



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 150×10^6 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 150×10^6 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 150×10^6 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 150×10^6 cells.

| Number of subjects in period 2 | IltamioceI | Placebo |
|---------------------------------------|-------------------|----------------|
| Started | 198 | 97 |
| Open Label Period | 166 | 97 |
| IltamioceI 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 iltamioceI 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 150×10^6 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 | IltamioceI |
| Reporting group description: AMDC is the study product (autologous muscle-derived cells). The generic name is iltamioceI. Single intraurethral injection of 150×10^6 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 | IltamioceI |
| Reporting group description: AMDC is the study product (autologous muscle-derived cells). The generic name is iltamioceI. 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 iltamioceI injection of 150×10^6 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 \geq 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 \geq 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 \geq 75% Reduction in Stress Incontinence Episodes From Baseline at 12 Months

| | |
|-----------------|--|
| End point title | Participants With at \geq 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 | Iltamioce | 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 | Iltamioce | 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 \geq 75% Reduction in Stress Incontinence Episodes From Baseline at 12 Months (Prior Surgery Participants Only)

| | |
|-----------------|--|
| End point title | Participants With at \geq 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 150×10^6 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 occurrences (all) | 7 / 199 (3.52%) 8 | 5 / 98 (5.10%) 6 | |
| Infections and infestations | | | |
| Sinusitis subjects affected / exposed occurrences (all) | 11 / 199 (5.53%) 11 | 1 / 98 (1.02%) 1 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 36 / 199 (18.09%) 53 | 14 / 98 (14.29%) 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