Clinical trial results:
A Double-blind, Randomized, Controlled Trial Comparing the Safety and Efficacy of AMDC-USR with Placebo in Female Subjects with Stress Urinary Incontinence

Summary

EudraCT number	2014-002919-41
Trial protocol	DE BE
Global end of trial date	10 November 2020

Results information

Result version number	v1 (current)
This version publication date	27 October 2022
First version publication date	27 October 2022

Trial information

Trial identification

Sponsor protocol code	13-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01893138
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cook MyoSite, Inc.
Sponsor organisation address	105 Delta Drive, Pittsburgh, PA, United States, 15238
Public contact	Kelly Cardello, Cook MyoSite, Inc., +1 412-963-7380, Kelly.Cardello@CookMyoSite.com
Scientific contact	Ron Jankowski, PhD, Cook MyoSite, Inc., +1 412-963-7380, Ron.Jankowski@CookMyoSite.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	10 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2020
Global end of trial reached?	Yes
Global end of trial date	10 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy and safety of Autologous Muscle Derived Cells (AMDC, generic name iltamiocel, preparation of a patient's own cells) compared to a placebo (vehicle) control dose in the treatment of stress urinary incontinence (SUI) in adult female patients.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki, including the International Council for Harmonization (ICH) Guideline for Good Clinical Practice and applicable regulations in the United States, Germany, and Belgium where the study took place.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 November 2013
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	Belgium: 3
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	United States: 287
Worldwide total number of subjects	297
EEA total number of subjects	10

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)	241

From 65 to 84 years	56
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were screened and enrolled at 30 sites globally; in the United States, Germany, and Belgium.

Pre-assignment

Screening details:

297 subjects were enrolled (underwent biopsy procedure) and 297 subjects received study treatment (iltamiocel injection). At randomization, participants were stratified by presence or absence of prior incontinence surgery and by < 10 or ≥10 stress incontinence episodes over 3-day diary at screening.

Period 1

Period 1 title	Double-blind Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Iltamiocel

Arm description:

AMDC is the study product (autologous muscle-derived cells). The generic name is iltamiocel. Single intraurethral injection of 150 x 10^6 cells.

Arm type	Experimental
Investigational medicinal product name	Iltamiocel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single intraurethral injection of 150 x 10^6 cells.

Arm title	Placebo

Arm description:

Placebo control is the vehicle solution used for the study product. Single intraurethral injection of vehicle control.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single intraurethral injection of placebo.

Number of subjects in period 1	Iltamiocel	Placebo
Started	199	98
Iltamiocel Injection	199	98
1 Month Follow-Up	199	97
3 Month Follow-Up	199	97
6 Month Follow-Up	198	97
12 Month Follow-Up	198	97
Completed	198	97
Not completed	1	1
Consent withdrawn by subject	1	1

Period 2

Period 2 title	Open Label - Unblinded Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Iltamiocel

Arm description:

AMDC is the study product (autologous muscle-derived cells). The generic name is iltamiocel. No additional treatment for this arm in the open label period.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Placebo

Arm description:

Subjects originally randomized to placebo received single, open-label iltamiocel injection of 150x10^6 cells.

Arm type	Experimental
Investigational medicinal product name	Iltamiocel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single intraurethral injection of 150 x 10^6 cells.

Number of subjects in period 2	Iltamiocel	Placebo
Started	198	97
Open Label Period	166	97
Iltamiocel Injection	0 [1]	92
2 Year Follow-Up	166	87
Completed	166	87
Not completed	32	10
Consent withdrawn by subject	18	7
Adverse event, non-fatal	1	-
Lost to follow-up	4	3
Lack of efficacy	9	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: No additional treatment for iltamiocel arm in the open-label period.

Baseline characteristics

Reporting groups	
Reporting group title	Iltamiocel
Reporting group description:	
AMDC is the study product (autologous muscle-derived cells). The generic name is iltamiocel. Single intraurethral injection of 150 x 10^6 cells.	
Reporting group title	Placebo
Reporting group description:	
Placebo control is the vehicle solution used for the study product. Single intraurethral injection of vehicle control.	

Reporting group values	Iltamiocel	Placebo	Total
Number of subjects	199	98	297
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	54.1	55.0	
standard deviation	± 10.9	± 10.7	-
Gender categorical			
Units: Subjects			
Female	199	98	297
Male	0	0	0
Stress Incontinence Episodes Over 3 Day Diary			
Participant recorded number of stress leaks over 3 days in electronic diary.			
Units: stress leaks			
arithmetic mean	14.2	15.0	
standard deviation	± 9.8	± 14.2	-
24 Hour Pad Test Weight			
A test in which the participant wears specific absorbent pads dispensed by the clinic. The pads are weighed to record the pre-test weight prior to dispensing to the participant. The participant must wear the absorbent pads for 24 hours. The participant returns the used absorbent pads to the clinic, and the clinic records the post-test weight to determine urinary leakage for the 24 hour period. The difference in weights represent the amount of urine leaked in which 24 hour pad weight = total weight of pads after test period - total weight of pads prior to test period.			
Units: grams			
arithmetic mean	47.6	40.9	
standard deviation	± 91.8	± 52.8	-
Incontinence Quality of Life (IQOL)			

Assessment -Total Score			
The I-QOL questionnaire is a validated, 22-item tool used to assess quality of life (QOL) of women with urinary incontinence, focused on avoidance and limiting behavior, psychosocial impacts, and social embarrassment. Score scale is 0-100; increased score indicates improvement.. Scored 0 to100, with higher scores indicating a better QOL.			
Units: scores on scales			
arithmetic mean	59.0	59.5	
standard deviation	± 21.0	± 20.2	-
7-Item Incontinence Impact Questionnaire – Short Form (IIQ-7)			
The IIQ-7 questionnaire is a validated, 7-item tool used to assess the impact of urinary incontinence on health-related quality of life, focused on physical activity, social relationships, travel, and emotional health. Scored 0 to 100, lower scores indicate better quality of life (QOL).			
Units: scores on scales			
arithmetic mean	44.4	43.7	
standard deviation	± 20.9	± 21.8	-
6-Item Urogenital Distress Inventory Score – Short Form (UDI-6)			
This questionnaire consists of 6 questions focused on symptoms related to stress urinary incontinence, detrusor overactivity, and bladder outlet obstruction. Score scale is 0-75; decreased score indicates improvement.			
Units: scores on scales			
arithmetic mean	38.5	40.5	
standard deviation	± 16.0	± 18.4	-
Global Quality of Life Assessment (GQOL)			
This questionnaire consists of 1 question focused on satisfaction with condition. Score scale is 0-6; decreased score indicates improvement.			
Units: scores on scales			
arithmetic mean	5.7	5.6	
standard deviation	± 1.0	± 1.1	-
Incontinence Severity Index (ISI)			
The ISI is a questionnaire consisting of two questions which assesses the frequency and quantity of urine leakage. Score scale is 0-12; decreased score indicates improvement.			
Units: scores on scales			
arithmetic mean	7.6	7.4	
standard deviation	± 2.4	± 2.8	-

End points

End points reporting groups

Reporting group title	Iltamiocel

Reporting group description:

AMDC is the study product (autologous muscle-derived cells). The generic name is iltamiocel. Single intraurethral injection of 150 x 10^6 cells.

Reporting group title	Placebo

Reporting group description:

Placebo control is the vehicle solution used for the study product. Single intraurethral injection of vehicle control.

Reporting group title	Iltamiocel

Reporting group description:

AMDC is the study product (autologous muscle-derived cells). The generic name is iltamiocel. No additional treatment for this arm in the open label period.

Reporting group title	Placebo

Reporting group description:

Subjects originally randomized to placebo received single, open-label iltamiocel injection of 150x10^6 cells.

Subject analysis set title	Durability of 50% Reduction in SIEF at Month 24
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The number of subjects with 50% reduction of stress incontinence episode frequency (SIEF) at 12 months and diary data at Month 24.

Subject analysis set title	Durability of 75% Reduction in SIEF at Month 24
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The number of subjects with 75% reduction of stress incontinence episode frequency (SIEF) at 12 months and diary data at Month 24.

Subject analysis set title	Durability of 0 to 1 SIEF at Month 24
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The number of subjects with 0 to 1 stress incontinence episode frequency (SIEF) at 12 months and diary data at Month 24.

Subject analysis set title	Durability of 50% Reduction in SIEF at Month 24(Prior Surgery)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The number of subjects with prior surgery with 50% reduction of stress incontinence episode frequency (SIEF) at 12 months and diary data at Month 24.

Subject analysis set title	Durability of 75% Reduction in SIEF at Month 24(Prior Surgery)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The number of subjects with prior surgery with 75% reduction of stress incontinence episode frequency (SIEF) at 12 months and diary data at Month 24.

Subject analysis set title	Durability of 0 to 1 SIEF at Month 24 (Prior Surgery)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The number of subjects with prior surgery with 0 to 1 stress incontinence episode frequency (SIEF) at 12 months and diary data at Month 24.

Primary: Participants With ≥ 50% Reduction in Stress Incontinence Episode Frequency From Baseline to 12 Months Post-treatment; as Assessed by 3 Day Diary

End point title	Participants With ≥ 50% Reduction in Stress Incontinence Episode Frequency From Baseline to 12 Months Post-treatment; as Assessed by 3 Day Diary

End point description:

All participants with baseline and 12 month 3 day diary data.

End point type	Primary

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	97		
Units: participants	103	52		

Statistical analyses

Statistical analysis title	Chi-square test between iltamiocel & placebo arms
Comparison groups	Iltamiocel v Placebo
Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7978
Method	Chi-squared

Secondary: Participants With at ≥ 75% Reduction in Stress Incontinence Episodes From Baseline at 12 Months

End point title	Participants With at ≥ 75% Reduction in Stress Incontinence Episodes From Baseline at 12 Months

End point description:

All participants with baseline and 12 month 3 day diary data.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	97		
Units: participants	73	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With 0 or 1 Stress Incontinence Episodes Based on 3 Day Diary Records at 12 Months

End point title	Participants With 0 or 1 Stress Incontinence Episodes Based on 3 Day Diary Records at 12 Months

End point description:

All participants with baseline and 12 month diary data.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	97		
Units: participants	53	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement (Reduction) in the Frequency of Stress Incontinence Episodes From Baseline at 12 Months

End point title	Improvement (Reduction) in the Frequency of Stress Incontinence Episodes From Baseline at 12 Months

End point description:

All participants with baseline and 12 month 3 day diary data.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	97		
Units: change in number of stress leaks				
arithmetic mean (standard deviation)	-5.8 (± 11)	-4.9 (± 13.5)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Association of Quality of Life Improvement With Stress Incontinence Episode Reduction

End point title	Association of Quality of Life Improvement With Stress Incontinence Episode Reduction

End point description:

All participants with baseline and 12 month diary data; Spearman's correlation used for analysis. Association of change in questionnaires with change in stress incontinence episode frequency (SIEF) at 12 months.

End point type	Other pre-specified

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	96		
Units: correlation coefficient				
number (not applicable)				
Change in IQOL vs change in SIEF	-0.556	-0.456		
Change in IIQ-7 vs change in SIEF	0.522	0.442		
Change in UDI-6 vs change in SIEF	0.408	0.433		
Change in GQOL vs change in SIEF	0.537	0.422		
Change in ISI vs change in SIEF	0.529	0.599		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Treatment Durability at 24 Months

End point title	Treatment Durability at 24 Months

End point description:

Treatment durability defined as iltamiocel-treated participants with categorical reduction in stress incontinence episode frequency (SIEF) at 12 months who maintained response at 24 months. All participants with 12 month and 24 month stress incontinence episode frequency (SIEF) diary data.

End point type	Other pre-specified

End point timeframe:

12 months to 24 months after injection with iltamiocel

End point values	Durability of 50% Reduction in SIEF at Month 24	Durability of 75% Reduction in SIEF at Month 24	Durability of 0 to 1 SIEF at Month 24	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	89	65	45	
Units: participants	80	50	36	

Statistical analyses

No statistical analyses for this end point

Post-hoc: Participants With at ≥ 75% Reduction in Stress Incontinence Episodes From Baseline at 12 Months (Prior Surgery Participants Only)

End point title	Participants With at ≥ 75% Reduction in Stress Incontinence Episodes From Baseline at 12 Months (Prior Surgery Participants Only)

End point description:

Participants with a history of prior SUI surgery with baseline and 12 month diary data.

End point type	Post-hoc

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	25		
Units: participants	20	4		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Participants With 0 or 1 Stress Incontinence Episodes Based on 3 Day Diary Records at 12 Months (Prior Surgery Participants Only)

End point title	Participants With 0 or 1 Stress Incontinence Episodes Based on 3 Day Diary Records at 12 Months (Prior Surgery Participants Only)

End point description:

Participants with a history of prior SUI surgery with baseline and 12 month diary data.

End point type	Post-hoc

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	25		
Units: participants	14	3		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Improvement (Reduction) in the Frequency of Stress Incontinence Episodes From Baseline at 12 Months (Prior Surgery Participants Only)

End point title	Improvement (Reduction) in the Frequency of Stress Incontinence Episodes From Baseline at 12 Months (Prior Surgery Participants Only)

End point description:

Participants with a history of prior SUI surgery with baseline and 12 month diary data.

End point type	Post-hoc

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	25		
Units: change in number of stress leaks				
arithmetic mean (standard deviation)	-6.7 (± 14.5)	-4.5 (± 11.5)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Association of Quality of Life Improvement With Stress Incontinence Episode Reduction (Prior Surgery Participants Only)

End point title	Association of Quality of Life Improvement With Stress Incontinence Episode Reduction (Prior Surgery Participants Only)

End point description:

All prior surgery participants with baseline and 12 month diary data; Spearman's correlation used for analysis. Association of change in questionnaires with change in stress incontinence episode frequency (SIEF) at 12 months.

End point type	Post-hoc

End point timeframe:

12 months

End point values	Iltamiocel	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	25		
Units: correlation coefficient				
number (not applicable)				
Change in IQOL vs change in SIEF	-0.489	-0.460		
Change in IIQ-7 vs change in SIEF	0.427	0.542		
Change in UDI-6 vs change in SIEF	0.424	0.604		
Change in GQOL vs change in SIEF	0.561	0.190		
Change in ISI vs change in SIEF	0.426	0.476		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Treatment Durability at 24 Months (Prior Surgery Participants)

End point title	Treatment Durability at 24 Months (Prior Surgery Participants)

End point description:

Treatment durability defined as iltamiocel-treated participants with reduction in stress incontinence episode frequency (SIEF) at 12 months who maintained response at 24 months. Prior surgery participants with 12 month and 24 month stress incontinence episode frequency (SIEF) diary data.

End point type	Post-hoc

End point timeframe:

12 months to 24 months after injection with iltamiocel

End point values	Durability of 50% Reduction in SIEF at Month 24(Prior Surgery)	Durability of 75% Reduction in SIEF at Month 24(Prior Surgery)	Durability of 0 to 1 SIEF at Month 24 (Prior Surgery)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	22	18	13	
Units: participants	19	12	11	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
12 month double-blind period	
Adverse event reporting additional description:	
Collection at injection, 1 month, 3 months, 6 months, and 12 months post-treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Iltamiocel
Reporting group description:	
AMDC is the study product (autologous muscle-derived cells). The generic name is iltamiocel. Single intraurethral injection of 150 x 10^6 cells.	
Reporting group title	Placebo
Reporting group description:	
Placebo control is the vehicle solution used for the study product. Single intraurethral injection of vehicle control.	

Serious adverse events	Iltamiocel	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 199 (5.53%)	9 / 98 (9.18%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			

subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural Pain			
subjects affected / exposed	2 / 199 (1.01%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery dissection			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major depression			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 199 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scoliosis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 199 (0.50%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	2 / 199 (1.01%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 199 (0.50%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Iltamiocel	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 199 (42.21%)	28 / 98 (28.57%)	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	10 / 199 (5.03%)	1 / 98 (1.02%)	
occurrences (all)	11	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	20 / 199 (10.05%)	7 / 98 (7.14%)	
occurrences (all)	20	8	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	7 / 199 (3.52%)	5 / 98 (5.10%)	
occurrences (all)	8	6	
Infections and infestations			
Sinusitis			
subjects affected / exposed	11 / 199 (5.53%)	1 / 98 (1.02%)	
occurrences (all)	11	1	
Urinary tract infection			
subjects affected / exposed	36 / 199 (18.09%)	14 / 98 (14.29%)	
occurrences (all)	53	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 June 2014	Substantial amendment to protocol (version 13-003-02, dated 03 June 2014) for use in United States.
03 November 2015	Substantial amendment 01 to protocol (version 13-003-04-BE, dated 06 October 2015) for use in Belgium.
30 November 2015	Substantial amendment to protocol (version 13-003-03, dated 02 November 2015) for use in United States.
01 February 2016	Substantial amendment to protocol (version 13-003-04, dated 14 January 2016) for use in United States.
08 March 2016	Substantial amendment to protocol (version 13-003-05, dated 18 February 2016) for use in United States.
27 January 2017	Substantial amendment to protocol (version 13-003-05-BE, dated 19 January 2017) for use in Belgium.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported