Clinical trial results:
A Prospective Nonrandomized Study of Autologous Muscle Derived Cell (AMDC) Transplantation for Treatment of Fecal Incontinence

Summary

EudraCT number	2013-004672-35
Trial protocol	GB
Global end of trial date	27 October 2021

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	09-025

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01600755
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cook MyoSite, Inc.
Sponsor organisation address	105 Delta Drive, Pittsburgh, United States, 15238
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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	27 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 October 2021
Global end of trial reached?	Yes
Global end of trial date	27 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety and feasibility of Autologous Muscle Derived Cells (AMDC, generic name iltamiocel, preparation of a patient's own cells) injection into the anal sphincter for treatment of patients with fecal incontinence. Iltamiocel therapy seeks to allow remodeling of the external anal sphincter in patients with fecal incontinence from either defined structural defects or a generalized weakening of the external anal sphincter. The primary objective of the study was to assess the frequency and severity of adverse events related to the study product and study procedures through 12 months following treatment of fecal incontinence in adult male and female subjects.

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 Canada and the United Kingdom where the study took place.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 March 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	United Kingdom: 15
Country: Number of subjects enrolled	Canada: 33
Worldwide total number of subjects	48
EEA total number of subjects	0

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)	24
From 65 to 84 years	23
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Subjects were screened and enrolled at 2 sites globally; 1 site in Canada and 1 site in the United Kingdom.

Pre-assignment

Screening details:

53 subjects were enrolled (underwent biopsy procedure) and 48 subjects received study treatment (iltamiocel injection). The analysis population is based on 48 subjects that received study treatment (iltamiocel injection).

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	Iltamiocel

Arm description:

AMDC is the study product (autologous muscle-derived cells). The generic name is iltamiocel. Single intrasphincteric injection of 250 x 10^6 cells.

Arm type	Experimental
Investigational medicinal product name	Iltamiocel
Investigational medicinal product code	
Other name	Autologous muscle-derived cells (AMDC)
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single intrasphincteric injection of 250 x 10^6 cells.

Number of subjects in period 1	Iltamiocel
Started	48
Iltamiocel Injection	48
3-Month Follow-Up	48
6-Month Follow-Up	48
12-Month Follow-Up	47
Completed	47
Not completed	1
Consent withdrawn by subject	1

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 intrasphincteric injection of 250 x 10^6 cells.	

Reporting group values	Iltamiocel	Total	
Number of subjects	48	48	
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)	24	24	
From 65-84 years	24	24	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	61.7		
standard deviation	± 13.3	-	
Gender categorical Units: Subjects			
Female	45	45	
Male	3	3	
28-Day Incontinence Diary (Number of Episodes) Units: incontinence episodes			
median	16		
full range (min-max)	0 to 92	-	
28-Day Incontinence Diary (Days with Episodes) Units: days with incontinence episodes			
median	12		
full range (min-max)	0 to 28	-	
Cleveland Clinic Incontinence Score (CCIS)			
CCIS is a validated 5-questions tool assessing the frequency and the type of incontinence episodes (solid, liquid, gas), pad use, and lifestyle alteration. Scored from 0 to 20, with lower scores indicating less severe symptoms.			
Units: scores on scales			
arithmetic mean	13.6		
standard deviation	± 2.9	-	
Fecal Incontinence Quality of Life (FIQL) Questionnaire - Lifestyle Scale			
FIQL is a validated, 29-item tool assessing quality of life (QOL) of subjects with FI with four scales:			

Lifestyle (10 items), Coping/Behavior (9 items), Depression/Self-Perception (7 items), and Embarrassment (3 items). Scored 0 to 4, with higher scores indicating a better QOL.			
Units: scores on scales arithmetic mean standard deviation	 2.5 ± 0.9	 -	
Fecal Incontinence Quality of Life (FIQL) Questionnaire - Coping/behavior Scale			
FIQL is a validated, 29-item tool assessing quality of life (QOL) of subjects with FI with four scales: Lifestyle (10 items), Coping/Behavior (9 items), Depression/Self-Perception (7 items), and Embarrassment (3 items). Scored 0 to 4, with higher scores indicating a better QOL.			
Units: scores on scales arithmetic mean standard deviation	 1.7 ± 0.6	 -	
Fecal Incontinence Quality of Life (FIQL) Questionnaire - Depression/perception Scale			
FIQL is a validated, 29-item tool assessing quality of life (QOL) of subjects with FI with four scales: Lifestyle (10 items), Coping/Behavior (9 items), Depression/Self-Perception (7 items), and Embarrassment (3 items). Scored 0 to 4, with higher scores indicating a better QOL.			
Units: scores on scales arithmetic mean standard deviation	 2.5 ± 0.9	 -	
Fecal Incontinence Quality of Life (FIQL) Questionnaire - Embarrassment Scale			
FIQL is a validated, 29-item tool assessing quality of life (QOL) of subjects with FI with four scales: Lifestyle (10 items), Coping/Behavior (9 items), Depression/Self-Perception (7 items), and Embarrassment (3 items). Scored 0 to 4, with higher scores indicating a better QOL.			
Units: scores on scales arithmetic mean standard deviation	 1.9 ± 0.8	 -	

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 intrasphincteric injection of 250 x 10^6 cells.

Primary: Incidence of Treatment-Related Adverse Events

End point title	Incidence of Treatment-Related Adverse Events[1]

End point description:

Assessment of frequency and severity of adverse events related to study product and study procedures through 12 months following treatment of FI in adult male and female subjects.

End point type	Primary

End point timeframe:

12 months

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: This study was not a randomized controlled clinical trial. Therefore there was no comparator group. Frequency of serious adverse events and non-serious adverse events was calculated as the number of subjects with an event divided by the total number of subjects in the analysis population.

End point values	Iltamiocel			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Events				
Study Product-related serious adverse events	0			
Study Product-related adverse events	1			
Injection procedure-related adverse events	5			
Biopsy procedure-related adverse events	27			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Fecal Incontinence (FI) Episodes (Median 28-day Fecal Incontinence Diary)

End point title	Number of Fecal Incontinence (FI) Episodes (Median 28-day Fecal Incontinence Diary)

End point description:

Median number of fecal incontinence (FI) episodes as assessed by 28-day FI diary at 3, 6, and 12 months post-treatment.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: incontinence episodes				
median (full range (min-max))				
Fecal incontinence diary at 3 months	8 (0 to 100)			
Fecal incontinence diary at 6 months	10 (0 to 206)			
Fecal incontinence diary at 12 months	7 (0 to 161)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days With FI Episodes (Median 28-day Fecal Incontinence Diary)

End point title	Number of Days With FI Episodes (Median 28-day Fecal Incontinence Diary)

End point description:

Median number of days with fecal incontinence (FI) episodes, as assessed by 28-day FI diary at 3, 6, and 12 months post-treatment.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: days with incontinence episodes				
median (full range (min-max))				
Fecal incontinence diary at 3 months	7 (0 to 28)			
Fecal incontinence diary at 6 months	7 (0 to 28)			
Fecal incontinence diary at 12 months	5 (0 to 28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Fecal Incontinence (FI) Episodes (Categorical ≥50%

Reduction in 28-day Fecal Incontinence Diary)	
End point title	Number of Fecal Incontinence (FI) Episodes (Categorical ≥50% Reduction in 28-day Fecal Incontinence Diary)

End point description:

Number of fecal incontinence (FI) episodes (categorical ≥50% reduction in episodes) as assessed by 28-day FI diary at 3, 6, and 12 months post-treatment.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: participants				
Fecal incontinence diary at 3 months	17			
Fecal incontinence diary at 6 months	19			
Fecal incontinence diary at 12 months	22			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Fecal Incontinence (FI) Episodes (Categorical ≥75% Reduction in 28-day Fecal Incontinence Diary)	
End point title	Number of Fecal Incontinence (FI) Episodes (Categorical ≥75% Reduction in 28-day Fecal Incontinence Diary)

End point description:

Number of fecal incontinence (FI) episodes (categorical ≥75% reduction in episodes) as assessed by 28-day FI diary at 3, 6, and 12 months post-treatment.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: participants				
Fecal incontinence diary at 3 months	7			
Fecal incontinence diary at 6 months	12			
Fecal incontinence diary at 12 months	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Fecal Incontinence (FI) Episodes (Categorical 100% Reduction in 28-day Fecal Incontinence Diary)

End point title	Number of Fecal Incontinence (FI) Episodes (Categorical 100% Reduction in 28-day Fecal Incontinence Diary)

End point description:

Number of fecal incontinence (FI) episodes (categorical 100% reduction in episodes) as assessed by 28-day FI diary at 3, 6, and 12 months post-treatment.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: participants				
Fecal incontinence diary at 3 months	1			
Fecal incontinence diary at 6 months	4			
Fecal incontinence diary at 12 months	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient-reported Quality of Life (Fecal Incontinence Quality of Life (FIQL) Questionnaire)

End point title	Change From Baseline in Patient-reported Quality of Life (Fecal Incontinence Quality of Life (FIQL) Questionnaire)

End point description:

Mean change from baseline in patient-reported quality of life, as assessed by the Fecal Incontinence Quality of Life (FIQL) questionnaire at 3, 6, and 12 months post-treatment. The FIQL is a validated, 29-item tool assessing the quality of life (QOL) of subjects with FI with four scales: Lifestyle (10 items), Coping/Behavior (9 items), Depression/Self-Perception (7 items), and Embarrassment (3 items). Scored 0 to 4, with higher scores indicating a better QOL.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: scores on scales				
arithmetic mean (standard deviation)				
Change in Lifestyle scale at 3 months	0.4 (± 0.7)			
Change in Lifestyle scale at 6 months	0.4 (± 0.7)			
Change in Lifestyle scale at 12 months	0.6 (± 0.7)			
Change in Coping/Behavior scale at 3 months	0.4 (± 0.7)			
Change in Coping/Behavior scale at 6 months	0.5 (± 0.7)			
Change in Coping/Behavior scale at 12 months	0.5 (± 0.7)			
Change in Depression/Perception scale at 3 months	0.3 (± 0.7)			
Change in Depression/Perception scale at 6 months	0.3 (± 0.6)			
Change in Depression/Perception scale at 12 months	0.4 (± 0.6)			
Change in Embarrassment scale at 3 months	0.5 (± 0.8)			
Change in Embarrassment scale at 6 months	0.5 (± 0.8)			
Change in Embarrassment scale at 12 months	0.6 (± 0.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient-reported Fecal Incontinence Symptom Severity (Cleveland Clinic Incontinence Score (CCIS))

End point title	Change From Baseline in Patient-reported Fecal Incontinence Symptom Severity (Cleveland Clinic Incontinence Score (CCIS))

End point description:

Mean change from baseline in patient-reported fecal incontinence symptom severity, as assessed by the Cleveland Clinic Incontinence Score (CCIS) questionnaire at 3, 6, and 12 months post-treatment. CCIS is a validated 5-questions tool assessing the frequency and the type of incontinence episodes (solid, liquid, gas), pad use, and lifestyle alteration. Scored from 0 to 20, with lower scores indicating less severe symptoms.

End point type	Secondary

End point timeframe:

12 months

End point values	Iltamiocel			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: scores on scales				
arithmetic mean (standard deviation)				
Change in CCIS score at 3 months	-2.2 (± 3.0)			
Change in CCIS score at 6 months	-2.0 (± 2.8)			
Change in CCIS score at 12 months	-2.9 (± 2.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Iltamiocel
Reporting group description:	
AMDC is the study product (autologous muscle-derived cells). The generic name is iltamiocel. Single intrasphincteric injection of 250 x 10^6 cells.	

Serious adverse events	Iltamiocel		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 48 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Sinus operation			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Small intestine obstruction			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			

subjects affected / exposed	2 / 48 (4.17%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Iltamiocel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 48 (62.50%)		
Injury, poisoning and procedural complications			
Post procedural contusion			
subjects affected / exposed	5 / 48 (10.42%)		
occurrences (all)	5		
Procedural pain			
subjects affected / exposed	13 / 48 (27.08%)		
occurrences (all)	13		
Nervous system disorders			
Hypoesthesia			
subjects affected / exposed	5 / 48 (10.42%)		
occurrences (all)	5		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	8 / 48 (16.67%)		
occurrences (all)	9		
Hemorrhoids			
subjects affected / exposed	3 / 48 (6.25%)		
occurrences (all)	3		

Proctalgia subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 4		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 3		
Infections and infestations Cystitis subjects affected / exposed occurrences (all) Lower respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 4 6 / 48 (12.50%) 6 4 / 48 (8.33%) 4 5 / 48 (10.42%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 June 2013	Substantial amendment 01 to protocol for use in Canada.
04 May 2015	Substantial amendment 03 to protocol for use in Canada.
30 September 2015	Substantial amendment 03 to protocol for use in United Kingdom.
26 May 2016	Substantial amendment 04 to protocol for use in Canada.
06 March 2017	Substantial amendment 08 to protocol for use in United Kingdom.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported