

Health Technology Briefing

May 2024

Neuro-Cells for treating traumatic spinal cord injury

Company/Developer

Neuroplast

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 27621

NICE ID: Not Available

UKPS ID: Not Available

Licensing and Market Availability Plans

Phase II/III clinical trial ongoing.

Summary

Neuro-Cells are in development for the treatment of patients with traumatic spinal cord injury (TSCI). The spinal cord can be injured through accidents or by internal causes such as tumours or bleeding within the spine putting pressure on the spinal cord. The resulting damage to the nerves that run through the cord and that branch out from it can stop the flow of nerve impulses between the brain and the body. This leads to loss of feeling, paralysis and even death, depending on the severity of the injury and where it is located. TSCI occurs when an external physical impact, for example, a motor vehicle injury, fall, sports-related injury or violence, acutely damages the spinal cord. TSCI can severely impact on physical, cognitive, and psychological functioning. TSCI has high morbidity and mortality, and currently there are no curative treatments available for TSCI.

Neuro-Cells are a stem cell treatment that is derived from the bone marrow of the patient and does not include any genetic engineering. It depends on the self-healing capacity of non-manipulated stem cells (special body cells), that the body itself is unable to use for neurodegenerative conditions (a condition that gradually damage and destroy parts of the nervous system) due to the blood brain barrier. The use of Neuro-Cells in the treatment of patients with traumatic spinal cord injury is expected to reduce cell death in the injured spinal cord, reduce scar tissue formation in the damaged spinal cord and create a cell regenerative environment in the injured spinal cord. If licenced, Neuro-Cells may provide a new treatment option for patients with traumatic spinal cord injury.

Proposed Indication

Adults with complete or incomplete traumatic spinal cord injury (TSCI).¹

Technology

Description

Stem cell therapy (Neuro-Cells®) is an autologous, human bone marrow-derived haematopoietic and mesenchymal stem cells that are depleted of erythrocytes, monocytes and lymphocytes.² The fresh stem cells are thought to modulate secondary inflammation following a traumatic spinal cord injury (TSCI). They reduce apoptosis (cell death) in the injured spinal cord, reduce scar tissue formation in the damaged spinal cord and create a cell regenerative environment in the injured spinal cord.^{1,2} The exact mechanism of action is not clear but when the bone-marrow derived stem cells are injected, intrathecally, back into the patient's spinal canal, they are expected to help repair the damaged nerve cells, improving the symptoms of patients with spinal cord injury.²

Neuro-Cells is currently in phase II/III clinical development for the treatment of TSCI. In the phase II/III clinical trial (NCT03935724), harvesting of the bone marrow derived stem cells and administration of Neuro-Cells was intrathecally (lumbar puncture), delivered at days 1- 2, between 6-10 weeks after the TSCI incident.¹

Key Innovation

Treatment with Neuro-Cells aims to use the patient's own stem cells to reduce irreversible damage to the central nervous system from secondary inflammation following trauma.³ Specifically, Neuro-Cells aim to prevent further loss of function, mobility and independence.³ Current therapies for TSCI are centred around pain management in the acute management stage and then physical, cognitive and psychological rehabilitation.⁴ There is a lack of curative pharmacological treatments for TSCI.⁵

Neuro-Cells for spinal cord injury was classified as an advanced therapy medicinal product (ATMP) by the European Medicines Agency (EMA) in July 2012.⁶ If licenced, Neuro-Cells may provide a new treatment option for TSCI.

Regulatory & Development Status

Neuro-Cells does not currently have Marketing Authorisation in the EU or UK for any indication.

Neuro-Cells was awarded an Orphan Drug designation by the European Medicines Agency (EMA) in April 2019 for the treatment of TSCI.²

Patient Group

Disease Area and Clinical Need

A spinal cord injury (SCI) is defined as damage to the spinal cord that temporarily or permanently causes changes in its function.⁷ SCI is divided into traumatic and non-traumatic aetiologies.⁷ Traumatic SCI (TSCI) occurs when an external physical impact, for example, a motor vehicle injury, fall, sports-related injury or violence, acutely damages the spinal cord.⁷ In TSCI, the primary insult damages cells and initiates a complex secondary injury cascade, which cyclically produces the death of neurons and glial cells, as well as ischaemia and inflammation. This cascade is followed by changes in the organisation and structural

architecture of the spinal cord, including the formation of a glial scar and cystic cavities. The glial scar and cystic cavities, in combination with poor endogenous remyelination and axonal regrowth, mean that the spinal cord has a poor intrinsic recovery potential, such that SCI causes permanent neurological deficits.⁷ TSCI is a devastating condition with high morbidity and mortality, it can have life-long impacts on physical, cognitive and psychological functioning.^{4,5}

The annual incidence of traumatic spinal cord injury is estimated to range from 12.1 to 57.8 per million worldwide.⁸ In the UK, every 8 hours, someone is paralysed by a spinal cord injury.⁹ In England (2022-23) there were 1,541 finished consultant episodes (FCEs) and 834 admissions for injury of nerves and spinal cord at the neck level (ICD-10 code S14), which resulted in 16 day cases and 41,744 FCE bed days.¹⁰

Recommended Treatment Options

There are currently no curative treatment options for TSCI. Rehabilitation following TSCI has been recommended by the National Institute for Health and Care Excellence (NICE).⁴ Also, NICE recommend the following medicines for pain management in pre-hospital and hospital settings:¹¹

- Intravenous morphine as the first-line analgesic, and where this is not possible
- Atomised delivery of diamorphine or ketamine, with ketamine considered as a second-line analgesic.

Clinical Trial Information

Trial	NCT03935724 ; A Multi-center, Double-blind, Randomized, Placebo-controlled, Delayed Start Phase II/III Study to Assess the Efficacy and Safety of Neuro-Cells in (Sub)Acute Spinal Cord Injury Patients. Phase II/III – Active, not recruiting Location(s) : Two EU countries Primary Completion Date : February 2024
Trial Design	Randomised, parallel assignment, quadruple masking, placebo-controlled
Population	N=16 (actual); patients aged between 18 and 65 years with complete (AIS grade A) or incomplete (AIS grade B or C) traumatic spinal cord injury (TSCI) assessed with the International Standards for Neurologic Classification of Spinal Cord Injury (ISNCSCI) at the time of randomisation.
Intervention(s)	Treatment with Neuro-Cells at days 1-2, administered between 6-10 weeks after TSCI incident
Comparator(s)	Treatment with placebo at days 1-2, administered between 6-10 weeks after TSCI incident, followed by treatment with Neuro-Cells at days 181-182 administered between 32-34 weeks after TSCI incident
Outcome(s)	Primary outcome measures: <ul style="list-style-type: none"> - Physical changes after intrathecal intervention with Neuro-Cells [Time frame: 9 months] - Increase of motor scores after intrathecal intervention with Neuro-Cells [Time frame: 6 months] See trial record for a full list of other outcomes

Results (efficacy)	-
Results (safety)	-

Trial	<p>NCT04205019; A 3 Months Open Phase I Study to Assess the Safety of the Intrathecal Application of Neuro-Cells in End Stage (Chronic) Traumatic Spinal Cord Injury Patients. Phase I – Completed Location(s): One EU country (Spain) Study Completion Date: March 2023</p>
Trial Design	Single group assignment and open-label
Population	N=10 (actual); patients aged between 18 and 40 years with complete (AIS grade A) or incomplete (AIS grade B or C) TSCI assessed with the ISNCSCI at the time of randomisation.
Intervention(s)	Treatment with Neuro-Cells administered to patient once at study onset and followed up for safety.
Comparator(s)	-
Outcome(s)	<p>Primary outcome measures:</p> <ul style="list-style-type: none"> - Characterise and confirm the safety of intrathecal administration of Neuro-Cells by ISNCSCI checklist [Time frame: 3 months] - Characterise and confirm the safety of intrathecal administration of Neuro-Cells assessed by blood [Time frame: 3 months] - Characterise and confirm the safety of intrathecal administration of Neuro-Cells assessed by urine [Time frame: 3 months] - Characterise and confirm the safety of intrathecal administration of Neuro-Cells by adverse events [Time frame: 3 months] <p>See trial record for a full list of other outcomes</p>
Results (efficacy)	-
Results (safety)	No product-related adverse events reported. ¹²

Estimated Cost

The cost for Neuro-Cells is not yet known.

Relevant Guidance

NICE Guidance

- NICE guideline. Rehabilitation after traumatic injury (NG211). January 2022
- NICE guideline. Spinal injury: assessment and initial management (NG41). February 2016
- NICE quality standard. Trauma (QS166). March 2018

NHS England (Policy/Commissioning) Guidance

- NHS England. 2019 NHS Service Specification: Spinal Cord Injury Services (Adults and children). 170119S
- NHS England. 2013 NHS Service Specification: Complex Spinal Surgery Services (All ages). URN 1738
- NHS England. 2013 NHS Standard Contract for Spinal Cord Injuries (All Ages). D13/S/a
- NHS England. 2013 Clinical Commissioning Policy: Phrenic Nerve Pacing Following Spinal Cord Injury. NHSCB/D13/P/a

Other Guidance

- Fehlings MG, Tetreault LA, Hachem L, Evaniew N, Ganau M, McKenna SL *et al.* An Update of a Clinical Practice Guideline for the Management of Patients with Acute Spinal Cord Injury: Recommendations on the Role and Timing of Decompressive Surgery. 2024.¹³
- Fehlings MG, Tetreault LA, Aarabi B, Anderson P, Arnold PM, Brodke DS *et al.* A Clinical Practice Guideline for the Management of Patients with Acute Spinal Cord Injury: Recommendations on the Type and Timing of Rehabilitation. 2017.¹⁴
- Fehlings MG, Martin AR, Tetreault LA, Aarabi B, Anderson P, Arnold PM *et al.* A Clinical Practice Guideline for the Management of Patients with Acute Spinal Cord Injury: Recommendations on the Role of Baseline Magnetic Resonance Imaging in Clinical Decision Making and Outcome Prediction. 2017.¹⁵
- Fehlings MG, Wilson JR, Tetreault LA, Aarabi B, Anderson P, Arnold PM *et al.* A Clinical Practice Guideline for the Management of Patients with Acute Spinal Cord Injury: Recommendations on the Use of Methylprednisolone Sodium Succinate. 2017.¹⁶
- Fehlings MG, Tetreault LA, Aarabi B, Anderson P, Arnold PM, Brodke DS *et al.* A Clinical Practice Guideline for the Management of Patients with Acute Spinal Cord Injury: Recommendations on the Type and Timing of Anticoagulant Thromboprophylaxis. 2017.¹⁷

Additional Information

Neuroplast did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

- 1 ClinicalTrials.gov. *Stem Cells in Spinal Cord Injury (SCI2)*. Trial ID: NCT03935724. 2019. Status: Active, not recruiting. Available from: <https://classic.clinicaltrials.gov/ct2/show/NCT03935724> [Accessed March 27, 2024].
- 2 European Medicines Agency (EMA). *EU/3/19/2153 - orphan designation for treatment of spinal cord injury*. 2019. Available from: <https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu-3-19-2153> [Accessed April 05, 2024].
- 3 Newswire P. *Stem cell biotech Neuroplast enrolls first patient in Phase II clinical trial of transformative Neuro-Cells® treatment for Traumatic Spinal Cord Injury*. 2022. Available from: <https://www.prnewswire.com/news-releases/stem-cell-biotech-neuroplast-enrolls-first-patient-in-phase-ii-clinical-trial-of-transformative-neuro-cells-treatment-for-traumatic-spinal-cord-injury-301512509.html> [Accessed April 05, 2024].
- 4 National Institute for Health and Care Excellence (NICE). *Rehabilitation after traumatic injury - NICE guideline [NG211]*. 2022. Available from: <https://www.nice.org.uk/guidance/ng211/resources> [Accessed April 04, 2024].
- 5 Jazayeri SB, Maroufi SF, Mohammadi E, Dabbagh Ohadi MA, Hagen EM, Chalangari M, et al. Incidence of traumatic spinal cord injury worldwide: A systematic review, data integration, and update. *World Neurosurg X*. 2023;18:100171. Available from: <https://doi.org/10.1016/j.wnsx.2023.100171>.
- 6 European Medicines Agency (EMA). *Scientific recommendation on classification of advanced therapy medicinal products: Article 17 – Regulation (EC) No 1394/2007*. 2012. Available from: https://www.ema.europa.eu/system/files/documents/report/wc500133062_en.pdf [Accessed March 27, 2024].
- 7 Ahuja CS, Wilson JR, Nori S, Kotter MRN, Druschel C, Curt A, Fehlings MG. Traumatic spinal cord injury. *Nature Reviews Disease Primers*. 2017;3(1):17018. Available from: <https://doi.org/10.1038/nrdp.2017.18>.
- 8 Melin J, Axwaller E, Åhrén G, Sunnerhagen KS, Lundgren-Nilsson Å, Wangdell J. Research priorities to enhance life for people with spinal cord injury: a Swedish priority setting partnership. *Spinal Cord*. 2023;61(10):570-7. Available from: <https://doi.org/10.1038/s41393-023-00913-2>.
- 9 National Health Service (NHS) England. *Spinal Injuries Association*. 2024. Available from: <https://www.nhs.uk/services/service-directory/spinal-injuries-association/N10957626> [Accessed March 28, 2024].
- 10 National Health Service (NHS) 75 Digital. *Hospital Admitted Patient Care Activity, 2022-23*. 2023. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity> [Accessed 19 March 2024].
- 11 National Institute for Health and Care Excellence (NICE). *Spinal injury: assessment and initial management: NICE guideline [NG41]*. 2016. Available from: <https://www.nice.org.uk/guidance/ng41/chapter/Recommendations#early-management-in-the-emergency-department-after-traumatic-spinal-cord-injury> [Accessed March 28, 2024].
- 12 BioPharma-Reporter.com. *Neuroplast reports successful Phase 1 trial for spinal cord injury stem cell treatment*. 2021. Available from: <https://www.biopharma-reporter.com/Article/2021/11/09/Neuroplast-reports-successful-Phase-1-trial-for-spinal-cord-injury-stem-cell-treatment> [Accessed April 05, 2024].
- 13 Fehlings MG, Tetreault LA, Hachem L, Evaniew N, Ganau M, McKenna SL, et al. An Update of a Clinical Practice Guideline for the Management of Patients With Acute Spinal Cord Injury:

- Recommendations on the Role and Timing of Decompressive Surgery. *Global Spine J.* 2024;14(3_suppl):174s-86s. Available from: <https://doi.org/10.1177/21925682231181883>.
- 14 Fehlings MG, Tetreault LA, Aarabi B, Anderson P, Arnold PM, Brodke DS, et al. A Clinical Practice Guideline for the Management of Patients With Acute Spinal Cord Injury: Recommendations on the Type and Timing of Rehabilitation. *Global Spine J.* 2017;7(3 Suppl):231s-8s. Available from: <https://doi.org/10.1177/2192568217701910>.
- 15 Fehlings MG, Martin AR, Tetreault LA, Aarabi B, Anderson P, Arnold PM, et al. A Clinical Practice Guideline for the Management of Patients With Acute Spinal Cord Injury: Recommendations on the Role of Baseline Magnetic Resonance Imaging in Clinical Decision Making and Outcome Prediction. *Global Spine J.* 2017;7(3 Suppl):221s-30s. Available from: <https://doi.org/10.1177/2192568217703089>.
- 16 Fehlings MG, Wilson JR, Tetreault LA, Aarabi B, Anderson P, Arnold PM, et al. A Clinical Practice Guideline for the Management of Patients With Acute Spinal Cord Injury: Recommendations on the Use of Methylprednisolone Sodium Succinate. *Global Spine J.* 2017;7(3 Suppl):203s-11s. Available from: <https://doi.org/10.1177/2192568217703085>.
- 17 Fehlings MG, Tetreault LA, Aarabi B, Anderson P, Arnold PM, Brodke DS, et al. A Clinical Practice Guideline for the Management of Patients With Acute Spinal Cord Injury: Recommendations on the Type and Timing of Anticoagulant Thromboprophylaxis. *Global Spine J.* 2017;7(3 Suppl):212s-20s. Available from: <https://doi.org/10.1177/2192568217702107>.

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