Clinical trial results:
NDisc Study: A Prospective Randomized Multicentre Phase I / II Clinical Trial to Evaluate Safety and Efficacy of NOVOCART® Disc plus Autologous Disc Chondrocyte Transplantation (ADCT) in the Treatment of Nucleotomized and Degenerative Lumbar Discs to Avoid Secondary Disease

Summary

EudraCT number	2010-023830-22
Trial protocol	DE AT
Global end of trial date	14 June 2021
Results information	
Result version number	v1 (current)
This version publication date	15 October 2022
First version publication date	15 October 2022
Summary attachment (see zip file)	Synoptic Clinical Study Report AAG-G-H-1102 (NDisc CSR FINAL_24May2022.pdf) AAG-G-H-1102 Listings (NDisc_Final_Listings_20211214.pdf) AAG-G-H-1102 Tables (NDisc_Final_Tables_20211214.pdf)

Trial information

Trial identification	
Sponsor protocol code	AAG-G-H-1102
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01640457
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	TETEC AG
Sponsor organisation address	Aspenhaustr. 18, Reutlingen, Germany, 72770
Public contact	Simone Steinert, Study Manager, TETEC AG, 0049 071211626 203, simone.steinert@tetec-ag.de
Scientific contact	Dr. Christoph Gaissmaier, CMO, TETEC AG, 0049 071211626 201, christoph.gaissmaier@tetec-ag.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	31 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To characterize the safe use of the investigational medicinal product and the transplantation/implantation procedures.
• To characterize the cumulative functional and radiographic effects of NDplus over NDbasic and SC.
• To characterize the effect of NDbasic alone over SC.
• To characterize the effect of the investigational medicinal product on the adjacent de-generative discs.
• To define metabolic parameters that measure identity, purity, and potency of the extracted tissue, of the isolated cells, and of the in vitro expanded cells.
• To define metabolic parameters in subjects to control the status of tissue repair.
• To define metabolic parameters in patients to control the status of tissue repair
• To define the prognostic value of metabolic and radiological parameters in the context of disc degeneration, functional status, and quality of life

Protection of trial subjects:

NDisc plus application: The required biomaterial for the cell culture is extracted in the context of an elective sequestrectomy. The material is taken from the extracted disc and therefore a by-product of the elective sequestrectomy with no additional risk for the patient.
Nutrition solution for cultivation of human chondrocytes contains a small amount of homologous serum, which is manufactured by Transfusion Medicine Tuebingen. EU-GMP-guidelines are fully applied.
The injection needle for the implantation must be inserted into the remaining disc tissue under the image converter tube (X-ray unit). The administered radiation dose is about the same as that of 2x-ray-chest images. For NDplus and NDbasic patients female patients are required to take contraceptive measures until the end of the therapy phase. Pregnancy tests are performed prior to sequestrectomy and prior implantation.
Local anaesthesia prior to implantation were conducted.
Investigators are specially trained for the process of implantation.

Background therapy:

Standard of care treatment: Sequestrectomy

Evidence for comparator:

NOVOCART® Disc plus (NDplus) was developed to provide rehydration and biological integrity of degenerative lumbar discs to prevent secondary disease such as disc herniation and segmental instability. It was hypothesized that by transplanting disc derived chondrocytes into degenerative discs, where the cells will be held in situ re-differentiate and produce new cartilaginous tissue. Thus patients were expected to experience better outcomes as compared to control (standard care [SC] sequestrectomy).
NOVOCART® Disc basic (NDbasic) alone has no active cell component, its hydrophilic characteristics and specific ingredients for influencing cell metabolism and anti-inflammatory as well as anti-angiogenic, anti-osteogenic, and anti-neurotropic milieu conditioning has a potential for disc regeneration and effective pain treatment.

Actual start date of recruitment	07 October 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 46
Country: Number of subjects enrolled	Germany: 74
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	120
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

FPFV: 07-OCT-2012
LPFV: 16-MAR-2016
Austria: Innsbruck
Germany: Halle, Düsseldorf, Murnau, Berlin DRK, Karlsruhe, Münster, Kiel, Berlin Chrité, Idar-Oberstein, Göttingen

Pre-assignment

Screening details:

1. The patient has a disc herniation with back and/or leg pain (radicular pain)
2. The patient has an indication for sequestrectomy according to the guidelines of DGNC and DGOOC (Börm, Steiger, Papavero, Herdmann, Ohmann, & Schwedtfeger, 2005.
3. The patient is between 18-60 years of age.

Period 1

Period 1 title	Phase I/II (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Assessor blinded for MRI analysis

Arms

Are arms mutually exclusive?	Yes
Arm title	NDplus

Arm description:

Patients who receive NOVOCART Disc plus (acitve cells)

Arm type	Active comparator
Investigational medicinal product name	NOVOCART Disc plus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implantation suspension
Routes of administration	Implantation, Injection

Dosage and administration details:

In situ cross-linking modified albumin-hyaluronic acid gel with autologous disc cells (1 mio. intervertebral disc chondrocytes/ml). The volume of the injection depends on the capacity of the treated disc. It may vary between 0.5 and 2 ml.

Arm title	NDbasic

Arm description:

Patients who receive NOVOCART Basic (no active cells)

Arm type	Active comparator
Investigational medicinal product name	NOVOCART Disc basic
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implantation suspension
Routes of administration	Implantation, Injection

Dosage and administration details:

In situ cross-linking modified albumin-hyaluronic acid gel. The volume of the injection depends on the capacity of the treated disc. It may vary between 0.5 and 2 ml.

Arm title	Standard of Care (SC)

Arm description:	
Patients who received standard of care, sequestrectomy only.	
Arm type	Standard of care
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	NDplus	NDbasic	Standard of Care (SC)
Started	58	37	25
Completed	58	37	25

Baseline characteristics

Reporting groups

Reporting group title	Phase I/II

Reporting group description: -

Reporting group values	Phase I/II	Total	
Number of subjects	120	120	
Age categorical			
Patients aged 18 to 60 years			
Units: Subjects			
Adults aged 18 to 60 years	120	120	
Age continuous			
18 to 60 years			
Units: years			
arithmetic mean	41.7		
standard deviation	± 10.54	-	
Gender categorical			
Gender distribution was analysed only for the safety set.			
Units: Subjects			
Female	48	48	
Male	72	72	
Weight			
Weight at timepoint enrolment			
Units: kg			
arithmetic mean	78.9		
standard deviation	± 13.56	-	
Height			
Height at timepoint enrolment			
Units: cm			
arithmetic mean	177.0		
standard deviation	± 9.62	-	

Subject analysis sets

Subject analysis set title	Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who received surgery with sequestrectomy for tissue harvest.

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

All patients randomised who underwent surgery (sequestrectomy for SC patients; transplantation in case of NDplus or NDbasic patients) and with at least one primary efficacy assessment after surgery/implantation. This is equivalent to the ITT population.

Reporting group values	Safety set	Full analysis set	
Number of subjects	120	98	
Age categorical			
Patients aged 18 to 60 years			
Units: Subjects			
Adults aged 18 to 60 years	120	98	
Age continuous			
18 to 60 years			
Units: years			
arithmetic mean	41.7		
standard deviation	± 10.54	±	
Gender categorical			
Gender distribution was analysed only for the safety set.			
Units: Subjects			
Female	48		
Male	72		
Weight			
Weight at timepoint enrolment			
Units: kg			
arithmetic mean	78.9		
standard deviation	± 13.56	±	
Height			
Height at timepoint enrolment			
Units: cm			
arithmetic mean	177.0		
standard deviation	± 9.62	±	

End points

End points reporting groups

Reporting group title	NDplus
Reporting group description:	
Patients who receive NOVOCART Disc plus (acitve cells)	
Reporting group title	NDbasic
Reporting group description:	
Patients who receive NOVOCART Basic (no active cells)	
Reporting group title	Standard of Care (SC)
Reporting group description:	
Patients who received standard of care, sequestrectomy only.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received surgery with sequestrectomy for tissue harvest.	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients randomised who underwent surgery (sequestrectomy for SC patients; transplantation in case of NDplus or NDbasic patients) and with at least one primary efficacy assessment after surgery/implantation. This is equivalent to the ITT population.	

Primary: Safety

End point title	Safety[1]
End point description:	
To characerize the safe use of the IMP and the transplantation/implantation procedures. - Adverse events (AEs) by event category, intensity, seriousness, and relationship to the graft and/or procedure.	
End point type	Primary
End point timeframe:	
Until the end of study.	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Results are only available as numbers and percentage of occurrence, no statistical analysis was done.	

End point values	NDplus	NDbasic	Standard of Care (SC)	Safety set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	58	37	25	120
Units: Prevalence	53	31	22	120

Statistical analyses

No statistical analyses for this end point

Primary: Functional effects of NDplus over SC, 60 months FU

End point title	Functional effects of NDplus over SC, 60 months FU[2]

End point description:

ODI: Mean total score changes from baseline to 60 months.

End point type	Primary

End point timeframe:

60 months after treatment

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses were done between NDplus arm versus SC arm and NDbasic arm versus SC. Therefore this endpoint is available twice (NDplus vs. SC, NDbasic vs. SC).

End point values	NDplus	Standard of Care (SC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	21		
Units: Oswestry Dissability Index (ODI)				
median (standard deviation)				
Changes from baseline	-32.6 (± 21.69)	-34.6 (± 21.33)		

Statistical analyses

Statistical analysis title	ODI total score changes NDplus vs. SC 60 month FU

Statistical analysis description:

Non-confirmatory study without pre-specified decision-making rules or hypotheses. NDplus vs. SC

Comparison groups	Standard of Care (SC) v NDplus
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.24 [4]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	12.44

Notes:

[3] - Non-confirmatory study without pre-specified decision-making rules or hypotheses. p-values for LS means NDplus vs. SC.
[4] - NDplus vs. SC at 60 months follow-up

Primary: Functional effects of NDplus over SC, 12 months follow-up

End point title	Functional effects of NDplus over SC, 12 months follow-up[5]

End point description:

ODI total score changes from 12 month follow-up to baseline (treatment).

End point type	Primary

End point timeframe:

12 months after treatment

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses were done between NDplus arm versus SC arm and NDbasic arm versus SC. Therefore this endpoint is available twice (NDplus vs. SC, NDbasic vs. SC).

End point values	NDplus	Standard of Care (SC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	20		
Units: ODI total score changes from baseline				
arithmetic mean (standard deviation)	-33.7 (± 19.91)	-33.8 (± 24.63)		

Statistical analyses

Statistical analysis title	ODI total score changes NDplus vs. SC 12 months FU

Statistical analysis description:

ODI totgal score changes 12 months to baseline NDplus to SC

Comparison groups	NDplus v Standard of Care (SC)
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.3062
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	12.67

Notes:

[6] - Non-confirmatory study without pre-specified decision-making rules or hypotheses.

Primary: Functional effects of NDplus over SC, 24 months follow-up

End point title	Functional effects of NDplus over SC, 24 months follow-up[7]

End point description:

ODI total score changes from baseline to 12 months follow-up.

End point type	Primary

End point timeframe:

12 months follow-up after treatment.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses were done between NDplus arm versus SC arm and NDbasic arm versus SC. Therefore this endpoint is available twice (NDplus vs. SC, NDbasic vs. SC).

End point values	NDplus	Standard of Care (SC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	22		
Units: ODI total score changes from baseline				
arithmetic mean (standard deviation)	-32.4 (± 20.00)	-36.7 (± 22.46)		

Statistical analyses

Statistical analysis title	ODI total score changes NDplus 24 months FU
Statistical analysis description:	
Non-confirmatory study without pre-specified decision-making rules or hypotheses.	
Comparison groups	Standard of Care (SC) v NDplus
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0.0788
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.33
upper limit	16

Notes:

[8] - Non-confirmatory study without pre-specified decision-making rules or hypotheses.

Primary: Functional effects of NDbasic over SC, 24 months follow-up

End point title	Functional effects of NDbasic over SC, 24 months follow-up[9]
End point description:	
End point type	Primary
End point timeframe:	
24 months follow-up after treatment	

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses were done between NDplus arm versus SC arm and NDbasic arm versus SC. Therefore this endpoint is available twice (NDplus vs. SC, NDbasic vs. SC).

End point values	NDbasic	Standard of Care (SC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	22		
Units: ODI total score changes from baseline				
arithmetic mean (standard deviation)	-41.3 (± 19.22)	-36.7 (± 22.46)		

Statistical analyses

Statistical analysis title	ODI total score change NDbasic 24 months FU

Statistical analysis description:

Non-confirmatory study without pre-specified decision-making rules or hypotheses.

Comparison groups	Standard of Care (SC) v NDbasic
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.4161
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-5.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18
upper limit	8

Notes:

[10] - Non-confirmatory study without pre-specified decision-making rules or hypotheses.

Primary: Functional effects of NDbasic over SC, 12 months follow-up

End point title	Functional effects of NDbasic over SC, 12 months follow-up[11]

End point description:

End point type	Primary

End point timeframe:

12 months follow-up after treatment

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses were done between NDplus arm versus SC arm and NDbasic arm versus SC. Therefore this endpoint is available twice (NDplus vs. SC, NDbasic vs. SC).

End point values	NDbasic	Standard of Care (SC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	20		
Units: ODI total score changes to baseline				
arithmetic mean (standard deviation)	-39.6 (± 19.20)	-33.8 (± 24.63)		

Statistical analyses

Statistical analysis title	ODI total score changes NDbasic 12 months FU
Comparison groups	NDbasic v Standard of Care (SC)
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.1506
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20
upper limit	8

Notes:

[12] - Non-confirmatory study without pre-specified decision-making rules or hypotheses.

Primary: Functional effects of NDbasic over SC, 60 months FU

End point title	Functional effects of NDbasic over SC, 60 months FU[13]

End point description:

End point type	Primary

End point timeframe:

60 months follow-up after treatment

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analyses were done between NDplus arm versus SC arm and NDbasic arm versus SC. Therefore this endpoint is available twice (NDplus vs. SC, NDbasic vs. SC).

End point values	NDbasic	Standard of Care (SC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	21		
Units: ODI total score changes from baseline				
arithmetic mean (standard deviation)	-39.1 (± 20.54)	-34.6 (± 21.33)		

Statistical analyses

Statistical analysis title	ODI total score changes NDbasic over SC 60 months

Statistical analysis description:

ODI total score changes NBasic over SC at 60 months after treatment

Comparison groups	NDbasic v Standard of Care (SC)

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.9826
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18
upper limit	6.67

Notes:

[14] - Non-confirmatory study without pre-specified decision-making rules or hypotheses.

Secondary: MRI changes disc height NDplus, NDbasic, SC 60 months FU

End point title	MRI changes disc height NDplus, NDbasic, SC 60 months FU

End point description:

Caudal disc height (mm) (from volume) at timepoint 60 month after treatment.

End point type	Secondary

End point timeframe:

Timepoint 60 months

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	11	6	
Units: Disc height				
arithmetic mean (standard deviation)				
Changes in total score ODI	-0.5 (± 2.57)	2.1 (± 6.99)	0.1 (± 1.67)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRI changes disc volume NDplus, NDbasic, SC 60 months FU

End point title	MRI changes disc volume NDplus, NDbasic, SC 60 months FU

End point description:

Caudal disc volume (mm3), changes from baseline to 60 months follow-up.

End point type	Secondary

End point timeframe:

60 months follow-up

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	11	6	
Units: Caudal disc volume				
arithmetic mean (standard deviation)	-488.6 (± 1378.36)	128.3 (± 2212.52)	-479.0 (± 711.81)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRI changes signal intensity NDplus, NDbasic, SC 60 months FU

End point title	MRI changes signal intensity NDplus, NDbasic, SC 60 months FU

End point description:

Caudal disc T2 (ms) Relaxations time of MRI measured as signal intensity .

End point type	Secondary

End point timeframe:

60 month follow-up

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	13	6	
Units: Signal intensity (T2 relaxation time)				
arithmetic mean (standard deviation)	-6.5 (± 8.27)	-3.0 (± 11.82)	1.9 (± 13.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRI changes disc height NDplus, NDbasic, SC 12 months FU

End point title	MRI changes disc height NDplus, NDbasic, SC 12 months FU

End point description:

Caudial disc height (mm) (from volume) at timepoint 12 months after treatment.

End point type	Secondary

End point timeframe:

Timepoint 12 months follow-up

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	12	7	
Units: Disc height				
arithmetic mean (standard deviation)	0.00 (± 2.01)	0.4 (± 0.98)	0.2 (± 0.90)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRI changes disc height NDplus, NDbasic, SC 24 months FU

End point title	MRI changes disc height NDplus, NDbasic, SC 24 months FU
End point description:	
Caudal disc height (mm) (from volume) at timepoint 24 months after treatment.	
End point type	Secondary
End point timeframe:	
Timepoint 24 months follow-up	

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	12	7	
Units: Disc height				
arithmetic mean (standard deviation)	-0.2 (± 1.52)	0.6 (± 0.99)	1.0 (± 0.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRI changes disc volume NDplus, NDbasic, SC 12 months FU

End point title	MRI changes disc volume NDplus, NDbasic, SC 12 months FU
End point description:	
Caudal disc volume (mm3) at timepoint 12 months after treatment.	
End point type	Secondary
End point timeframe:	
Timepoint 12 months follow-up	

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	12	6	
Units: Disc volume				
arithmetic mean (standard deviation)	169.9 (± 971.39)	319.9 (± 1336.64)	496.9 (± 1280.50)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRI changes disc volume NDplus, NDbasic, SC 24 months FU

End point title	MRI changes disc volume NDplus, NDbasic, SC 24 months FU
End point description:	
Caudal disc volume (mm3) at timepoint 24 months after treatment.	
End point type	Secondary
End point timeframe:	
Timepoint 24 months follow-up	

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	12	7	
Units: Disc volume				
arithmetic mean (standard deviation)	-180.1 (± 1166.15)	1.8 (± 1689.02)	802.7 (± 1364.16)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRI changes signal intensity NDplus, NDbasic, SC 12 months FU

End point title	MRI changes signal intensity NDplus, NDbasic, SC 12 months FU
End point description:	
Caudal disc T2 (ms) at timepoint 12 months after treatment.	
End point type	Secondary
End point timeframe:	
Timepoint 12 months follow-up	

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	12	7	
Units: Disc signal intensity (T2 relaxation tim				
arithmetic mean (standard deviation)	-1.6 (± 8.89)	0 (± 7.12)	2.9 (± 10.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRI changes signal intensity NDplus, NDbasic, SC 24 months FU

End point title	MRI changes signal intensity NDplus, NDbasic, SC 24 months FU

End point description:

Caudal disc T2 (ms) at timepoint 24 months after treatment.

End point type	Secondary

End point timeframe:

Timepoint 24 months follow-up

End point values	NDplus	NDbasic	Standard of Care (SC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	13	7	
Units: Disc signal intensity (2 relaxation time				
arithmetic mean (standard deviation)	-3.3 (± 9.64)	-1.3 (± 7.04)	5.9 (± 15.42)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Study start to study finish.	
Adverse event reporting additional description: Reporting by investigator after becoming aware of it with reporting form.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	actual

Reporting groups	
Reporting group title	Any AE NDplus group
Reporting group description: All NDplus patients	
Reporting group title	Any AE NDbasic
Reporting group description: All NDbasic patients	
Reporting group title	Any AE SC patients
Reporting group description: All patients from SC group	

Serious adverse events	Any AE NDplus group	Any AE NDbasic	Any AE SC patients
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 53 (75.47%)	12 / 37 (32.43%)	6 / 25 (24.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			

subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	1 / 53 (1.89%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post laminectomy syndrome			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 53 (0.00%)	0 / 37 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facet joint syndrome			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Diastolic dysfunction			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Sciatica			
subjects affected / exposed	2 / 53 (3.77%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperaesthesia			

subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersomnia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 37 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic generalised epilepsy			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Arrested labour			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical incompetence			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastritis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 53 (0.00%)	0 / 37 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal infarct			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric stenosis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			

subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	11 / 53 (20.75%)	4 / 37 (10.81%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	7 / 11	3 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	2 / 53 (3.77%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 53 (0.00%)	2 / 37 (5.41%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sacroiliac joint dysfunction			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon calcification			

subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral foraminal stenosis			
subjects affected / exposed	0 / 53 (0.00%)	0 / 37 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 53 (0.00%)	0 / 37 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 53 (1.89%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 53 (0.00%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Any AE NDplus group	Any AE NDbasic	Any AE SC patients
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 53 (41.51%)	31 / 37 (83.78%)	22 / 25 (88.00%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 53 (3.77%)	2 / 37 (5.41%)	0 / 25 (0.00%)
occurrences (all)	2	2	0
Skin laceration			
subjects affected / exposed	1 / 53 (1.89%)	2 / 37 (5.41%)	0 / 25 (0.00%)
occurrences (all)	1	2	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 53 (3.77%)	1 / 37 (2.70%)	2 / 25 (8.00%)
occurrences (all)	2	1	2
Nervous system disorders			
Sciatica			
subjects affected / exposed	12 / 53 (22.64%)	6 / 37 (16.22%)	6 / 25 (24.00%)
occurrences (all)	12	6	6
Headache			
subjects affected / exposed	5 / 53 (9.43%)	4 / 37 (10.81%)	2 / 25 (8.00%)
occurrences (all)	5	4	2
Radiculopathy			
subjects affected / exposed	3 / 53 (5.66%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences (all)	3	1	0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	3 / 53 (5.66%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences (all)	3	1	0
Nausea			
subjects affected / exposed	3 / 53 (5.66%)	0 / 37 (0.00%)	1 / 25 (4.00%)
occurrences (all)	3	0	1
Toothache			
subjects affected / exposed	3 / 53 (5.66%)	0 / 37 (0.00%)	1 / 25 (4.00%)
occurrences (all)	3	0	1

Diarrhoea			
subjects affected / exposed	1 / 53 (1.89%)	2 / 37 (5.41%)	0 / 25 (0.00%)
occurrences (all)	1	2	0
Gastrooesophageal reflux disiease			
subjects affected / exposed	0 / 53 (0.00%)	0 / 37 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Respiratory tract infection			
subjects affected / exposed	1 / 53 (1.89%)	1 / 37 (2.70%)	2 / 25 (8.00%)
occurrences (all)	1	1	2
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 53 (1.89%)	2 / 37 (5.41%)	0 / 25 (0.00%)
occurrences (all)	1	2	0
Psychiatric disorders			
Depression			
subjects affected / exposed	4 / 53 (7.55%)	3 / 37 (8.11%)	2 / 25 (8.00%)
occurrences (all)	4	3	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	16 / 53 (30.19%)	9 / 37 (24.32%)	12 / 25 (48.00%)
occurrences (all)	16	9	12
Intervertebral disc protrusion			
subjects affected / exposed	17 / 53 (32.08%)	10 / 37 (27.03%)	1 / 25 (4.00%)
occurrences (all)	17	10	1
Arthralgia			
subjects affected / exposed	5 / 53 (9.43%)	3 / 37 (8.11%)	1 / 25 (4.00%)
occurrences (all)	5	3	1
Procedural pain			
subjects affected / exposed	1 / 53 (1.89%)	4 / 37 (10.81%)	1 / 25 (4.00%)
occurrences (all)	1	4	1
Facet joint syndrome			
subjects affected / exposed	2 / 53 (3.77%)	2 / 37 (5.41%)	1 / 25 (4.00%)
occurrences (all)	2	2	1
Pain in extremity			

subjects affected / exposed	2 / 53 (3.77%)	2 / 37 (5.41%)	1 / 25 (4.00%)
occurrences (all)	2	2	1
Ligament sprain			
subjects affected / exposed	2 / 53 (3.77%)	2 / 37 (5.41%)	0 / 25 (0.00%)
occurrences (all)	2	2	0
Meniscus injury			
subjects affected / exposed	3 / 53 (5.66%)	1 / 37 (2.70%)	0 / 25 (0.00%)
occurrences (all)	3	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	20 / 53 (37.74%)	9 / 37 (24.32%)	7 / 25 (28.00%)
occurrences (all)	20	9	7
Bacterial infection			
subjects affected / exposed	1 / 53 (1.89%)	1 / 37 (2.70%)	3 / 25 (12.00%)
occurrences (all)	1	1	3
Influenza			
subjects affected / exposed	2 / 53 (3.77%)	2 / 37 (5.41%)	1 / 25 (4.00%)
occurrences (all)	2	2	1
Urinary tract infection			
subjects affected / exposed	4 / 53 (7.55%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences (all)	4	0	0
Bronchitis			
subjects affected / exposed	3 / 53 (5.66%)	0 / 37 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Final Safety results and brief summary of efficacy are reported in this synoptic clinical study report due to the Sponsor's decision to permanently discontinue the NDplus and NDbasic development program.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27567635

http://www.ncbi.nlm.nih.gov/pubmed/26920137