



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 legal representative in the EU, Prof. Dr. Norbert Weidner, +49 6221 5626321, norbert.weidner@med.uni-heidelberg.de |
| Scientific contact | Sponsors legal 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 screening period, the patient was assessed for study eligibility. The following assessments 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 | 46.83 | 46.60 | |
| full range (min-max) | 19 to 70 | 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 | 46.25 | 46,34 | |
| full range (min-max) | 19 to 70 | 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 (\pm 24.407) | 52.62 (\pm 30.521) | | |
| Day 168 | 71.84 (\pm 27.192) | 64.24 (\pm 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 (\pm 24.407) | 34.42 (\pm 27.985) | | |
| Day 168 | 47.73 (\pm 30.434) | 46.94 (\pm 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 occurrences (all) | 6 / 48 (12.50%) 6 | 14 / 78 (17.95%) 17 | |
| General disorders and administration site conditions All AEs in the SOC general disorders and administration site conditions subjects affected / exposed occurrences (all) | 15 / 48 (31.25%) 22 | 15 / 78 (19.23%) 21 | |
| Respiratory, thoracic and mediastinal disorders All AEs in the SOC respiratory, thoracic and mediastinal disorders subjects affected / exposed occurrences (all) | 10 / 48 (20.83%) 11 | 14 / 78 (17.95%) 18 | |
| Psychiatric disorders All AEs in the SOC psychiatric disorders subjects affected / exposed occurrences (all) | 11 / 48 (22.92%) 13 | 14 / 78 (17.95%) 19 | |
| Investigations All AEs in the SOC Investigations subjects affected / exposed occurrences (all) | 11 / 48 (22.92%) 19 | 9 / 78 (11.54%) 10 | |
| Injury, poisoning and procedural complications All AEs in the SOC injury, poisoning and procedural complications subjects affected / exposed occurrences (all) | 19 / 48 (39.58%) 29 | 21 / 78 (26.92%) 31 | |
| Cardiac disorders All AEs in the SOC Cardiac Disorders subjects affected / exposed occurrences (all) | 4 / 48 (8.33%) 5 | 8 / 78 (10.26%) 11 | |
| Nervous system disorders All AEs in the SOC nervous system disorders subjects affected / exposed occurrences (all) | 32 / 48 (66.67%) 73 | 41 / 78 (52.56%) 82 | |
| Gastrointestinal disorders All AEs in the SOC gastrointestinal disorders | | | |

| | | | |
|---|---|------------------------|--|
| subjects affected / exposed occurrences (all) | 11 / 48 (22.92%) 19 | 14 / 78 (17.95%) 40 | |
| Skin and subcutaneous tissue disorders All AEs in the SOC Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all) | 14 / 48 (29.17%) 20 | 36 / 78 (46.15%) 69 | |
| Renal and urinary disorders All AEs in the SOC renal and urinary disorders subjects affected / exposed occurrences (all) | 12 / 48 (25.00%) 12 | 16 / 78 (20.51%) 19 | |
| Musculoskeletal and connective tissue disorders All AEs in the SOC Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all) | 23 / 48 (47.92%) 43 | 36 / 78 (46.15%) 72 | |
| Infections and infestations All AEs in the SOC Infections and Infestations subjects affected / exposed occurrences (all) | <div>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)</div> <div>44 / 48 (91.67%) 126</div> <div>65 / 78 (83.33%) 182</div> | | |
| Metabolism and nutrition disorders All AEs in the SOC Metabolism and nutritional disorders subjects affected / exposed occurrences (all) | 10 / 48 (20.83%) 12 | 13 / 78 (16.67%) 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>