Clinical trial results:
Skeletal muscle-derived cell implantation in female patients with stress urinary incontinence: a multinational and multicenter open follow-up study

Summary

EudraCT number	2014-001656-34
Trial protocol	BG
Global end of trial date	02 April 2015

Results information

Result version number	v1 (current)
This version publication date	29 September 2021
First version publication date	29 September 2021

Trial information

Trial identification

Sponsor protocol code	IC-01-01-05-015

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Innovacell AG
Sponsor organisation address	Mitterweg 24, Innsbruck, Austria, 6020
Public contact	Clinical Development, Innovacell AG, office@innovacell.com
Scientific contact	Clinical Development, Innovacell 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	06 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 March 2015
Global end of trial reached?	Yes
Global end of trial date	02 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To show the long term efficacy and safety of the skeletal muscle-derived cell therapy

Protection of trial subjects:

This study was conducted in full accordance with the International Conference of Harmonisation Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	28
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No treatment was administered within the study. Only patients were allowed to participate in the study who were part of the preceeding phase IIb study.

Pre-assignment

Screening details:

Only patients from the previously performed phase IIb study who received cells and who were randomized to one of the two cell groups (0.2 x 10e6 [low cell count] aSMDC or 10 x 10e6 [high cell count] aSMDC).

Period 1

Period 1 title	Follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Low Cell Count

Arm description:

0.2 x 10e6 autologous skeletal muscle-derived cells (aSMDCs) were administered with a standardized, ultrasound-directed, transurethral injection device under general anesthesia.

Arm type	Experimental
Investigational medicinal product name	Autologous skeletal muscle-derived cells
Investigational medicinal product code	
Other name	ICES13
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

The IMP (0.2 ± 1 x 10e6 cells) is stored and transported as one vial, frozen in liquid nitrogen in 2 mL cell transportation medium. aSMDC were obtained from each patient by muscle biopsy. After in vitro purification and appropriate passages, the aSMDC were injected into the rhabdosphincter of the respective patient using a standarddized, ultrasoud-directed, transurethral injection tool. The administration of the aSMDC was performed under general anesthesia.

Arm title	High Cell Group

Arm description:

10 x 10e6 autologous skeletal muscle-derived cells (aSMDCs) were administered with a standardized, ultrasound-directed, transurethral injection device under general anesthesia.

Arm type	Experimental
Investigational medicinal product name	Autologous skeletal muscle-derived cells
Investigational medicinal product code	
Other name	ICES13
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

The IMP (10 x 10e6 cells) is stored and transported as one vial, frozen in liquid nitrogen in 2 mL cell transportation medium. aSMDC were obtained from each patient by muscle biopsy. After in vitro purification and appropriate passages, the aSMDC were injected into the rhabdosphincter of the respective patient using a standarddized, ultrasoud-directed, transurethral injection tool. The administration of the aSMDC was performed under general anesthesia.

Number of subjects in period 1	Low Cell Count	High Cell Group
Started	23	19
Completed	23	19

Baseline characteristics

Reporting groups	
Reporting group title	Low Cell Count
Reporting group description:	
0.2 x 10e6 autologous skeletal muscle-derived cells (aSMDCs) were administered with a standardized, ultrasound-directed, transurethral injection device under general anesthesia.	
Reporting group title	High Cell Group
Reporting group description:	
10 x 10e6 autologous skeletal muscle-derived cells (aSMDCs) were administered with a standardized, ultrasound-directed, transurethral injection device under general anesthesia.	

Reporting group values	Low Cell Count	High Cell Group	Total
Number of subjects	23	19	42
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	60.96	55.56	
standard deviation	± 12.6	± 10.75	-
Gender categorical			
Units: Subjects			
Female	23	19	42
Male	0	0	0

End points

End points reporting groups

Reporting group title	Low Cell Count
Reporting group description:	
0.2 x 10e6 autologous skeletal muscle-derived cells (aSMDCs) were administered with a standardized, ultrasound-directed, transurethral injection device under general anesthesia.	
Reporting group title	High Cell Group
Reporting group description:	
10 x 10e6 autologous skeletal muscle-derived cells (aSMDCs) were administered with a standardized, ultrasound-directed, transurethral injection device under general anesthesia.	

Primary: Incontinence Episode Frequency

End point title	Incontinence Episode Frequency
End point description:	
Change in the Incontinence Episode Frequency (IEF) score compared to pre-treatment baseline measured in predecessor phase II study (2009-011797-15).	
End point type	Primary
End point timeframe:	
48 months post treatment	

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: IEF change				
arithmetic mean (standard deviation)	-19.21 (± 11.89)	-13.95 (± 10.78)		

Statistical analyses

Statistical analysis title	High cell group versus Low cell group
Comparison groups	Low Cell Count v High Cell Group
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05 [1]
Method	t-test, 1-sided

Notes:

[1] - A p-value of <0.05 refers to statistical difference

Secondary: VAS scale assessment

End point title	VAS scale assessment

End point description:

The individual perception of SUI complaints was evaluated by each patient using a standardized VAS; an instrument that measures a characteristic or attitude believed to range across a continuum of values and cannot be easily measured directly. The VAS used was a line of 100 mm in length, anchored by word descriptors at each end. Two endpoints were defined on the VAS: "no complaint at all" (0 mm) and "worst complaints imaginable" (100 mm).

End point type	Secondary

End point timeframe:

48 months post implantation

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: mm				
arithmetic mean (standard deviation)	15.5 (± 17.55)	23.08 (± 26.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Responder Rate 25%

End point title	Responder Rate 25%

End point description:

Responders were defined as patients with a decrease in the IEF score by 25% at V2 (48M) compared to baseline.

End point type	Secondary

End point timeframe:

48 months post implantation

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: 25%	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Responder Rate 50%

End point title	Responder Rate 50%

End point description:

Responders were defined as patients with a decrease in the IEF score by 50% at V2 (48M) compared to baseline

End point type	Secondary

End point timeframe:

48 months post implantation

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: number of patients	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Responder Rate 75%

End point title	Responder Rate 75%

End point description:

Responders were defined as patients with a decrease in the IEF score by 75% at V2 (48M) compared to baseline

End point type	Secondary

End point timeframe:

48 months post implantation

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: number of patients	5	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Responder rate 90%

End point title	Responder rate 90%

End point description:

End point type	Secondary

End point timeframe:

Responders were defined as patients with a decrease in the IEF score by 90% at V2 (48M) compared to baseline

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: number of patients	9	8		

Statistical analyses

No statistical analyses for this end point

Secondary: I-QoL (Scale Score total)

End point title	I-QoL (Scale Score total)

End point description:

atients' health-related quality of life was assessed using the urinary I-QoL score, a self-administered quality of life instrument specific to persons 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. I-QoL includes 22 items divided into three domains: Avoidance and Limiting Behavior (ALB), Psychosocial Impacts (PSI), and Social Embarrassment (SE). Each item scores on a 5-point Likert scale comprising the categories “extremely”, “quite a bit”, “moderately”, “a little”, and “none at all”. The best health state is assessed with a score of 5, standing for “none at all”, and the worst health state has a score of 1 standing for “extremely”. Higher scores indicate better health related quality of life.

End point type	Secondary

End point timeframe:

Baseline

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: Total Score				
arithmetic mean (standard deviation)	35.27 (± 21.09)	45.23 (± 24.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: I-QoL (Scale Score total)

End point title	I-QoL (Scale Score total)

End point description:

Patients' health-related quality of life was assessed using the urinary I-QoL score, a self-administered quality of life instrument specific to persons 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. I-QoL includes 22 items divided into three domains: Avoidance and Limiting Behavior (ALB), Psychosocial Impacts (PSI), and Social Embarrassment (SE). Each item scores on a 5-point Likert scale comprising the categories "extremely", "quite a bit", "moderately", "a little", and "none at all". The best health state is assessed with a score of 5, standing for "none at all", and the worst health state has a score of 1 standing for "extremely". Higher scores indicate better health related quality of life.

End point type	Secondary

End point timeframe:

48 months post implantation

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: Total Score				
arithmetic mean (standard deviation)	82.78 (± 18.7)	83.84 (± 18.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global impression (CGI) score

End point title	Clinical Global impression (CGI) score

End point description:

The CGI scale is a standardized assessment tool which allows physicians to rate severity of illness, changes over time and treatment efficiency, taking into account patients' clinical condition and the severity of side effects (1, normal, not at all ill, 2, borderline ill, 3, mildly ill, 4, moderately ill, 5, markedly ill, 6, severly ill, 7, among the most extremely ill patients).

End point type	Secondary

End point timeframe:

Baseline

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: CGI score				
arithmetic mean (standard deviation)	3.53 (± 0.75)	3.7 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Gobal Impression (CGI)

End point title	Clinical Gobal Impression (CGI)

End point description:

The CGI scale is a standardized assessment tool which allows physicians to rate severity of illness, changes over time and treatment efficiency, taking into account patients' clinical condition and the severity of side effects (1, normal, not at all ill, 2, borderline ill, 3, mildly ill, 4, moderately ill, 5, markedly ill, 6, severly ill, 7, among the most extremely ill patients).

End point type	Secondary

End point timeframe:

48 months post implantation

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: CGI Score				
arithmetic mean (standard deviation)	2.57 (± 1.21)	2.84 (± 1.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression - Improvement (PGI-I)

End point title	Patient Global Impression - Improvement (PGI-I)

End point description:

The Patient Global Impression of improvement (PGI-I) score is the patient reported outcomes counterpart to the CGI and was published in 1976 by the National Institute of Mental Health (US). This scale evaluates all aspects of patients' health and assesses if there has been an improvement or decline in clinical status (1, very much better, 2, much better, 3, a little better, 4, no change, 5, a little worse, 6, much worse, 7, very much worse)

End point type	Secondary

End point timeframe:

48 months post implantation

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: PGI-I score				
arithmetic mean (standard deviation)	2.52 (± 1.21)	2.53 (± 1.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS scale assessment

End point title	VAS scale assessment

End point description:

The individual perception of SUI complaints was evaluated by each patient using a standardized VAS; an instrument that measures a characteristic or attitude believed to range across a continuum of values and cannot be easily measured directly. The VAS used was a line of 100 mm in length, anchored by word descriptors at each end. Two endpoints were defined on the VAS: "no complaint at all" (0 mm) and "worst complaints imaginable" (100 mm).

End point type	Secondary

End point timeframe:

Baseline

End point values	Low Cell Count	High Cell Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	19		
Units: mm				
arithmetic mean (standard deviation)	36.65 (± 16.9)	30.37 (± 17.17)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Adverse events reporting was performed from September 2014 to April 2015.	
Adverse event reporting additional description:	
This was a follow-up study without any treatment administered. No adverse events were observed, thus no analysis, reporting and follow-up regarding adverse events was required.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No treatment was administered during this follow-up study.

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

None reported