



## Clinical trial results:

### PHASE III PROTOCOL COMPARING A MICROFRACTURE TREATMENT TO A CARTIPATCH® CHONDROCYTE GRAFT TREATMENT IN FEMORAL CONDYLE LESIONS

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2007-003481-18 |
| Trial protocol           | BE             |
| Global end of trial date | 31 July 2013   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 22 July 2021 |
| First version publication date | 22 July 2021 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | CART.III. |
|-----------------------|-----------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | TBF Genie Tissulaire   |
| Sponsor organisation address | 6 rue d'Italie, Mions, France, 69780   |
| Public contact               | Laurence BARNOUIN, TBF Genie Tissulaire, +33 (0)4 72 68 69 09, laurence.barnouin@tbf-lab.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:

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**Results analysis stage**

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|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 16 May 2014   |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 04 April 2013 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 31 July 2013  |
| Was the trial ended prematurely?                     | Yes           |

Notes:

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**General information about the trial**

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Main objective of the trial:

Compare the clinical improvement of the IKDC subjective score between the microfracture-treated group and the Cartipatch® chondrocyte graft-treated groups

Protection of trial subjects:

Every cartilage biopsy received was checked to verify their compliance before CARTIPATCH® implantation. Investigators were informed if, for unexpected reasons, the chondrocyte expansion through cell culture could not be initiated. Possible reasons can be either initial poor quality of collected cartilage, or failure during CARTIPATCH® manufacturing. Any adverse event related to cell culture was discussed with the main surgeon and the surgeons in relation with the patient to find a satisfactory solution (performing of a second procurement for instance).

Background therapy: -

Evidence for comparator:

Comparison of CARTIPATCH® to reference therapy (microfracture treatment).

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 11 November 2008 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Efficacy         |
| Long term follow-up duration                              | 18 Months        |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Hong Kong: 3 |
| Country: Number of subjects enrolled | Norway: 8    |
| Country: Number of subjects enrolled | Croatia: 2   |
| Country: Number of subjects enrolled | Belgium: 9   |
| Country: Number of subjects enrolled | Israel: 10   |
| Worldwide total number of subjects   | 32           |
| EEA total number of subjects         | 19           |

Notes:

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**Subjects enrolled per age group**

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|   |   |
|---|---|
| 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)                     | 32 |
| From 65 to 84 years                      | 0  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

64 patients were expected to be included in the study and to be distributed in two groups of equal size (32 patients per group). As the overall trial enrolment could not be reached in time, inclusion period was delayed several times and study was then early terminated. Finally, a total of 32 patients were included in 6 centers.

### Pre-assignment

Screening details:

Forty-six patients were recorded in the study. On this 46 recorded patients, 32 patients were included.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Not blinded                    |

### Arms

|                              |       |
|------------------------------|-------|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | Arm A |

Arm description:

Reference arm : microfracture treatment

|   |                     |
|---|---------------------|
| Arm type  | Reference treatment |
| No investigational medicinal product assigned in this arm |                     |
| <b>Arm title</b>  | Arm B               |

Arm description:

Experimental arm, CARTIPATCH®

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | CARTIPATCH®  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Implant      |
| Routes of administration               | Implantation |

Dosage and administration details:

Dosage : not applicable

Surgical treatment :

- 1st operative step: Arthroscopy to collect cartilage
- 2nd operative step: Implantation by arthrotomy about 6 weeks following arthroscopy

| Number of subjects in period 1           | Arm A | Arm B |
|--|-------|-------|
| Started                                  | 18    | 14    |
| Completed                                | 12    | 9     |
| Not completed                            | 6     | 5     |
| Graft washed out 1.5 months post-surgery | -     | 1     |
| Lost to follow-up                        | 2     | -     |
| Missing data                             | 1     | 2     |

|             |   |   |
|-------------|---|---|
| Not treated | 3 | 2 |
|-------------|---|---|

## Baseline characteristics

### Reporting groups

|   |       |
|---|-------|
| Reporting group title                   | Arm A |
| Reporting group description:            |       |
| Reference arm : microfracture treatment |       |
| Reporting group title                   | Arm B |
| Reporting group description:            |       |
| Experimental arm, CARTIPATCH®           |       |

| Reporting group values                             | Arm A        | Arm B        | Total |
|--|--------------|--------------|-------|
| Number of subjects                                 | 18           | 14           | 32    |
| 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)                               | 18           | 14           | 32    |
| From 65-84 years                                   | 0            | 0            | 0     |
| 85 years and over                                  | 0            | 0            | 0     |
| Age continuous                                     |              |              |       |
| Units: years                                       |              |              |       |
| arithmetic mean                                    | 33           | 34           |       |
| full range (min-max)                               | 20 to 45     | 19 to 46     | -     |
| Gender categorical                                 |              |              |       |
| Units: Subjects                                    |              |              |       |
| Female   | 8            | 3            | 11    |
| Male   | 10           | 11           | 21    |
| Lesion size  |              |              |       |
| Units: cm2   |              |              |       |
| arithmetic mean                                    | 3.46         | 4.08         |       |
| full range (min-max)                               | 2.52 to 5.76 | 2.50 to 6.25 | -     |

### Subject analysis sets

|   |                  |
|---|------------------|
| Subject analysis set title  | Treated patients |
| Subject analysis set type   | Per protocol     |
| Subject analysis set description:   |                  |
| Analysis was done by study arm. All treated patients followed up to 18 months post-surgery were included in the analysis. |                  |

| Reporting group values | Treated patients |  |  |
|------------------------|------------------|--|--|
| Number of subjects     | 21               |  |  |

|   |    |  |  |
|---|----|--|--|
| Age categorical                                       |    |  |  |
| Units: Subjects                                       |    |  |  |
| In utero  | 0  |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0  |  |  |
| Newborns (0-27 days)                                  | 0  |  |  |
| Infants and toddlers (28 days-23<br>months)           | 0  |  |  |
| Children (2-11 years)                                 | 0  |  |  |
| Adolescents (12-17 years)                             | 0  |  |  |
| Adults (18-64 years)                                  | 21 |  |  |
| From 65-84 years                                      | 0  |  |  |
| 85 years and over                                     | 0  |  |  |
| Age continuous  |    |  |  |
| Units: years  |    |  |  |
| arithmetic mean                                       |    |  |  |
| full range (min-max)                                  |    |  |  |
| Gender categorical                                    |    |  |  |
| Units: Subjects                                       |    |  |  |
| Female  |    |  |  |
| Male  |    |  |  |
| Lesion size   |    |  |  |
| Units: cm2  |    |  |  |
| arithmetic mean                                       |    |  |  |
| full range (min-max)                                  |    |  |  |

## End points

### End points reporting groups

|   |                  |
|---|------------------|
| Reporting group title   | Arm A            |
| Reporting group description:  |                  |
| Reference arm : microfracture treatment   |                  |
| Reporting group title   | Arm B            |
| Reporting group description:  |                  |
| Experimental arm, CARTIPATCH®   |                  |
| Subject analysis set title  | Treated patients |
| Subject analysis set type   | Per protocol     |
| Subject analysis set description:   |                  |
| Analysis was done by study arm. All treated patients followed up to 18 months post-surgery were included in the analysis. |                  |

### Primary: Patient part of IKDC subjective score

|                        |                                       |
|------------------------|---------------------------------------|
| End point title        | Patient part of IKDC subjective score |
| End point description: |                                       |
| End point type         | Primary                               |
| End point timeframe:   |                                       |
| 18 months post-surgery |                                       |

| End point values                       | Arm A           | Arm B           | Treated patients     |  |
|--|-----------------|-----------------|----------------------|--|
| Subject group type                     | Reporting group | Reporting group | Subject analysis set |  |
| Number of subjects analysed            | 12              | 9               | 21                   |  |
| Units: scale from 0 to 100             |                 |                 |                      |  |
| arithmetic mean (full range (min-max)) | 66 (34 to 86)   | 59 (32 to 98)   | 63 (32 to 98)        |  |

### Statistical analyses

|   |                         |
|---|-------------------------|
| Statistical analysis title  | No statistical analysis |
| Statistical analysis description:   |                         |
| Statistical analysis to assess difference between treatments was not performed. |                         |
| Comparison groups   | Arm A v Arm B           |
| Number of subjects included in analysis   | 21                      |
| Analysis specification  | Pre-specified           |
| Analysis type   | superiority             |
| Parameter estimate  | Not assessed            |
| Point estimate  | 0                       |
| Confidence interval   |                         |
| level   | 95 %                    |
| sides   | 2-sided                 |
| lower limit   | 0                       |
| upper limit   | 0                       |



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**Primary: Surgeon part of IKDC score**

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|                 |                            |
|-----------------|----------------------------|
| End point title | Surgeon part of IKDC score |
|-----------------|----------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

18 months post-surgery

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| End point values            | Arm A           | Arm B           | Treated patients     |  |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type          | Reporting group | Reporting group | Subject analysis set |  |
| Number of subjects analysed | 12              | 9               | 21                   |  |
| Units: Grade                |                 |                 |                      |  |
| Grade A                     | 7               | 6               | 13                   |  |
| Grade B                     | 4               | 0               | 4                    |  |
| Grade C                     | 0               | 2               | 2                    |  |
| Grade D                     | 0               | 1               | 1                    |  |

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**Statistical analyses**

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|                            |                            |
|----------------------------|----------------------------|
| Statistical analysis title | Surgeon part of IKDC score |
|----------------------------|----------------------------|

Statistical analysis description:

Statistical analysis to assess difference between treatments was not performed.

|                   |               |
|-------------------|---------------|
| Comparison groups | Arm A v Arm B |
|-------------------|---------------|

|   |    |
|---|----|
| Number of subjects included in analysis | 21 |
|---|----|

|                        |               |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

|               |             |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

|                    |              |
|--------------------|--------------|
| Parameter estimate | Not assessed |
|--------------------|--------------|

|                |   |
|----------------|---|
| Point estimate | 0 |
|----------------|---|

Confidence interval

|       |      |
|-------|------|
| level | 95 % |
|-------|------|

|       |         |
|-------|---------|
| sides | 2-sided |
|-------|---------|

|             |   |
|-------------|---|
| lower limit | 0 |
|-------------|---|

|             |   |
|-------------|---|
| upper limit | 0 |
|-------------|---|

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**Secondary: KOOS clinical scores: SYMPTOMS**

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|                 |                                |
|-----------------|--------------------------------|
| End point title | KOOS clinical scores: SYMPTOMS |
|-----------------|--------------------------------|

End point description:

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

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End point timeframe:  
18 months post-surgery

| End point values                       | Arm A               | Arm B              | Treated patients     |  |
|--|---------------------|--------------------|----------------------|--|
| Subject group type                     | Reporting group     | Reporting group    | Subject analysis set |  |
| Number of subjects analysed            | 12                  | 9                  | 21                   |  |
| Units: 0-100                           |                     |                    |                      |  |
| arithmetic mean (full range (min-max)) | 81.6 (53.6 to 92.9) | 71.8 (42.9 to 100) | 77.4 (42.9 to 100)   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: KOOS clinical scores: PAIN

End point title KOOS clinical scores: PAIN

End point description:

End point type Secondary

End point timeframe:  
18 months post-surgery

| End point values                       | Arm A               | Arm B              | Treated patients     |  |
|--|---------------------|--------------------|----------------------|--|
| Subject group type                     | Reporting group     | Reporting group    | Subject analysis set |  |
| Number of subjects analysed            | 12                  | 9                  | 21                   |  |
| Units: 0-100                           |                     |                    |                      |  |
| arithmetic mean (full range (min-max)) | 78.9 (50.0 to 97.2) | 73.5 (47.2 to 100) | 76.6 (47.2 to 100)   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: KOOS clinical scores: ACTIVITY OF DAILY LIVING

End point title KOOS clinical scores: ACTIVITY OF DAILY LIVING

End point description:

End point type Secondary

End point timeframe:  
18 months post-surgery

| End point values                       | Arm A              | Arm B              | Treated patients     |  |
|--|--------------------|--------------------|----------------------|--|
| Subject group type                     | Reporting group    | Reporting group    | Subject analysis set |  |
| Number of subjects analysed            | 12                 | 9                  | 21                   |  |
| Units: 0-100                           |                    |                    |                      |  |
| arithmetic mean (full range (min-max)) | 84.6 (63.2 to 100) | 77.1 (39.7 to 100) | 81.3 (39.7 to 100)   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: KOOS Clinical scores: SPORTS & RECREATIONAL ACTIVITIES

|                        |  |
|------------------------|--|
| End point title        | KOOS Clinical scores: SPORTS & RECREATIONAL ACTIVITIES |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| 18 months post-surgery |  |

| End point values                       | Arm A           | Arm B           | Treated patients     |  |
|--|-----------------|-----------------|----------------------|--|
| Subject group type                     | Reporting group | Reporting group | Subject analysis set |  |
| Number of subjects analysed            | 12              | 9               | 21                   |  |
| Units: 0-100                           |                 |                 |                      |  |
| arithmetic mean (full range (min-max)) | 56 (0 to 90)    | 42 (0 to 100)   | 50 (0 to 100)        |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: KOOS clinical scores: QUALITY OF LIFE

|                        |                                       |
|------------------------|---------------------------------------|
| End point title        | KOOS clinical scores: QUALITY OF LIFE |
| End point description: |                                       |
| End point type         | Secondary                             |
| End point timeframe:   |                                       |
| 18 months post-surgery |                                       |

| <b>End point values</b>                | Arm A               | Arm B             | Treated patients     |  |
|--|---------------------|-------------------|----------------------|--|
| Subject group type                     | Reporting group     | Reporting group   | Subject analysis set |  |
| Number of subjects analysed            | 12                  | 9                 | 21                   |  |
| Units: 0-100                           |                     |                   |                      |  |
| arithmetic mean (full range (min-max)) | 45.8 (12.5 to 87.5) | 52.1 (6.3 to 100) | 48.5 (6.3 to 100)    |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events had to be reported during the whole study period.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Arm A (microfracture) |
|-----------------------|-----------------------|

Reporting group description:

No adverse events declared in microfracture group.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Arm B (CARTIPATCH®) |
|-----------------------|---------------------|

Reporting group description:

9 adverse events were declared in CARTIPATCH® group affecting 5 patients. 7 of them were probably related to the treatment, 2 were not. 4 of the adverse events were serious adverse events.

Serious adverse events:

- Septic arthritis
- Knee contracture probably due to rehabilitation protocol and chondral defect of medial condyle
- Infection of surgical scar, suspected septic arthritis

Adverse events:

- Fracture of contralateral ankle
- Pain, high blood pressure (not related to CARTIPATCH® graft), tachycardia (not related to CARTIPATCH® graft)
- Knee stiffness in range from 90° to full flexion due to adhesions

| Serious adverse events                            | Arm A<br>(microfracture)   | Arm B<br>(CARTIPATCH®) |  |
|---|--|------------------------|--|
| Total subjects affected by serious adverse events |  |                        |  |
| subjects affected / exposed                       | 0 / 18 (0.00%)   | 3 / 14 (21.43%)        |  |
| number of deaths (all causes)                     | 0  | 0                      |  |
| number of deaths resulting from adverse events    |  |                        |  |
| Musculoskeletal and connective tissue disorders   |  |                        |  |
| Chondral defect                                   | Additional description: Chondral defect of medial condyle                        |                        |  |
| subjects affected / exposed                       | 0 / 18 (0.00%)   | 1 / 14 (7.14%)         |  |
| occurrences causally related to treatment / all   | 0 / 0  | 1 / 1                  |  |
| deaths causally related to treatment / all        | 0 / 0  | 1 / 1                  |  |
| Knee contracture                                  | Additional description: Knee contracture probably due to rehabilitation protocol |                        |  |
| subjects affected / exposed                       | 0 / 18 (0.00%)   | 1 / 14 (7.14%)         |  |
| occurrences causally related to treatment / all   | 0 / 0  | 1 / 1                  |  |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0                  |  |
| Infections and infestations                       |  |                        |  |

|   |  |                |  |
|---|--|----------------|--|
| Septic arthritis                                |  |                |  |
| subjects affected / exposed                     | 0 / 18 (0.00%)   | 1 / 14 (7.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |
| Incision site infection                         | Additional description: Infection of surgical scar with suspected septic arthritis |                |  |
| subjects affected / exposed                     | 0 / 18 (0.00%)   | 1 / 14 (7.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Arm A<br>(microfracture)  | Arm B<br>(CARTIPATCH®) |  |
|---|---|------------------------|--|
| Total subjects affected by non-serious adverse events |   |                        |  |
| subjects affected / exposed                           | 0 / 18 (0.00%)  | 3 / 14 (21.43%)        |  |
| Injury, poisoning and procedural complications        |   |                        |  |
| Fracture of ankle                                     | Additional description: Fracture of contralateral ankle                                   |                        |  |
| subjects affected / exposed                           | 0 / 18 (0.00%)  | 1 / 14 (7.14%)         |  |
| occurrences (all)                                     | 0   | 1                      |  |
| Cardiac disorders                                     |   |                        |  |
| High blood pressure                                   |   |                        |  |
| subjects affected / exposed                           | 0 / 18 (0.00%)  | 1 / 14 (7.14%)         |  |
| occurrences (all)                                     | 0   | 1                      |  |
| Tachycardia   |   |                        |  |
| subjects affected / exposed                           | 0 / 18 (0.00%)  | 1 / 14 (7.14%)         |  |
| occurrences (all)                                     | 0   | 1                      |  |
| General disorders and administration site conditions  |   |                        |  |
| Pain  |   |                        |  |
| subjects affected / exposed                           | 0 / 18 (0.00%)  | 1 / 14 (7.14%)         |  |
| occurrences (all)                                     | 0   | 1                      |  |
| Musculoskeletal and connective tissue disorders       |   |                        |  |
| Knee stiffness  | Additional description: Knee stiffness in range from 90° to full flexion due to adhesions |                        |  |
| subjects affected / exposed                           | 0 / 18 (0.00%)  | 1 / 14 (7.14%)         |  |
| occurrences (all)                                     | 0   | 1                      |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

|   |
|---|
| <p>The study was terminated prematurely because of difficulties in recruiting patients. The decision did not involve any safety reason.<br/>As the statistical analysis of the collected data was not performed, it is impossible to conclude on the product.</p> |
|---|

Notes: