male	107		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	NG-101
Reporting group description: -	
Subject analysis set title	Full analysis set, placebo arm
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set (FAS) comprises all patients, with a valid informed consent, who were randomized into the placebo arm and received the placebo at least once.	
Subject analysis set title	Full analysis set, NG-101 arm
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients randomised to the treatment arm, receiving study treatment at least once	

Primary: Mean bilateral upper extremity motor scores

End point title	Mean bilateral upper extremity motor scores
End point description:	
End point type	Primary
End point timeframe:	
Day 168	

End point values	Full analysis set, placebo arm	Full analysis set, NG-101 arm		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	68		
Units: Score value				
arithmetic mean (standard deviation)	29.98 (± 11.87)	29.69 (± 14.62)		

Statistical analyses

Statistical analysis title	Primary endpoint
Statistical analysis description:	
The UEMS change 168 days after randomization, as the primary response, was estimated using a linear mixed model with 1 month, 12 weeks and 24 weeks measurements as response. All analyses were performed on the full analysis set using all randomized patients.	
Comparison groups	Full analysis set, NG-101 arm v Full analysis set, placebo arm

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.868
Method	Linear mixed model
Parameter estimate	Mean difference (final values)

Secondary: Mean lower extremity motor scores day 168

End point title	Mean lower extremity motor scores day 168

End point description:

End point type	Secondary

End point timeframe:

Day 168

End point values	Full analysis set, placebo arm	Full analysis set, NG-101 arm		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	68		
Units: Score value				
arithmetic mean (standard deviation)	24.82 (± 19.568)	25.04 (± 21.580)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Light touch scores bilateral mean values

End point title	Mean Light touch scores bilateral mean values

End point description:

End point type	Secondary

End point timeframe:

Baseline to day 168

End point values	Full analysis set, placebo arm	Full analysis set, NG-101 arm		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: Score readings				
arithmetic mean (standard deviation)				
Baseline	60.91 (± 24.407)	52.62 (± 30.521)		
Day 168	71.84 (± 27.192)	64.24 (± 29.568)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pin Prick score bilateral

End point title	Pin Prick score bilateral

End point description:

End point type	Secondary

End point timeframe:

From Baseline to day 168

End point values	Full analysis set, placebo arm	Full analysis set, NG-101 arm		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47[1]	78[2]		
Units: Score values				
arithmetic mean (standard deviation)				
Baseline	34.40 (± 24.407)	34.42 (± 27.985)		
Day 168	47.73 (± 30.434)	46.94 (± 31.162)		

Notes:

[1] - Day 168: 44 patients analysed

[2] - Analysed at time point day 168: 68 patients

Statistical analyses

No statistical analyses for this end point

Secondary: SCIM-III (FAS), aspect Self Care, mean values

End point title	SCIM-III (FAS), aspect Self Care, mean values

End point description:

There was no significant treatment effect of NG-101 against Placebo at day 168 in the self care score: The effect estimate was 1.121 (standard error 1.141, 95% CI [-1.13,3.37].
However, in an additional analysis, the numerical superiority observed in this analysis translated into functional recovery according to the Spinal Cord Independence Measure (SCIM self-care

change +1.58, 95% CI: [0.13, 3.03], p = 0.033).

End point type	Secondary

End point timeframe:

From Baseline to day 168

End point values	Full analysis set, placebo arm	Full analysis set, NG-101 arm		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[3]	78[4]		
Units: Score values				
arithmetic mean (standard deviation)				
Baseline	0.79 (± 1.556)	0.67 (± 1.576)		
Day 168	8.00 (± 6.310)	8.55 (± 7.415)		

Notes:

[3] - Analysed at time point day 168 45 patients

[4] - Analysed at day 168: 69 patients.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from first application to day 168 after application	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	NG-101
Reporting group description: -	

Serious adverse events	Placebo	NG-101	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 48 (12.50%)	11 / 78 (14.10%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 48 (0.00%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Low cardiac output syndrome			

subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasticity			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Acute abdomen			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal rupture			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 48 (2.08%)	3 / 78 (3.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax spontaneous			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary infarction			
subjects affected / exposed	0 / 48 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Cholangitis sclerosing			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 48 (2.08%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	NG-101	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 48 (100.00%)	78 / 78 (100.00%)	
Vascular disorders			

All AEs in the SOC Vascular disorders			
subjects affected / exposed	6 / 48 (12.50%)	14 / 78 (17.95%)	
occurrences (all)	6	17	
General disorders and administration site conditions			
All AEs in the SOC general disorders and administration site conditions			
subjects affected / exposed	15 / 48 (31.25%)	15 / 78 (19.23%)	
occurrences (all)	22	21	
Respiratory, thoracic and mediastinal disorders			
All AEs in the SOC respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	10 / 48 (20.83%)	14 / 78 (17.95%)	
occurrences (all)	11	18	
Psychiatric disorders			
All AEs in the SOC psychiatric disorders			
subjects affected / exposed	11 / 48 (22.92%)	14 / 78 (17.95%)	
occurrences (all)	13	19	
Investigations			
All AEs in the SOC Investigations			
subjects affected / exposed	11 / 48 (22.92%)	9 / 78 (11.54%)	
occurrences (all)	19	10	
Injury, poisoning and procedural complications			
All AEs in the SOC injury, poisoning and procedural complications			
subjects affected / exposed	19 / 48 (39.58%)	21 / 78 (26.92%)	
occurrences (all)	29	31	
Cardiac disorders			
All AEs in the SOC Cardiac Disorders			
subjects affected / exposed	4 / 48 (8.33%)	8 / 78 (10.26%)	
occurrences (all)	5	11	
Nervous system disorders			
All AEs in the SOC nervous system disorders			
subjects affected / exposed	32 / 48 (66.67%)	41 / 78 (52.56%)	
occurrences (all)	73	82	
Gastrointestinal disorders			
All AEs in the SOC gastrointestinal disorders			

subjects affected / exposed	11 / 48 (22.92%)	14 / 78 (17.95%)	
occurrences (all)	19	40	
Skin and subcutaneous tissue disorders			
All AEs in the SOC Skin and subcutaneous tissue disorders			
subjects affected / exposed	14 / 48 (29.17%)	36 / 78 (46.15%)	
occurrences (all)	20	69	
Renal and urinary disorders			
All AEs in the SOC renal and urinary disorders			
subjects affected / exposed	12 / 48 (25.00%)	16 / 78 (20.51%)	
occurrences (all)	12	19	
Musculoskeletal and connective tissue disorders			
All AEs in the SOC Musculosceletal and connective tissue disorders			
subjects affected / exposed	23 / 48 (47.92%)	36 / 78 (46.15%)	
occurrences (all)	43	72	
Infections and infestations			
All AEs in the SOC Infections and Infestations	Additional description: A total of 214 non-serious events in this SOC was documented under the preferred terms 'urinary tract infection' or 'cystitis' (90 in the placebo group and 124 in the NG-101 group)		
subjects affected / exposed	44 / 48 (91.67%)	65 / 78 (83.33%)	
occurrences (all)	126	182	
Metabolism and nutrition disorders			
All AEs in the SOC Metabolism and nutritional disorders			
subjects affected / exposed	10 / 48 (20.83%)	13 / 78 (16.67%)	
occurrences (all)	12	22	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 November 2020	No amendments were made in the Czech Republic. In Germany and Switzerland the treatment allocation was changed from 1:1 to an aim of 1:2 (placebo: NG-101)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/39706632