



## Clinical trial results:

### A Double blind, Randomized, Placebo-Controlled Study Evaluating the Safety and Effectiveness of Cook MyoSite Incorporated AMDC in Female Patients with Stress Urinary Incontinence

#### Summary

EudraCT number	2011-003599-35
Trial protocol	DE GB BE NL
Global end of trial date	29 January 2017

#### Results information

Result version number	v1 (current)
This version publication date	01 April 2018
First version publication date	01 April 2018

#### Trial information

##### Trial identification

Sponsor protocol code	10-019
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01382602
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Cook MyoSite Incorporated
Sponsor organisation address	105 Delta Drive, Pittsburgh, United States, 15238
Public contact	Maja Skytte Jensen, William Cook Europe ApS, +45 56868686, DNK-Clinical-Studies@CookMedical.com
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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	18 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 February 2016
Global end of trial reached?	Yes
Global end of trial date	29 January 2017
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To assess the safety and efficacy of Autologous Muscle Derived Cells for Urinary Sphincter Repair (AMDC-USR) compared with placebo control in women with stress urinary incontinence (SUI).

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 Europe where the study took place.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Canada: 140
Worldwide total number of subjects	143
EEA total number of subjects	3

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)	125
From 65 to 84 years	18

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details:

Subjects were screened and enrolled at 10 sites globally; 8 sites in Canada, 1 site in Germany, and 1 site in United Kingdom.

### Pre-assignment

Screening details:

227 subjects consented to study participation and were screened for eligibility, of whom 150 subjects were enrolled (underwent biopsy procedure) and 143 subjects underwent at least 1 study treatment of AMDC-USR (93 subjects) or placebo (50 subjects). Analysis population is based on 143 subjects that underwent at least 1 study treatment.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	AMDC-USR

Arm description:

Subjects received 1 or 2 treatments of 150 million AMDC-USR delivered via transurethral intrasphincteric injection. After completing 12 months follow-up subjects were unblinded. Subjects were followed for 2 years after initial AMDC-USR treatment. Analysis population is based on subjects that received at least 1 treatment of AMDC-USR at the 12 months follow-up.

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

Dosage and administration details:

Subjects received 1 or 2 treatments of 150 million AMDC-USR delivered via transurethral intrasphincteric injection.

<b>Arm title</b>	Placebo
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Arm description:

Subjects received 1 or 2 treatments of placebo delivered via transurethral intrasphincteric injection. After completing 12 months follow-up subjects were unblinded and could elect to receive open-label AMDC-USR treatment. Subjects that received open-label AMDC-USR treatment were followed for 2 years after initial AMDC-USR treatment. Analysis population is based on subjects that received at least 1 treatment of placebo at the 12 months follow-up.

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:

Subjects received 1 or 2 treatments of placebo delivered via transurethral intrasphincteric injection.

<b>Number of subjects in period 1</b>	AMDC-USR	Placebo
Started	93	50
Completed	93	50

## Baseline characteristics

### Reporting groups

Reporting group title	AMDC-USR
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Reporting group description:

Subjects received 1 or 2 treatments of 150 million AMDC-USR delivered via transurethral intrasphincteric injection. After completing 12 months follow-up subjects were unblinded. Subjects were followed for 2 years after initial AMDC-USR treatment. Analysis population is based on subjects that received at least 1 treatment of AMDC-USR at the 12 months follow-up.

Reporting group title	Placebo
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Reporting group description:

Subjects received 1 or 2 treatments of placebo delivered via transurethral intrasphincteric injection. After completing 12 months follow-up subjects were unblinded and could elect to receive open-label AMDC-USR treatment. Subjects that received open-label AMDC-USR treatment were followed for 2 years after initial AMDC-USR treatment. Analysis population is based on subjects that received at least 1 treatment of placebo at the 12 months follow-up.

Reporting group values	AMDC-USR	Placebo	Total
Number of subjects	93	50	143
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	82	43	125
From 65-84 years	11	7	18
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	51.4	51.7	
standard deviation	± 11.1	± 9.9	-
Gender categorical Units: Subjects			
Female	93	50	143
Male	0	0	0

## End points

### End points reporting groups

Reporting group title	AMDC-USR
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Reporting group description:

Subjects received 1 or 2 treatments of 150 million AMDC-USR delivered via transurethral intrasphincteric injection. After completing 12 months follow-up subjects were unblinded. Subjects were followed for 2 years after initial AMDC-USR treatment. Analysis population is based on subjects that received at least 1 treatment of AMDC-USR at the 12 months follow-up.

Reporting group title	Placebo
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Reporting group description:

Subjects received 1 or 2 treatments of placebo delivered via transurethral intrasphincteric injection. After completing 12 months follow-up subjects were unblinded and could elect to receive open-label AMDC-USR treatment. Subjects that received open-label AMDC-USR treatment were followed for 2 years after initial AMDC-USR treatment. Analysis population is based on subjects that received at least 1 treatment of placebo at the 12 months follow-up.

### Primary: Responder Rate (Based on Stress IEF, or In-office Pad Weight Test, or 24-hour Pad Weight Test) at 12 Months

End point title	Responder Rate (Based on Stress IEF, or In-office Pad Weight Test, or 24-hour Pad Weight Test) at 12 Months
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End point description:

A composite primary endpoint of responder rate was used, where a subject was considered a responder if she had  $\geq 50\%$  reduction from baseline in stress Incontinence Episode Frequency (stress IEF; reported stress leaks from 3-day diary) or  $\geq 50\%$  reduction in leakage from baseline as determined by either the in-office pad weight test or the 24-hour pad weight test.

End point type	Primary
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End point timeframe:

12 months

End point values	AMDC-USR	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	50		
Units: Percentage of Subjects				
number (confidence interval 95%)	82 (73 to 90)	90 (78 to 97)		

### Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	AMDC-USR v Placebo

Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05 <sup>[1]</sup>
Method	t-test, 1-sided

Notes:

[1] - Enrollment was halted early due to limitations in study design related to the primary efficacy endpoint. Therefore, official p-value for primary endpoint was not calculated.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were monitored from consent through study exit. Reporting groups were based on adverse events that occurred between initial blinded injection treatment and unblinding of subjects after 12-months follow-up.

Adverse event reporting additional description:

Adverse events that occurred between initial blinded injection and unblinding of subjects after 12-months follow-up were compared between AMDC-USR and Placebo groups. No deaths, SAEs, or discontinuation of a subject due to adverse events were reported.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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### Reporting groups

Reporting group title	AMDC-USR
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Reporting group description:

Subjects received 1 or 2 treatments of 150 million AMDC-USR delivered via transurethral intrasphincteric injection. Analysis population is based on subjects that received at least 1 treatment of AMDC-USR at the 12 months follow-up.

Reporting group title	Placebo
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Reporting group description:

Subjects received 1 or 2 treatments of placebo delivered via transurethral intrasphincteric injection. Analysis population is based on subjects that received at least 1 treatment of placebo at the 12 months follow-up.

Serious adverse events	AMDC-USR	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 93 (0.00%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	AMDC-USR	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 93 (34.41%)	13 / 50 (26.00%)	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	5 / 93 (5.38%)	1 / 50 (2.00%)	
occurrences (all)	5	1	

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 93 (8.60%)	0 / 50 (0.00%)	
occurrences (all)	8	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	5 / 93 (5.38%)	3 / 50 (6.00%)	
occurrences (all)	6	3	
Pollakiuria			
subjects affected / exposed	2 / 93 (2.15%)	4 / 50 (8.00%)	
occurrences (all)	2	4	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	12 / 93 (12.90%)	5 / 50 (10.00%)	
occurrences (all)	18	5	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2011	Amendment 01 to protocol for use in Canada.
21 February 2012	Substantial Amendment 01, to protocol for use in United Kingdom.
04 July 2012	Amendment during CTA review, to protocol for use in Germany.
04 September 2012	Substantial Amendment 02, to protocol for use in United Kingdom.
15 October 2012	Substantial Amendment 02, to protocol for use in Germany.
02 January 2013	Amendment 02 to protocol for use in Canada.
09 August 2013	Substantial Amendment 03, to protocol for use in United Kingdom.
04 March 2014	Substantial Amendment 04, to protocol for use in United Kingdom.
04 March 2014	Substantial Amendment 03, to protocol for use in Germany.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
05 May 2014	Planned study enrollment was 246 subjects; due to limitations in study design related to the primary efficacy endpoint, enrollment was halted early after 150 subjects.	-

Notes:

### Limitations and caveats

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

Planned study enrollment was 246 patients; due to limitations in study design related to the primary efficacy endpoint, enrollment was halted at 150 subjects.

Notes: