



Clinical trial results:

An open, monocentric study to evaluate the urodynamic properties of a local implantation of autologous skeletal muscle-derived cells (aSMDCs) in female patients with stress urinary incontinence

Summary

EudraCT number	2010-021867-34
Trial protocol	SI
Global end of trial date	12 August 2015

Results information

Result version number	v1 (current)
This version publication date	02 April 2026
First version publication date	02 April 2026
Summary attachment (see zip file)	Intrasphincteric autologous myoblast injections with electrical stimulation for stress urinary incontinence (2012-Blaganje_ICES13.pdf)

Trial information

Trial identification

Sponsor protocol code	IC-01-01-5-006
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Innovacell Biotechnologie AG
Sponsor organisation address	Mitterweg 24, Innsbruck, Austria, 6020
Public contact	Clinical Department Innovacell , Innovacell Biotechnologie AG, office@innovacell.com
Scientific contact	Clinical Department Innovacell , Innovacell Biotechnologie AG, office@innovacell.com

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	19 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 August 2015
Global end of trial reached?	Yes
Global end of trial date	12 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate the functional status of the urethra and particularly the urethral rhabdosphincter by means of urodynamic measures after SMDCs implantation procedure in female patients with SUI.

Protection of trial subjects:

The rights, safety, and well-being of trial participants are the primary considerations of this clinical trial and prevail over interests of science and society. The trial is conducted in full accordance with the International Conference of Harmonisation Good Clinical Practice (GCP), the Declaration of Helsinki, and applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovenia: 46
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	34

From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited in a single study center. Recruitment started in December 2012 and was planned to last 7 months.

Pre-assignment

Screening details:

In total, 46 patients were screened, and 38 who received cell therapy implantation were included in the ITT set. Long-term follow up was completed by 31 patients.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	aSMDC
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Arm description:

All patients of the ITT set were treated with the IMP consisting of 0.2×10^6 autologous skeletal muscle-derived cells are implanted in female patients with SUI.

Arm type	Experimental
Investigational medicinal product name	aSMDC
Investigational medicinal product code	
Other name	ICES13
Pharmaceutical forms	Implantation suspension
Routes of administration	Injection

Dosage and administration details:

The IMP containing 0.2×10^6 aSMDC are stored in 2 ml cell transport medium. Before the implantation, 20 aliquots containing 100 µl are prepared. The IMP aliquots were single administrated by using a standardized, ultrasound-directed, transurethral injection device with electromyography (EMG) needle to validate sonographic image and correct position of needle for implantation by EMG (passive) or electrostimulation (active).

Number of subjects in period 1 ^[1]	aSMDC
Started	38
Completed	31
Not completed	7
Consent withdrawn by subject	2
Lost to follow-up	5

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Of the overall enrolled 46 patients, 38 received treatment, and 8 patients were not eligible and not exposed to any trial treatment; the ITT set comprises 38 patients.

Baseline characteristics

Reporting groups

Reporting group title	aSMDC
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Reporting group description:

All patients of the ITT set were treated with the IMP consisting of 0.2×10^6 autologous skeletal muscle-derived cells are implanted in female patients with SUI.

Reporting group values	aSMDC	Total	
Number of subjects	38	38	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	31	31	
From 65-84 years	7	7	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	55.79		
standard deviation	± 10.68	-	
Gender categorical			
Units: Subjects			
Female	38	38	
Male	0	0	

End points

End points reporting groups

Reporting group title	aSMDC
Reporting group description: All patients of the ITT set were treated with the IMP consisting of 0.2 x 10e6 autologous skeletal muscle-derived cells are implanted in female patients with SUI.	
Subject analysis set title	ES compliant participants
Subject analysis set type	Sub-group analysis
Subject analysis set description: The performance of electrical stimulation (ES) before and after the implantation of aSMDC was amended as concomitant by the sponsor (substantial amendment protocol version 4.0 (May 2013)). The Sponsor reviewed individual ES data, and allocated patients in the 2 ES sub-groups, defined as compliant and non-compliant to ES. The same methodology as described above for primary and secondary endpoints did apply, and analyses were on the ITT population, according to these two groups of patients.	
Subject analysis set title	ES non-compliant participants
Subject analysis set type	Sub-group analysis
Subject analysis set description: The performance of electrical stimulation (ES) before and after the implantation of aSMDC was amended as concomitant by the sponsor (substantial amendment protocol version 4.0 (May 2013)). The Sponsor reviewed individual ES data, and allocated patients in the 2 ES sub-groups, defined as compliant and non-compliant to ES. The same methodology as described above for primary and secondary endpoints did apply, and analyses were on the ITT population, according to these two groups of patients.	

Primary: Change in the USP transmission ratio of Visit 2 from baseline (screening visit)

End point title	Change in the USP transmission ratio of Visit 2 from baseline (screening visit) ^[1]
End point description: Change from baseline in the urethral stress profile (USP) measured by the transmission ratio in percent in the midurethra.	
End point type	Primary
End point timeframe: Changes of USP at Visit 2 (day 90 post implantation) compared to screening visit (37 days prior implantation) in the ITT set.	
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: As no control or comparator group was included, statistical analyses aimed at testing treatment effects between groups were not applicable. Instead, outcomes were assessed by comparing follow-up observations with the baseline values of the same participants in order to describe potential trends or changes over time.	

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Transmission ratio (%)				
arithmetic mean (standard deviation)	-3.95 (± 15.01)			

Statistical analyses

No statistical analyses for this end point

Primary: Change in the USP transmission ratio of Visit 4 from baseline (screening visit)

End point title	Change in the USP transmission ratio of Visit 4 from baseline (screening visit) ^[2]
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End point description:

Change from baseline in the urethral stress profile (USP) measured by the transmission ratio in percent in the midurethra.

End point type	Primary
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End point timeframe:

Changes of USP at Visit 4 (day 365 post implantation) compared to screening visit (37 days prior implantation) in the ITT set.

Notes:

[2] - 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: As no control or comparator group was included, statistical analyses aimed at testing treatment effects between groups were not applicable. Instead, outcomes were assessed by comparing follow-up observations with the baseline values of the same participants in order to describe potential trends or changes over time.

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Transmission rate (%)				
arithmetic mean (standard deviation)	-3.87 (± 13.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of MUCP of V2 compared to baseline

End point title	Change of MUCP of V2 compared to baseline
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End point description:

The maximum urethral closure pressure is determined through the urethral pressure profile at rest and given by the subtraction of the intravesical pressure at rest from the maximum urethral pressure at rest.

End point type	Secondary
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End point timeframe:

MUCP at Visit 2 (day 90 post implantation) compared to screening visit (37 days prior to implantation) in the ITT set.

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: cmH2O				
arithmetic mean (standard deviation)	-10.13 ($\pm$ 19.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of MUCP of V4 compared to baseline

End point title	Change of MUCP of V4 compared to baseline
End point description: The maximum urethral closure pressure is determined through the urethral pressure profile at rest and given by the subtraction of the intravesical pressure at rest from the maximum urethral pressure at rest.	
End point type	Secondary
End point timeframe: MUCP at Visit 4 (day 365 post implantation) compared to screening visit (37 days prior to implantation) in the ITT set.	

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: cmH2O				
arithmetic mean (standard deviation)	-9.34 ($\pm$ 16.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in functional urethral length of V2 compared to baseline

End point title	Change in functional urethral length of V2 compared to baseline
End point description: The functional urethral length is the part of the urethra, where the intraurethral pressure at rest is lying above the intravesical pressure at rest. The length is determined automatically through the mechanical retraction of the catheter during USP.	
End point type	Secondary
End point timeframe: Change in functional urethral length at Visit 2 (day 90 post implantation) compared to screening visit (37 days prior implantation) in the ITT set.	

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: mm				
arithmetic mean (standard deviation)	0.74 ($\pm$ 7.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in functional urethral length of V4 compared to baseline

End point title	Change in functional urethral length of V4 compared to baseline
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End point description:

The functional urethral length is the part of the urethra, where the intraurethral pressure at rest is lying above the intravesical pressure at rest. The length is determined automatically through the mechanical retraction of the catheter during USP.

End point type	Secondary
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End point timeframe:

Change in functional urethral length at Visit 4 (day 365 post implantation) compared to screening visit (37 days prior implantation) in the ITT set.

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: mm				
arithmetic mean (standard deviation)	-0.29 ($\pm$ 6.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of AUC of the urethral pressure curve at rest of V2 compared to baseline

End point title	Change of AUC of the urethral pressure curve at rest of V2 compared to baseline
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End point description:

This value corresponds to the area under the curve of the urethral pressure profile at rest, depending on the maximum urethral closure pressure and the functional urethral length.

End point type	Secondary
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End point timeframe:

Absolute change in area under the curve of the urethral closure pressure (cm² H2O) of Visit 2 (day 90 post implantation) compared to screening visit (37 days prior implantation) in the ITT set.

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: cm ² H2O				
arithmetic mean (standard deviation)	-35.26 (± 48.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of AUC of the urethral pressure curve at rest of V4 compared to baseline

End point title	Change of AUC of the urethral pressure curve at rest of V4 compared to baseline
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End point description:

This value corresponds to the area under the curve of the urethral pressure profile at rest, depending on the maximum urethral closure pressure and the functional urethral length.

End point type	Secondary
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End point timeframe:

Absolute change in area under the curve of the urethral closure pressure (cm² H2O) of Visit 4 (day 365 post implantation) compared to screening visit (37 days prior implantation) in the ITT set.

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: cm ² H2O				
arithmetic mean (standard deviation)	-46.45 (± 47.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incontinence Episode Frequency Reduction ≥75% (V4 compared to baseline)

End point title	Incontinence Episode Frequency Reduction ≥75% (V4 compared to baseline)
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End point description:

The Incontinence Episodes Frequency (IEF) is calculated as number of incontinence episodes that occurred during 7 days preceding a visit.

End point type	Secondary
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End point timeframe:

Frequency of response measured as a reduction of the frequency of incontinence episodes by more than 75% under treatment from V4 (365 days post implantation) compared to screening visit 8 (37 days prior implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Incontinence Episode Frequency Reduction $\geq 90\%$ (V4 compared to baseline)

End point title	Incontinence Episode Frequency Reduction $\geq 90\%$ (V4 compared to baseline)
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End point description:

The Incontinence Episodes Frequency (IEF) is calculated as number of incontinence episodes that occurred during 7 days preceding a visit.

End point type	Secondary
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End point timeframe:

Frequency of response measured as a reduction of the frequency of incontinence episodes by more than 90% under treatment from V4 (365 days post implantation) compared to screening visit 8 (37 days prior implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of visual analogue scale (VAS) of Visit 4 from baseline

End point title	Change of visual analogue scale (VAS) of Visit 4 from baseline
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End point description:

The individual perception of UI complaints will be evaluated by each patient using a standardized VAS. The VAS is an instrument that measures a characteristic or attitude believed to range across a continuum of values and cannot easily be directly measured. It is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patient should mark the VAS with a vertical line representing his or her perception of the individual UI status. In the study, the two endpoints of the VAS are defined as "no complaints at all" (0 cm) and "worst complaints imaginable" (10 cm).

End point type	Secondary
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End point timeframe:

Changes of visual analogue scale (VAS) from Visit 4 (365 days post implantation) compared to screening visit (37 day prior to implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: cm				
arithmetic mean (standard deviation)	-1.83 (± 2.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incontinence Quality of Life (I-QoL) (V4 compared to screening)

End point title	Incontinence Quality of Life (I-QoL) (V4 compared to screening)
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End point description:

The patients' health-related QoL is assessed using the urinary I-QoL scale with 22-items specific to people with stress and mixed types of UI. It includes general questions on eliciting all areas of concern and specific probes into hypothesized areas of impact: social life, family life, job/work, intimate relationships, activities of daily life, household activities recreation and travel, mental health, physical health, and anxiety/depression.

End point type	Secondary
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End point timeframe:

Change of Patient's assessment based on the Quality of Life questionnaire (QoL) lifestyle score of V4 (365 days post implantation) compared to baseline (screening visit 37 days prior to implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Total I-QoL score				
arithmetic mean (standard deviation)	29.88 (± 25.66)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: very much improved

End point title	Clinical Global Impression (CGI) improvement: very much improved
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure

End point type	Secondary
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End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V4 (365 days post implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	15			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: much improved

End point title	Clinical Global Impression (CGI) improvement: much improved
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.

End point type	Secondary
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End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V4 (365 days post implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: minimally improved

End point title	Clinical Global Impression (CGI) improvement: minimally improved
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.

End point type	Secondary
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End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V4 (365 days post implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: no change

End point title	Clinical Global Impression (CGI) improvement: no change
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.

End point type	Secondary
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End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V4 (365 days post implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: minimally worse

End point title	Clinical Global Impression (CGI) improvement: minimally worse
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.

End point type	Secondary
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End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V4 (365 days post implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: much worse

End point title	Clinical Global Impression (CGI) improvement: much worse
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.

End point type	Secondary
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End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V4 (365 days post implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: very much worse

End point title	Clinical Global Impression (CGI) improvement: very much worse
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.

End point type	Secondary
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End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V4 (365 days post implantation).

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Number of Patients	0			

Statistical analyses

No statistical analyses for this end point

Secondary: USP transmission ratio at visit 4 (ES vs. no ES)

End point title	USP transmission ratio at visit 4 (ES vs. no ES)
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End point description:

End point type	Secondary
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End point timeframe:

Transmission ratio at V4 (365 days post-implantation),

End point values	ES compliant participants	ES non-compliant participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	12		
Units: Transmission ratio (%)				
arithmetic mean (standard deviation)	81.0 (± 8.1)	71.4 (± 10.7)		

Statistical analyses

Statistical analysis title	ES vs. no ES
Comparison groups	ES non-compliant participants v ES compliant participants
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.01
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	Other: 2.5 %

Secondary: Change in the USP transmission ratio of Visit 4 to baseline (ES vs. no ES)

End point title	Change in the USP transmission ratio of Visit 4 to baseline (ES vs. no ES)
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End point description:

End point type	Secondary
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End point timeframe:

Changes of USP at Visit 4 (day 365 post implantation) compared to screening visit (37 days prior implantation).

End point values	ES compliant participants	ES non-compliant participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	12		
Units: Transmission ratio (%)				
arithmetic mean (standard deviation)	-2.28 (± 12.77)	-6.92 (± 14.92)		

Statistical analyses

Statistical analysis title	ES vs. no ES
Comparison groups	ES compliant participants v ES non-compliant participants
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.322
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	Other: 2.5 %

Secondary: Change of IEF of Visit 4 to baseline (ES vs. no ES)

End point title	Change of IEF of Visit 4 to baseline (ES vs. no ES)
End point description: The frequencies of incontinence episodes were documented by a bowel diary that was completed by the patient. The Incontinence Episodes Frequency (IEF) is calculated as number of incontinence episodes that occurred during 7 days preceding a visit.	
End point type	Secondary
End point timeframe: Changes in IEF at V4 (365 days post implantation) compared to baseline (screening visit).	

End point values	ES compliant participants	ES non-compliant participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	12		
Units: IEF change				
arithmetic mean (standard deviation)	-18.24 ($\pm$ 22.50)	-9.38 ($\pm$ 15.76)		

Statistical analyses

Statistical analysis title	ES vs. no ES
Comparison groups	ES compliant participants v ES non-compliant participants
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.208
Method	Wilcoxon (Mann-Whitney)

Secondary: Change of visual analogue scale (VAS) of Visit 4 to baseline (ES vs. no ES)

End point title	Change of visual analogue scale (VAS) of Visit 4 to baseline (ES vs. no ES)
End point description: The individual perception of UI complaints will be evaluated by each patient using a standardized VAS. The VAS is an instrument that measures a characteristic or attitude believed to range across a continuum of values and cannot easily be directly measured. It is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patient should mark the VAS with a vertical line representing his or her perception of the individual UI status. In the study, the two endpoints of the VAS are defined as "no complaints at all" (0 cm) and "worst complaints imaginable" (10 cm).	
End point type	Secondary
End point timeframe: Changes of visual analogue scale (VAS) from Visit 4 (365 days post implantation) compared to baseline (screening visit, 37 days prior implantation).	

End point values	ES compliant participants	ES non-compliant participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	12		
Units: cm				
arithmetic mean (standard deviation)	-1.81 ($\pm$ 2.76)	-1.86 ($\pm$ 2.14)		

Statistical analyses

Statistical analysis title	ES vs. no ES
Comparison groups	ES compliant participants v ES non-compliant participants
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.954
Method	Wilcoxon (Mann-Whitney)

Secondary: Incontinence Quality of Life (I-QoL) V4 compared to baseline (ES vs. no ES)

End point title	Incontinence Quality of Life (I-QoL) V4 compared to baseline (ES vs. no ES)
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End point description:

The patients' health-related QoL is assessed using the urinary I-QoL scale with 22-items specific to people with stress and mixed types of UI. It includes general questions on eliciting all areas of concern and specific probes into hypothesized areas of impact: social life, family life, job/work, intimate relationships, activities of daily life, household activities recreation and travel, mental health, physical health, and anxiety/depression.

End point type	Secondary
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End point timeframe:

Change of Patient's assessment based on the Quality of Life questionnaire (QoL) lifestyle score of V4 (365 days post implantation) compared to screening (37 days prior implantation).

End point values	ES compliant participants	ES non-compliant participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	13		
Units: I-QoL total score				
arithmetic mean (standard deviation)	35.70 ($\pm$ 24.34)	19.14 ($\pm$ 25.44)		

Statistical analyses

Statistical analysis title	ES vs. no ES
Comparison groups	ES compliant participants v ES non-compliant participants
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.06
Method	Wilcoxon (Mann-Whitney)

Secondary: Change of IEF of Visit 4 from baseline

End point title	Change of IEF of Visit 4 from baseline
End point description: The frequencies of incontinence episodes were documented by a bowel diary that was completed by the patient. The Incontinence Episodes Frequency (IEF) is calculated as number of incontinence episodes that occurred during 7 days preceding a visit.	
End point type	Secondary
End point timeframe: Changes in IEF at V4 (365 days post implantation) compared to baseline (screening visit).	

End point values	aSMDC			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: IEF change				
arithmetic mean (standard deviation)	-15.51 ($\pm$ 20.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of AUC of the urethral pressure curve (ES vs. no ES)

End point title	Change of AUC of the urethral pressure curve (ES vs. no ES)
End point description: This value corresponds to the area under the curve of the urethral pressure profile at rest, depending on the maximum urethral closure pressure and the functional urethral length.	

End point type	Secondary
End point timeframe:	
Absolute change in area under the curve of the urethral closure pressure (cm ² H2O) at Visit 4 (day 365 post implantation) compared to screening visit (37 days prior to implantation).	

End point values	ES compliant participants	ES non-compliant participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	13		
Units: cm ² H2O				
arithmetic mean (standard deviation)	-32.6 (± 47)	-73.1 (± 38.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum urethral closure pressure at V4 (ES vs. no ES)

End point title	Maximum urethral closure pressure at V4 (ES vs. no ES)
End point description:	
The maximum urethral closure pressure is determined through the urethral pressure profile at rest and given by the subtraction of the intravesical pressure at rest from the maximum urethral pressure at rest.	
End point type	Secondary
End point timeframe:	
MUCP at Visit 4 (d365 days post implantation)	

End point values	ES compliant participants	ES non-compliant participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	13		
Units: cm H2O				
median (standard deviation)	47.6 (± 17.65)	42.5 (± 16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Functional urethral length at Visit 4 (ES vs. no ES)

End point title	Functional urethral length at Visit 4 (ES vs. no ES)
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End point description:

The functional urethral length is the part of the urethra, where the intraurethral pressure at rest is lying above the intravesical pressure at rest. The length is determined automatically through the mechanical retraction of the catheter during USP.

End point type	Secondary
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End point timeframe:

Functional urethral length at Visit 4 (365 days post implantation)

End point values	ES compliant participants	ES non-compliant participants		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	13		
Units: mm				
arithmetic mean (standard deviation)	31.5 (± 6.8)	27.9 (± 5.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

December 2012 - August 2015

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.0
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Reporting groups

Reporting group title	aSMDC
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Reporting group description: -

Serious adverse events	aSMDC		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 38 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	aSMDC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 38 (44.74%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	1		
Vascular disorders			
All PT's in this SOC			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Surgical and medical procedures			
Obesity surgery			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	1		
General disorders and administration site conditions			

Pyrexia subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1		
Reproductive system and breast disorders Menometrorrhagia subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3		
Injury, poisoning and procedural complications Ligmanet sprain subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1		
Nervous system disorders All PT's in this SOC subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1		
Gastrointestinal disorders Mouth ulceration subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1		
Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1		
Renal and urinary disorders All PT's in this SOC subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	1 / 38 (2.63%) 1		
Infections and infestations All PT's in this SOC subjects affected / exposed occurrences (all)	9 / 38 (23.68%) 12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 May 2012	- The sponsor made decision to replace the initial CRO - One primary endpoint "Change from baseline in the Valsalva Leak Point Pressure" was added because this is an important parameter to describe urethral closure function and yields important information on the function and activity of the external urethral sphincter. - The study duration per patient was extended and is 13 months. An assessment of 12 months with interim analysis at 3 months appeared the most appropriate to increase probability of detecting any pre-post difference. - The definition of response in liaison with IEF scores was modified from 50% and 75% to 75% and 90%.
06 May 2013	Addition of pelvic floor electrical stimulation as concomitant treatment all new patients enrolled into the study for 4 weeks after screening and prior to the cell implantation and 4 weeks starting immediately after cell implantation.
20 December 2013	Valsalva Leak-Point Pressure (VLLP) measure was considered as not appropriate further to the interim data reviews occurred on 24SEP2013 and 19DEC2013. The sponsor decided to skip this test from the primary endpoint and so at Visit 4 for all patients.
17 March 2014	An additional follow-up period was directly integrated into the current study instead of a separate follow up study.

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/34355391>