



## Clinical trial results:

**Randomized Clinical Trial comparing the endometrial transformation with 25 mg/day of subcutaneous progesterone (Prolutex) versus 50 mg/day intramuscular progesterone (Prontogest)**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-000290-12  |
| Trial protocol           | ES              |
| Global end of trial date | 29 January 2016 |

### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 31 October 2020                                       |
| First version publication date    | 31 October 2020                                       |
| Summary attachment (see zip file) | 1412-BCN-087-AB Results (1412-BCN-087-AB Results.pdf) |

### Trial information

#### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | 1412-BCN-087-AB |
|-----------------------|-----------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02567552 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | IVI Barcelona  |
| Sponsor organisation address | Ronda del General Mitre, 14, 08017 Barcelona, Barcelona, Spain,                            |
| Public contact               | Medicina Reproductiva, Clínica IVI Barcelona, 0034 932 063 000, agustin.ballesteros@ivi.es |
| Scientific contact           | Medicina Reproductiva, Clínica IVI Barcelona, 0034 932 063 000, agustin.ballesteros@ivi.es |

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**

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 14 December 2016 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 29 January 2016  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 29 January 2016  |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

To study the predecidualización endometrial (ie, measuring the effects of progesterone in the endometrial glands and stroma in the luteal phase) and endometrial receptivity on Day 5 as gene expression, following daily administration of 25 mg / day of subcutaneous progesterone and 50 mg / day intramuscular progesterone, both for 5 days, to see if there are differences in the use of both progesterone.

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 07 April 2015 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects****Subjects enrolled per country**

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Spain: 24 |
| Worldwide total number of subjects   | 24        |
| EEA total number of subjects         | 24        |

Notes:

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**Subjects enrolled per age group**

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 24 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

1 year

### Pre-assignment

Screening details:

Female aged between 18 and 34 years

- BMI between 18 and 28 kg/m<sup>2</sup>
- Endometrial thickness > 7 mm the day of progesterone treatment initiation (day of follicular puncture)
- Follicular maturation with a single bolus of GnRH agonist
- Egg donors who undergo a cycle of ovarian stimulation in the IVI Barcelona Centre
- Egg donors selected in accor

### Period 1

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

Blinding implementation details:

Masked samples for histological evaluation and assessment of gene expression

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Prolutex |
|------------------|----------|

Arm description: -

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | Prolutex                  |
| Investigational medicinal product code |                           |
| Other name                             | Subcutaneous progesterona |
| Pharmaceutical forms                   | Injection                 |
| Routes of administration               | Subcutaneous use          |

Dosage and administration details:

25 mg/day

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Prontogest |
|------------------|------------|

Arm description: -

|  |                            |
|--|----------------------------|
| Arm type                               | Active comparator          |
| Investigational medicinal product name | Prontogest                 |
| Investigational medicinal product code |                            |
| Other name                             | Intramuscular Progesterone |
| Pharmaceutical forms                   | Injection                  |
| Routes of administration               | Intramuscular use          |

Dosage and administration details:

50 mg/day

| <b>Number of subjects in period 1</b> | Prolutex | Prontogest |
|---------------------------------------|----------|------------|
| Started                               | 12       | 12         |
| Completed                             | 12       | 11         |
| Not completed                         | 0        | 1          |
| Adverse event, non-fatal              | -        | 1          |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                                | overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 24            | 24    |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero  | 0             | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0             | 0     |  |
| Children (2-11 years)                                 | 0             | 0     |  |
| Adolescents (12-17 years)                             | 0             | 0     |  |
| Adults (18-64 years)                                  | 24            | 24    |  |
| From 65-84 years                                      | 0             | 0     |  |
| 85 years and over                                     | 0             | 0     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female  | 24            | 24    |  |
| Male  | 0             | 0     |  |

## End points

### End points reporting groups

|                                |            |
|--------------------------------|------------|
| Reporting group title          | Prolutex   |
| Reporting group description: - |            |
| Reporting group title          | Prontogest |
| Reporting group description: - |            |

### Primary: Predecidual Transformation

|   |                            |
|---|----------------------------|
| End point title   | Predecidual Transformation |
| End point description:  |                            |
| Histologic dating of the endometrium at day 5: early secretory phase, media secretory phase or late secretory phase |                            |
| End point type  | Primary                    |
| End point timeframe:  |                            |
| 5 days  |                            |

| End point values            | Prolutex        | Prontogest      |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 12              | 11              |  |  |
| Units: %                    |                 |                 |  |  |
| early secretory phase       | 1               | 2               |  |  |
| media secretory phase       | 7               | 8               |  |  |
| late secretory phase        | 4               | 1               |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Statistical Analysis for Predecidual Transformat |
| Comparison groups                       | Prolutex v Prontogest                            |
| Number of subjects included in analysis | 23   |
| Analysis specification                  | Post-hoc   |
| Analysis type                           | other <sup>[1]</sup>                             |
| P-value                                 | = 0.3395   |
| Method                                  | Chi-squared                                      |

Notes:

[1] - Pilot study

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

1 year

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 20 |
|--------------------|----|

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | Prolutex |
|-----------------------|----------|

Reporting group description: -

|                       |            |
|-----------------------|------------|
| Reporting group title | Prontogest |
|-----------------------|------------|

Reporting group description: -

| Serious adverse events                            | Prolutex       | Prontogest     |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 12 (0.00%) | 0 / 12 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |

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

| Non-serious adverse events                            | Prolutex        | Prontogest      |  |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                 |                 |  |
| subjects affected / exposed                           | 5 / 12 (41.67%) | 4 / 12 (33.33%) |  |
| General disorders and administration site conditions  |                 |                 |  |
| Discomfort in injection site                          |                 |                 |  |
| subjects affected / exposed                           | 3 / 12 (25.00%) | 0 / 12 (0.00%)  |  |
| occurrences (all)                                     | 0               | 0               |  |
| Pain in injection site                                |                 |                 |  |
| subjects affected / exposed                           | 0 / 12 (0.00%)  | 4 / 12 (33.33%) |  |
| occurrences (all)                                     | 0               | 0               |  |
| Reproductive system and breast disorders              |                 |                 |  |
| Breast inflammation                                   |                 |                 |  |
| subjects affected / exposed                           | 2 / 12 (16.67%) | 0 / 12 (0.00%)  |  |
| occurrences (all)                                     | 0               | 0               |  |



## 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

None reported