



## Clinical trial results:

**A phase IIa, unicenter, prospective, randomized, parallel, two-arms, single-dose, open-label with blinded assessor pilot clinical trial to assess ex vivo expanded adult autologous mesenchymal stromal cells fixed in allogeneic bone tissue (XCEL-MT-OSTEO-ALPHA) in non hypertrophic pseudoarthrosis of long bones**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2013-005025-23   |
| Trial protocol           | ES               |
| Global end of trial date | 20 December 2019 |

### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 18 May 2022   |
| First version publication date    | 18 May 2022   |
| Summary attachment (see zip file) | A Phase IIa, Single Center, Prospective, Randomized, Parallel, Two-arms, Single-dose, Open-label With Blinded Assessor Pilot Clinical Trial to Assess ex Vivo Expanded Adult Autologous Mesenchymal Stro (CSR Synopsis.pdf) |

### Trial information

#### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | XCEL-PSART-01 |
|-----------------------|---------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Banc de Sang i Teixits   |
| Sponsor organisation address | Passeig Taulat 116, Barcelona, Spain, 08005  |
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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                       | 05 March 2019    |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 05 March 2019    |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 20 December 2019 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

-To assess the efficacy of XCEL-MT-OSTEO-ALPHA in the treatment of non-hypertrophic pseudarthrosis of long bones through quantifying of the Hounsfield units by TC at month 12 posttreatment.

Protection of trial subjects:

Patients were sedated and locally anesthetized for the bone marrow extraction and were discharged after recovery.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 14 January 2015 |
| 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 | Spain: 20 |
| Worldwide total number of subjects   | 20        |
| EEA total number of subjects         | 20        |

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)                      | 20 |
| From 65 to 84 years                       | 0  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited between January 2015 and February 2018 in a single centre (Hospital ASEPEYO Sant Cugat (Barcelona)).

### Pre-assignment

Screening details:

Patients between 18 and 65 years of age affected with acquired metaphysodiaphyseal non-hypertrophic pseudoarthrosis of long bones, visited at Hospital ASEPEYO Sant Cugat (Barcelona)

### Period 1

|                              |                           |
|------------------------------|---------------------------|
| Period 1 title               | Period 1 (overall period) |
| Is this the baseline period? | Yes                       |
| Allocation method            | Randomised - controlled   |
| Blinding used                | Single blind              |
| Roles blinded                | Assessor <sup>[1]</sup>   |

Blinding implementation details:

As the tested product is from autologous bone marrow meaning randomised patients had to undergo for a previous bone marrow extraction, the only person that could be blinded was the radiologist who assessed the radiological images.

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | XCEL-MT-OSTEO-ALPHA |

Arm description:

Mechanical stabilization and XCEL-MT-OSTEO-ALPHA (ex Vivo Expanded Adult Autologous Mesenchymal Stromal Cells Fixed in Allogeneic Bone Tissue).

|  |                     |
|--|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | XCEL-MT-OSTEO-ALPHA |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Implant             |
| Routes of administration               | Local use           |

Dosage and administration details:

Product: XCEL-MT-OSTEO-ALPHA

- Dose: 3x10<sup>5</sup> y 1x10<sup>6</sup> mesenchymal stromal cells per cubic centimeter of bone (5 or 10 cc)
- Pharmaceutical form: Solid particles.
- Administration route: Surgically implanted
- Administration periodicity: Single dose.

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | Standar of care |
|------------------|-----------------|

Arm description:

Mechanical stabilization and autologous graft

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Autologous graft  |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Implant           |
| Routes of administration               | Local use         |

Dosage and administration details:

Autologous graft. Dosage is not applicable.

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Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Being an autologous treatment requiring previous bone marrow extraction, the only person that could be blind was the radiologist.

| <b>Number of subjects in period 1</b> | XCEL-MT-OSTEO-<br>ALPHA | Standar of care |
|---------------------------------------|-------------------------|-----------------|
| Started                               | 10                      | 10              |
| Completed                             | 10                      | 10              |

## Baseline characteristics

### Reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | XCEL-MT-OSTEO-ALPHA |
| Reporting group description:<br>Mechanical stabilization and XCEL-MT-OSTEO-ALPHA (ex Vivo Expanded Adult Autologous Mesenchymal Stromal Cells Fixed in Allogeneic Bone Tissue). |                     |
| Reporting group title   | Standar of care     |
| Reporting group description:<br>Mechanical stabilization and autologous graft   |                     |

| Reporting group values                             | XCEL-MT-OSTEO-ALPHA | Standar of care | Total |
|--|---------------------|-----------------|-------|
| Number of subjects                                 | 10                  | 10              | 20    |
| 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)                               | 10                  | 10              | 20    |
| From 65-84 years                                   | 0                   | 0               | 0     |
| 85 years and over                                  | 0                   | 0               | 0     |
| Age continuous                                     |                     |                 |       |
| Units: years                                       |                     |                 |       |
| arithmetic mean                                    | 43.7                | 51.8            |       |
| standard deviation                                 | ± 9.9               | ± 7.9           | -     |
| Gender categorical                                 |                     |                 |       |
| Units: Subjects                                    |                     |                 |       |
| Female   | 1                   | 2               | 3     |
| Male   | 9                   | 8               | 17    |

## End points

### End points reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | XCEL-MT-OSTEO-ALPHA |
| Reporting group description:<br>Mechanical stabilization and XCEL-MT-OSTEO-ALPHA (ex Vivo Expanded Adult Autologous Mesenchymal Stromal Cells Fixed in Allogeneic Bone Tissue). |                     |
| Reporting group title   | Standar of care     |
| Reporting group description:<br>Mechanical stabilization and autologous graft   |                     |

### Primary: Change in mean percentage of Housfield Units by CT

|                                   |  |
|-----------------------------------|--|
| End point title                   | Change in mean percentage of Housfield Units by CT |
| End point description:            |  |
| End point type                    | Primary  |
| End point timeframe:<br>12 months |  |

| End point values                     | XCEL-MT-OSTEO-ALPHA | Standar of care      |  |  |
|--------------------------------------|---------------------|----------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group      |  |  |
| Number of subjects analysed          | 7                   | 8                    |  |  |
| Units: percent                       |                     |                      |  |  |
| arithmetic mean (standard deviation) | 46 ( $\pm$ 19.25)   | 54.39 ( $\pm$ 21.63) |  |  |

### Statistical analyses

|   |                                       |
|---|---------------------------------------|
| Statistical analysis title              | Change in mean percentage of HU       |
| Comparison groups                       | XCEL-MT-OSTEO-ALPHA v Standar of care |
| Number of subjects included in analysis | 15                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.4835                              |
| Method                                  | Regression, Linear                    |

|                            |                                       |
|----------------------------|---------------------------------------|
| Statistical analysis title | Change in mean percentage of HU       |
| Comparison groups          | Standar of care v XCEL-MT-OSTEO-ALPHA |

|   |                    |
|---|--------------------|
| Number of subjects included in analysis | 15                 |
| Analysis specification                  | Pre-specified      |
| Analysis type                           | superiority        |
| P-value                                 | = 0.4835           |
| Method                                  | Regression, Linear |

### Secondary: Change in mean percentage of Housfield Units by CT

|                        |  |
|------------------------|--|
| End point title        | Change in mean percentage of Housfield Units by CT |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| 6 months               |  |

| End point values                     | XCEL-MT-OSTEO-ALPHA  | Standar of care      |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed          | 8                    | 8                    |  |  |
| Units: percent                       |                      |                      |  |  |
| arithmetic mean (standard deviation) | 29.70 ( $\pm$ 13.86) | 40.50 ( $\pm$ 19.88) |  |  |

### Statistical analyses

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Change in mean percentage of HU       |
| Comparison groups                       | XCEL-MT-OSTEO-ALPHA v Standar of care |
| Number of subjects included in analysis | 16                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.3761                              |
| Method                                  | Regression, Linear                    |

### Secondary: Degree of consolidation according to TUS scale (Tomographic union Score)

|                        |  |
|------------------------|--|
| End point title        | Degree of consolidation according to TUS scale (Tomographic union Score) |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| 6 months               |  |



| <b>End point values</b>     | XCEL-MT-<br>OSTEO-ALPHA | Standar of care |  |  |
|-----------------------------|-------------------------|-----------------|--|--|
| Subject group type          | Reporting group         | Reporting group |  |  |
| Number of subjects analysed | 8                       | 8               |  |  |
| Units: Units                |                         |                 |  |  |
| Consolidated                | 1                       | 5               |  |  |
| Not consolidated            | 7                       | 3               |  |  |

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | degree of consolidation according to TUS scale |
| Comparison groups                       | XCEL-MT-OSTEO-ALPHA v Standar of care          |
| Number of subjects included in analysis | 16   |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | superiority                                    |
| P-value                                 | = 0.119  |
| Method                                  | Fisher exact                                   |

### Secondary: Degree of consolidation according to TUS scale (Tomographic union Score)

|                        |  |
|------------------------|--|
| End point title        | Degree of consolidation according to TUS scale (Tomographic union Score) |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| 12 months              |  |

| <b>End point values</b>     | XCEL-MT-<br>OSTEO-ALPHA | Standar of care |  |  |
|-----------------------------|-------------------------|-----------------|--|--|
| Subject group type          | Reporting group         | Reporting group |  |  |
| Number of subjects analysed | 7                       | 8               |  |  |
| Units: Units                |                         |                 |  |  |
| Consolidated                | 3                       | 6               |  |  |
| Not consolidated            | 4                       | 2               |  |  |

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | degree of consolidation according to TUS scale |
| Comparison groups                       | XCEL-MT-OSTEO-ALPHA v Standar of care          |
| Number of subjects included in analysis | 15   |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | superiority                                    |
| P-value                                 | = 0.315  |
| Method                                  | Fisher exact                                   |

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**Secondary: Degree of consolidation according to RUS scale (Radiographic Union Score)**

|                 |   |
|-----------------|---|
| End point title | Degree of consolidation according to RUS scale (Radiographic Union Score) |
|-----------------|---|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

6 months

|                             |                     |                 |  |  |
|-----------------------------|---------------------|-----------------|--|--|
| <b>End point values</b>     | XCEL-MT-OSTEO-ALPHA | Standar of care |  |  |
| Subject group type          | Reporting group     | Reporting group |  |  |
| Number of subjects analysed | 8                   | 8               |  |  |
| Units: Units                |                     |                 |  |  |
| Consolidated                | 4                   | 5               |  |  |
| Not Consolidated            | 4                   | 3               |  |  |

**Statistical analyses**

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | degree of consolidation according to RUS scale |
| Comparison groups                       | XCEL-MT-OSTEO-ALPHA v Standar of care          |
| Number of subjects included in analysis | 16   |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | superiority                                    |
| P-value                                 | = 1  |
| Method                                  | Fisher exact                                   |

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**Secondary: Degree of consolidation according to RUS scale (Radiographic Union Score)**

|                 |   |
|-----------------|---|
| End point title | Degree of consolidation according to RUS scale (Radiographic Union Score) |
|-----------------|---|

End point description:

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| 12 months            |           |

| End point values            | XCEL-MT-OSTEO-ALPHA | Standar of care |  |  |
|-----------------------------|---------------------|-----------------|--|--|
| Subject group type          | Reporting group     | Reporting group |  |  |
| Number of subjects analysed | 7                   | 8               |  |  |
| Units: Units                |                     |                 |  |  |
| Consolidated                | 5                   | 7               |  |  |
| Not consolidated            | 2                   | 1               |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | degree of consolidation according to RUS scale |
| Comparison groups                       | XCEL-MT-OSTEO-ALPHA v Standar of care          |
| Number of subjects included in analysis | 15   |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | superiority                                    |
| P-value                                 | = 0.569  |
| Method                                  | Fisher exact                                   |

### Secondary: Changes in the EUROQoL-5D

|                        |                           |
|------------------------|---------------------------|
| End point title        | Changes in the EUROQoL-5D |
| End point description: |                           |
| End point type         | Secondary                 |
| End point timeframe:   |                           |
| 6 months               |                           |

| End point values                     | XCEL-MT-OSTEO-ALPHA    | Standar of care        |  |  |
|--------------------------------------|------------------------|------------------------|--|--|
| Subject group type                   | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed          | 8                      | 8                      |  |  |
| Units: mean                          |                        |                        |  |  |
| arithmetic mean (standard deviation) | 0.6217 ( $\pm$ 0.2248) | 0.5451 ( $\pm$ 0.1931) |  |  |

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Changes in punctuation on the Euroqol-5D |
| Comparison groups                       | XCEL-MT-OSTEO-ALPHA v Standar of care    |
| Number of subjects included in analysis | 16                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.3708                                 |
| Method                                  | Regression, Linear                       |

### Secondary: Changes in the EUROQoL-5D

|                        |                           |
|------------------------|---------------------------|
| End point title        | Changes in the EUROQoL-5D |
| End point description: |                           |
| End point type         | Secondary                 |
| End point timeframe:   |                           |
| 12 months              |                           |

|                                      |                     |                   |  |  |
|--------------------------------------|---------------------|-------------------|--|--|
| <b>End point values</b>              | XCEL-MT-OSTEO-ALPHA | Standar of care   |  |  |
| Subject group type                   | Reporting group     | Reporting group   |  |  |
| Number of subjects analysed          | 8                   | 7                 |  |  |
| Units: mean                          |                     |                   |  |  |
| arithmetic mean (standard deviation) | 0.5795 (± 0.1782)   | 0.7176 (± 0.2060) |  |  |

### Statistical analyses

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Changes in the EUROQoL-5D             |
| Comparison groups                       | XCEL-MT-OSTEO-ALPHA v Standar of care |
| Number of subjects included in analysis | 15                                    |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | = 0.4204                              |
| Method                                  | Regression, Linear                    |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the signature of the informed consent form to the end of the trial

Adverse event reporting additional description:

Safety analyzes were performed with the available data, without using missing data imputation techniques.

The analysis techniques were descriptive, including graphs and individual data listings. The AE were described by means of lists of the AE, organized by treatment group and patient, which included the preferred terms (MedDRA), as well as the c

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | XCEL-MT-OSTEO-ALPHA |
|-----------------------|---------------------|

Reporting group description:

Patients randomized to XCEL-MT-OSTEO-ALPHA

|                       |                  |
|-----------------------|------------------|
| Reporting group title | STANDARD OF CARE |
|-----------------------|------------------|

Reporting group description:

Patients randomized to standard of care treatment (autologous iliac crest)

| Serious adverse events                               | XCEL-MT-OSTEO-ALPHA | STANDARD OF CARE |  |
|--|---------------------|------------------|--|
| Total subjects affected by serious adverse events    |                     |                  |  |
| subjects affected / exposed                          | 3 / 10 (30.00%)     | 2 / 10 (20.00%)  |  |
| number of deaths (all causes)                        | 0                   | 0                |  |
| number of deaths resulting from adverse events       | 0                   | 0                |  |
| General disorders and administration site conditions |                     |                  |  |
| Medical device site joint pain                       |                     |                  |  |
| subjects affected / exposed                          | 1 / 10 (10.00%)     | 0 / 10 (0.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 1               | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0               | 0 / 0            |  |
| Musculoskeletal and connective tissue disorders      |                     |                  |  |
| Pseudarthrosis                                       |                     |                  |  |
| subjects affected / exposed                          | 0 / 10 (0.00%)      | 1 / 10 (10.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 0               | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0               | 0 / 0            |  |
| Infections and infestations                          |                     |                  |  |
| postprocedural infection                             |                     |                  |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Product issues                                  |                 |                 |  |
| Device breakage                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 2 / 10 (20.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | XCEL-MT-OSTEO-ALPHA | STANDARD OF CARE |  |
|---|---------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                     |                  |  |
| subjects affected / exposed                           | 5 / 10 (50.00%)     | 4 / 10 (40.00%)  |  |
| Injury, poisoning and procedural complications        |                     |                  |  |
| Post procedural discomfort                            |                     |                  |  |
| subjects affected / exposed                           | 0 / 10 (0.00%)      | 1 / 10 (10.00%)  |  |
| occurrences (all)                                     | 0                   | 1                |  |
| Surgical and medical procedures                       |                     |                  |  |
| Limb operation  |                     |                  |  |
| subjects affected / exposed                           | 1 / 10 (10.00%)     | 0 / 10 (0.00%)   |  |
| occurrences (all)                                     | 1                   | 0                |  |
| Nervous system disorders                              |                     |                  |  |
| Dysaesthesia  |                     |                  |  |
| subjects affected / exposed                           | 0 / 10 (0.00%)      | 1 / 10 (10.00%)  |  |
| occurrences (all)                                     | 0                   | 1                |  |
| Hypoaesthesia   |                     |                  |  |
| subjects affected / exposed                           | 1 / 10 (10.00%)     | 0 / 10 (0.00%)   |  |
| occurrences (all)                                     | 1                   | 0                |  |
| General disorders and administration site conditions  |                     |                  |  |
| Medical device site discomfort                        |                     |                  |  |
| subjects affected / exposed                           | 1 / 10 (10.00%)     | 2 / 10 (20.00%)  |  |
| occurrences (all)                                     | 1                   | 2                |  |
| Discomfort  |                     |                  |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Gait disturbance                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Medical device site joint discomfort            |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                               | 0               | 1               |  |
| Medical device site pain                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Pain  |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Haemorrhoids                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Psychiatric disorders                           |                 |                 |  |
| Anxiety   |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Encopresis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                               | 0               | 1               |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Musculoskeletal discomfort                      |                 |                 |  |
| subjects affected / exposed                     | 3 / 10 (30.00%) | 1 / 10 (10.00%) |  |
| occurrences (all)                               | 3               | 1               |  |
| Pain in extremity                               |                 |                 |  |
| subjects affected / exposed                     | 3 / 10 (30.00%) | 1 / 10 (10.00%) |  |
| occurrences (all)                               | 3               | 1               |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                               | 0               | 1               |  |
| Muscle atrophy                                  |                 |                 |  |

|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                  | 1               | 0               |  |
| Muscle contracture                 |                 |                 |  |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                  | 0               | 1               |  |
| Tendonitis                         |                 |                 |  |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                  | 0               | 1               |  |
| Infections and infestations        |                 |                 |  |
| Cystitis                           |                 |                 |  |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                  | 1               | 0               |  |
| Viral infection                    |                 |                 |  |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 10 (0.00%)  |  |
| occurrences (all)                  | 1               | 0               |  |
| Metabolism and nutrition disorders |                 |                 |  |
| Vitamin D deficiency               |                 |                 |  |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 1 / 10 (10.00%) |  |
| occurrences (all)                  | 0               | 1               |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 25 September 2015 | The dose to be used in this study was increased from 10 to 20 cc, with a minimum cell content of $30 \times 10^5$ and a maximum of $20 \times 10^6$ |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported