

**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
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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

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
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Arm title	Experimental
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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
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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
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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/m ²			
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]
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End point description:

End point type	Primary
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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]
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End point description:

End point type	Primary
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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 (± 43.64)	165.26 (± 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 (± 25.81)	44.18 (± 25.29)		
Corrective daily insulin (IU)	11.45 (± 7.84)	9.87 (± 8.03)		
Total daily insulin (IU/kg)	0.69 (± 0.37)	0.62 (± 0.32)		
Corrective daily insulin (IU/kg)	0.16 (± 0.11)	0.14 (± 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19
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Reporting groups

Reporting group title	both groups
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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: