



Clinical trial results:

Subcutaneous versus intravenous basal insulin in non-critical hospitalized diabetic patients receiving total parenteral nutrition

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-003954-42 |
| Trial protocol | ES |
| Global end of trial date | 19 February 2019 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 01 April 2021 |
| First version publication date | 01 April 2021 |
| Summary attachment (see zip file) | FPS-INSUPAR-2015-01 (Resumen resultados final_FPS-INSUPAR-2015-01_19_02_19.pdf) |

Trial information

Trial identification

| | |
|-----------------------|---------------------|
| Sponsor protocol code | FPS-INSUPAR-2015-01 |
|-----------------------|---------------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Fundación Pública Andaluza Progreso y Salud |
| Sponsor organisation address | Parque Científico y Tecnológico Cartuja, Avda. Américo Vespucio, 15. Edificio S-2. 41092 Sevilla, Seville, Spain, 41092 |
| Public contact | Unidad de Apoyo a Ensayos Clínicos, Fundación Pública Andaluza Progreso y Salud, 34 955040450, gestionensayosclinicos.fps@juntadeandalucia.es |
| Scientific contact | Unidad de Apoyo a Ensayos Clínicos, Fundación Pública Andaluza Progreso y Salud, 34 955040450, gestionensayosclinicos.fps@juntadeandalucia.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:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 19 February 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 February 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 February 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Analyze the degree of metabolic control achieved by a pattern of regular insulin in the stock of parenteral nutrition (PN) plus glargine subcutaneous insulin, compared to regular insulin in the stock of PN.

Protection of trial subjects:

This trial should be conducted in accordance with the protocol following the sponsor's SOPs. The trial shall be conducted in accordance with the recommendations for Clinical Trials and Investigational Product Evaluation in humans, as contained in the Declaration of Helsinki, as revised at successive World Assemblies (WMA, 2013), and the current Spanish Clinical Trial Legislation (RD 1090/2015). The ICH-GCP standards (CPMP/ICH/135/95) will be followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 February 2016 |
| 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: 161 |
| Worldwide total number of subjects | 161 |
| EEA total number of subjects | 161 |

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) | 31 |
| From 65 to 84 years | 117 |

| | |
|-------------------|----|
| 85 years and over | 13 |
|-------------------|----|

Subject disposition

Recruitment

Recruitment details:

- Adults (>18 years)
- Diagnosed with diabetes mellitus.
- Admitted to a non-intensive care hospital ward.
- Who have an indication for total parenteral nutritional support (TPN, understood as that which covers more than 70% of the estimated daily parenteral requirements) and it is foreseen that they will require it for a minimum of 5 days.

Pre-assignment

Screening details:

- Adults (>18 years)
- Diagnosed with diabetes mellitus.
- Admitted to a non-intensive care hospital ward.
- Who have an indication for total parenteral nutritional support (TPN, understood as that which covers more than 70% of the estimated daily parenteral requirements) and it is foreseen that they will require it for a minimum of 5 days.

Period 1

| | |
|------------------------------|---------------------------|
| Period 1 title | Recruitment and follow up |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Experimental |

Arm description: -

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Insulin glargine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Single-dose insulin glargine (basal component) + regular insulin within NPT (prandial component). Fifty percent of the total calculated insulin dose would be administered as regular insulin within the NPT bag. The other 50 % of the total calculated insulin dose would be administered as subcutaneous basal insulin (insulin glargine in unidose).

| | |
|------------------|---------|
| Arm title | Control |
|------------------|---------|

Arm description: -

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Regular Insuline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Parenteral use |

Dosage and administration details:

Regular insulin within NPT (basal + prandial component). The total calculated insulin dose would be administered as regular insulin within the NPT bag.

| Number of subjects in period 1 | Experimental | Control |
|--------------------------------|--------------|---------|
| Started | 81 | 80 |
| Completed | 81 | 80 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Data analysis |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|--|------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Experimental |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Insulin glargine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Single-dose insulin glargine (basal component) + regular insulin within NPT (prandial component). Fifty percent of the total calculated insulin dose would be administered as regular insulin within the NPT bag. The other 50 % of the total calculated insulin dose would be administered as subcutaneous basal insulin (insulin glargine in unidose).

| | |
|--|------------------------|
| Arm title | Control |
| Arm description: - | |
| Arm type | Active comparator |
| Investigational medicinal product name | Regular Insuline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Parenteral use |

Dosage and administration details:

Regular insulin within NPT (basal + prandial component). The total calculated insulin dose would be administered as regular insulin within the NPT bag.

| Number of subjects in period 2 | Experimental | Control |
|---------------------------------------|--------------|---------|
| Started | 81 | 80 |
| Completed | 81 | 80 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|--------------|
| Reporting group title | Experimental |
| Reporting group description: - | |
| Reporting group title | Control |
| Reporting group description: - | |

| Reporting group values | Experimental | Control | Total |
|------------------------|--------------|---------|-------|
| Number of subjects | 81 | 80 | 161 |
| Age categorical | | | |
| Units: Subjects | | | |
| 18 years and over | 81 | 80 | 161 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 70.8 | 71.2 | - |
| standard deviation | ± 9 | ± 10.8 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 28 | 23 | 51 |
| Male | 53 | 57 | 110 |
| Insulin patients | | | |
| Units: Subjects | | | |
| Insulin patients | 21 | 25 | 46 |
| Non-insulin patients | 60 | 55 | 115 |
| BMI | | | |
| Units: kg/m2 | | | |
| arithmetic mean | 26.8 | 27.6 | - |
| standard deviation | ± 4.8 | ± 6.5 | - |
| Duration of diabetes | | | |
| Units: Years | | | |
| arithmetic mean | 12.2 | 10.1 | - |
| standard deviation | ± 8.5 | ± 7.3 | - |
| HbA1c | | | |
| Units: HbA1c | | | |
| arithmetic mean | 6.6 | 6.6 | - |
| standard deviation | ± 1.1 | ± 1 | - |
| Albumin | | | |
| Units: Albumin | | | |
| arithmetic mean | 2.5 | 2.8 | - |
| standard deviation | ± 0.5 | ± 0.5 | - |
| NPT | | | |
| Units: Days | | | |
| arithmetic mean | 10.49 | 9.72 | - |
| standard deviation | ± 7.35 | ± 6.80 | - |
| Estimated requirements | | | |
| Units: kcal/day | | | |
| arithmetic mean | 1632.7 | 1602.3 | - |
| standard deviation | ± 242.0 | ± 218.4 | - |

End points

End points reporting groups

| | |
|--------------------------------|--------------|
| Reporting group title | Experimental |
| Reporting group description: - | |
| Reporting group title | Control |
| Reporting group description: - | |
| Reporting group title | Experimental |
| Reporting group description: - | |
| Reporting group title | Control |
| Reporting group description: - | |

Primary: Degree of metabolic control

| | |
|------------------------|--|
| End point title | Degree of metabolic control ^[1] |
| End point description: | |

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| During the study | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not all the required data is available. However, the final results report is attached, explaining the statistical analysis carried out.

| End point values | Experimental | Control | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 80 | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| <70 mg/dL | 1.52 (± 3.04) | 0.6 (± 1.91) | | |
| 70-180 mg/dL | 61.24 (± 30.01) | 66.73 (± 27.16) | | |
| >180 mg/dL | 37.24 (± 30.54) | 32.67 (± 27.20) | | |
| 70-100 mg/dL | 7.23 (± 9.15) | 7.68 (± 10.60) | | |
| 100-140 mg/dL | 27.57 (± 23.29) | 29.21 (± 20.27) | | |
| 140-180 mg/dL | 25.36 (± 15.55) | 29.12 (± 15.87) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Variability and hypoglycaemia

| | |
|-----------------|--|
| End point title | Variability and hypoglycaemia ^[2] |
|-----------------|--|

End point description:

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| During the study | |

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not all the required data is available. However, the final results report is attached, explaining the statistical analysis carried out.

| End point values | Experimental | Control | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 80 | | |
| Units: mg/dL, %, hypoglycaemia/100 days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Standard deviation (mg/dL) | 43.44 (± 18.97) | 40.39 (± 16.04) | | |
| Variation coefficient (%) | 25.46 (± 10.23) | 24.49 (± 8.08) | | |
| Hypoglycaemia/100 days of TPN | 4.89 (± 9.79) | 1.88 (± 6.05) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Patients with glucose ≤ 70 mg/dL

| | |
|------------------------|---|
| End point title | Patients with glucose ≤ 70 mg/dL ^[3] |
| End point description: | |

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| During the study | |

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not all the required data is available. However, the final results report is attached, explaining the statistical analysis carried out.

| End point values | Experimental | Control | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 80 | | |
| Units: Participants | | | | |
| Patients with glucose ≤ 70 mg/dL | 21 | 9 | | |
| Patients with glucose > 70 mg/dL | 60 | 71 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Patients with glucose < 54 mg/dL

End point title Patients with glucose < 54 mg/dL^[4]

End point description:

End point type Primary

End point timeframe:

During the study

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not all the required data is available. However, the final results report is attached, explaining the statistical analysis carried out.

| End point values | Experimental | Control | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 80 | | |
| Units: Participants | | | | |
| Patients with glucose < 54 mg/dL | 7 | 1 | | |
| Patients with glucose ≥ 54 mg/dL | 74 | 79 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Severe hypoglycaemia

End point title Severe hypoglycaemia^[5]

End point description:

End point type Primary

End point timeframe:

During the study

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not all the required data is available. However, the final results report is attached, explaining the statistical analysis carried out.

| End point values | Experimental | Control | | |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 80 | | |
| Units: Number of hypoglycaemia | | | | |
| Severe hypoglycaemia | 0 | 0 | | |
| No severe hypoglycaemia | 81 | 80 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Mean capillary glucose

End point title Mean capillary glucose^[6]

End point description:

End point type Primary

End point timeframe:

During the study

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Not all the required data is available. However, the final results report is attached, explaining the statistical analysis carried out.

| End point values | Experimental | Control | | |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 80 | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Mean capillary glucose | 172.52 (\pm 43.64) | 165.26 (\pm 35.43) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin dose

End point title Insulin dose

End point description:

End point type Secondary

End point timeframe:

During the study

| End point values | Experimental | Control | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 80 | | |
| Units: IU and IU/kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| Total daily insulin (IU) | 48.91 (\pm 25.81) | 44.18 (\pm 25.29) | | |
| Corrective daily insulin (IU) | 11.45 (\pm 7.84) | 9.87 (\pm 8.03) | | |
| Total daily insulin (IU/kg) | 0.69 (\pm 0.37) | 0.62 (\pm 0.32) | | |
| Corrective daily insulin (IU/kg) | 0.16 (\pm 0.11) | 0.14 (\pm 0.12) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean post-TPN blood glucose

| | |
|-----------------|-----------------------------|
| End point title | Mean post-TPN blood glucose |
|-----------------|-----------------------------|

End point description:

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

End point timeframe:

During the study

| End point values | Experimental | Control | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 80 | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| capillar post-TPN 48 hours | 141.67 (± 43.77) | 160.32 (± 45.07) | | |
| capillar post-TPN day 1 | 143.09 (± 53.76) | 161.31 (± 47.69) | | |
| capillar post-TPN day 2 | 143.33 (± 39.75) | 160.61 (± 47.30) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

During the study

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 19 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | both groups |
|-----------------------|-------------|

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: 112 non-serious adverse events were detected, but it is not specified exactly which ones.

| Serious adverse events | both groups | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 24 / 161 (14.91%) | | |
| number of deaths (all causes) | 18 | | |
| number of deaths resulting from adverse events | | | |
| Blood and lymphatic system disorders | | | |
| Arterial Bleeding | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oligoanuria and hypotension. Analytical deterioration | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Reintervention with anastomosis and ileostomy | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Jejunostomy loop ischaemia | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute lung oedema | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Death | | | |
| subjects affected / exposed | 18 / 161 (11.18%) | | |
| occurrences causally related to treatment / all | 0 / 18 | | |
| deaths causally related to treatment / all | 0 / 18 | | |
| Dehiscence sutures haematoma in splenic cell | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Severe hypoglycaemia | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cervical flap necrosis, haemorrhage and infection | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Desaturation | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 161 (0.62%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 4 %

| | | | |
|---|-----------------|--|--|
| Non-serious adverse events | both groups | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 28 July 2016 | <ul style="list-style-type: none">- Updating of the regulations governing clinical trials from Royal Decree 223/2004 to Royal Decree 1090/2015.- Addition of the protocol acceptance signature sheet by the principal investigator of each centre.- Addition of new abbreviations.- Updating of the study calendar.- Modification of section 2.6 Research Ethics Committee that has assessed the trial.- Change of Principal Investigator at the Hospital Universitario Severo Ochoa centre.- Change of Principal Investigator at the Hospital Universitario Virgen de la Arrixaca.- Modification of section 6.5 Withdrawal criteria and planned analysis of withdrawals and abandonments.- Modification of section 7.2 Safety assessment. |
| 18 April 2017 | <ul style="list-style-type: none">- Change of Principal Investigator at the Virgen del Rocío University Hospital.- Elimination of the centre Hospital de Cabueñes.- Modification of section 2.7 Trial duration.- Modification of section 7.3 Trial conduct.- Modification of the schedule of visits.- Change of minimum starting dose from 0.3 to 0.2 IU/kg. |
| 01 June 2017 | <ul style="list-style-type: none">- Enlargement of centres: inclusion of the centre "Hospital Universitario Central de Asturias". |
| 26 September 2017 | <ul style="list-style-type: none">- Change of Principal Investigator at the Complejo Asistencial Universitario de León centre.- Extension of the trial duration |

Notes:

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.

As we focus on people with non-critical type 2 diabetes mellitus we cannot apply the conclusions to another group of patients. The sample size was calculated to detect differences in mean capillary glucose but not in complications.

Notes: