

**Clinical trial results:****Phase IV Study to Evaluate the Safety and Efficacy of the Treatment of Hyperglycemia with Gla-300 in Basal-Bolus Regimen in Hospitalised Type 2 Diabetes Mellitus (T2D) Patients Poorly Controlled with Basal Insulin and/or Non-Insulin Treatments and Therapy Intensification at Discharge with Basal Insulin****Summary**

| | |
|--------------------------|----------------|
| EudraCT number | 2015-004715-20 |
| Trial protocol | ES |
| Global end of trial date | 17 July 2018 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 01 August 2019 |
| First version publication date | 01 August 2019 |

Trial information**Trial identification**

| | |
|-----------------------|-------------|
| Sponsor protocol code | GLARGL07710 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | STUDY NAME: COBALTA |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sanofi aventis recherche & développement |
| Sponsor organisation address | 1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380 |
| Public contact | Trial Transparency Team, Sanofi aventis recherche & développement, contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi aventis recherche & développement, contact-US@sanofi.com |

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 | 01 October 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 July 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of therapy intensification on discharge with basal insulin in hospitalized type 2 diabetes subjects poorly controlled with basal insulin and/or non-insulin antidiabetic agents (glycated hemoglobin [HbA1c] \geq 8.0% on admission) measured by the decrease in HbA1c at 6 months post-discharge.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

During hospitalization, the treatment regimen consisted of a basal-bolus-correction (BBC) insulin therapy. The initial total daily insulin dose was calculated according to the site protocol and distributed 50% as bolus insulin and 50% as basal insulin (Gla-300). Both insulins were titrated according to a pre-defined titration algorithm. Non-insulin antidiabetic drugs (NIADs) were retired during hospitalization and re-established at hospital discharge according to clinical criteria.

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 10 June 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: 112 |
| Worldwide total number of subjects | 112 |
| EEA total number of subjects | 112 |

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) | 27 |
| From 65 to 84 years | 71 |
| 85 years and over | 14 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 15 sites in Spain. A total of 115 subjects were screened between 10 June 2016 and 20 December 2017, of which 3 subjects were screening failure. Screen failures were mainly due to exclusion criteria met.

Pre-assignment

Screening details:

A total of 112 subjects were included in the study.

Period 1

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

Arms

| | |
|------------------|---------------------------|
| Arm title | Insulin glargine 300 U/mL |
|------------------|---------------------------|

Arm description:

Subjects received Insulin glargine 300 U/mL once daily for around 26 weeks (maximum 2 weeks hospitalization and 6 months follow-up).

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Insulin glargine |
| Investigational medicinal product code | HOE901 |
| Other name | Toujeo® |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

HOE901-U300 was administered by subcutaneous injection once daily in the evening using a pre-filled pen. The dose was self-titrated every 3-4 days to achieve fasting blood glucose levels in the target range of 90-140mg/dL.

| | |
|---------------------------------------|---------------------------|
| Number of subjects in period 1 | Insulin glargine 300 U/mL |
| Started | 112 |
| Completed | 93 |
| Not completed | 19 |
| Death | 6 |
| Discontinuation of study treatment | 1 |
| Adverse event | 2 |
| Not allowed concomitant medication | 1 |
| Revocation of informed consent | 2 |
| Posterior diagnose of cancer | 1 |
| Lost to follow-up | 4 |
| Exclusion criteria | 1 |

| | |
|--------------------|---|
| Protocol deviation | 1 |
|--------------------|---|

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description:

Subjects received Insulin glargine 300 U/mL once daily for around 26 weeks (maximum 2 weeks hospitalization and 6 months follow-up).

| Reporting group values | Overall Study | Total | |
|---|---------------|-------|--|
| Number of subjects | 112 | 112 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 72.3 | | |
| standard deviation | ± 10.8 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 44 | 44 | |
| Male | 68 | 68 | |
| Body Weight | | | |
| Units: kilogram (kg) | | | |
| arithmetic mean | 80.1 | | |
| standard deviation | ± 16.6 | - | |
| Body Mass Index | | | |
| Units: kilogram per square meter (kg/m ²) | | | |
| arithmetic mean | 30.1 | | |
| standard deviation | ± 5.9 | - | |
| Hemoglobin A1C (HbA1C) | | | |
| Units: percentage of hemoglobin | | | |
| arithmetic mean | 8.9 | | |
| standard deviation | ± 0.7 | - | |
| Fasting Blood Glucose | | | |
| Units: milligrams per deciliter (mg/dL) | | | |
| arithmetic mean | 205.4 | | |
| standard deviation | ± 83.9 | - | |

End points

End points reporting groups

| | |
|--|---------------------------|
| Reporting group title | Insulin glargine 300 U/mL |
| Reporting group description: Subjects received Insulin glargine 300 U/mL once daily for around 26 weeks (maximum 2 weeks hospitalization and 6 months follow-up). | |

Primary: Change From Discharge in Glycated Hemoglobin (HbA1c) to Month 6

| | |
|-----------------|--|
| End point title | Change From Discharge in Glycated Hemoglobin (HbA1c) to Month 6 ^[1] |
|-----------------|--|

End point description:

Change in HbA1c was calculated by subtracting discharge value from Month 6 value. Analysis was performed on intent-to-treat (ITT) population that included all subjects who received at least one dose of Gla-300 study insulin and had a primary or secondary measure of effectiveness evaluation both at baseline and in at least one follow-up visit.

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

End point timeframe:

Discharge, Month 6 (post discharge)

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: As the endpoint contains single arm, no statistical analysis is provided.

| | | | | |
|--------------------------------------|---------------------------|--|--|--|
| End point values | Insulin glargine 300 U/mL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 94 | | | |
| Units: percentage of HbA1c | | | | |
| arithmetic mean (standard deviation) | 1.6 (± 1.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Hospital Admission in 7-Point Capillary Glycaemia to Hospital Discharge

| | |
|-----------------|--|
| End point title | Mean Change From Hospital Admission in 7-Point Capillary Glycaemia to Hospital Discharge |
|-----------------|--|

End point description:

7-Point Capillary blood glucose were measured at the following 7 time points at baseline (hospital admission) and hospital discharge: before breakfast, 2 hours after breakfast, before lunch, 2 hours after lunch, before dinner, 2 hours after dinner, at bedtime. Analysis was performed on ITT population. Here, "n" signifies number of subjects with available data for specified category.

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

End point timeframe:

Baseline (hospital admission), discharge

| End point values | Insulin glargine 300 U/mL | | | |
|---|------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 94 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Glycaemia before breakfast (n= 87) | 25.1 (± 66.6) | | | |
| Glycaemia 2 hours after breakfast (n=61) | 44.0 (± 87.3) | | | |
| Food glucose before lunch (n=90) | 43.6 (± 70.6) | | | |
| Glycaemia 2 hours after lunch (n= 68) | 63.0 (± 85.4) | | | |
| Glycaemia before dinner (n= 91) | 53.8 (± 83.4) | | | |
| Glycaemia 2 hours after dinner (n= 66) | 43.4 (± 81.1) | | | |
| Glycaemia at bedtime (n= 76) | 47.9 (± 78.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Hospital Admission in Fasting Plasma Glucose (FPG) to Discharge, Month 3 and Month 6

| | |
|--|---|
| End point title | Mean Change From Hospital Admission in Fasting Plasma Glucose (FPG) to Discharge, Month 3 and Month 6 |
| End point description: | |
| Mean Change in FPG was calculated by subtracting baseline (hospital admission) value from hospital discharge value, Month 3 value and Month 6 value. Analysis was performed on ITT population. Here, 'n' signifies number of subjects with available data for each specified category. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (hospital admission), discharge, Month 3, Month 6 (post discharge) | |

| End point values | Insulin glargine 300 U/mL | | | |
|--------------------------------------|------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 94 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Discharge (n= 94) | 51.5 (± 90.9) | | | |
| Month 3 (n=92) | 68.2 (± 96.0) | | | |
| Month 6 (n=93) | 77.6 (± 86.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Diabetes Treatment Satisfaction Questionnaire (DTSQ) Mean Score at Month 6

| | |
|-----------------|--|
| End point title | Diabetes Treatment Satisfaction Questionnaire (DTSQ) Mean Score at Month 6 |
|-----------------|--|

End point description:

The DTSQs is a validated questionnaire to assess subject's satisfaction with their diabetes treatment. Total DTSQ score consists of the sum of 6 items (Q1 and Q4 - Q8), each rated on a 7-point scale (from 0 to 6). Total DTSQ score ranged from 0 (very dissatisfied) to 36 (very satisfied); higher score = more satisfaction. Analysis was performed on ITT population. Here, subjects analysed signifies subjects with available data for this endpoint.

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

End point timeframe:

Month 6 (post discharge)

| | | | | |
|--------------------------------------|------------------------------|--|--|--|
| End point values | Insulin glargine 300 U/mL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 91 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | 31.0 (± 4.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Body Weight From Discharge to Month 6

| | |
|-----------------|---|
| End point title | Change in Body Weight From Discharge to Month 6 |
|-----------------|---|

End point description:

Change in body weight was calculated by subtracting discharge value from Month 6 value. Analysis was performed on safety population that consisted of all included all subjects who received at least one dose of the Gla-300 study insulin. Here, subjects analysed signifies number of subjects with available data for this endpoint.

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

End point timeframe:

Discharge, Month 6 (post discharge)

| | | | | |
|--------------------------------------|------------------------------|--|--|--|
| End point values | Insulin glargine 300 U/mL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 86 | | | |
| Units: kilogram (Kg) | | | | |
| arithmetic mean (standard deviation) | 0.0 (± 6.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Confirmed or Severe Hypoglycemia During Hospitalisation and at Month 6 After Discharge

| | |
|-----------------|--|
| End point title | Number of Subjects With Confirmed or Severe Hypoglycemia During Hospitalisation and at Month 6 After Discharge |
|-----------------|--|

End point description:

Severe hypoglycemia was an event in which the subject required the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions. Analysis was performed on safety population. Here, 'n' = subjects with available data for each specified category.

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

End point timeframe:

From Baseline to discharge, Month 6 (post discharge)

| | | | | |
|--------------------------------|------------------------------|--|--|--|
| End point values | Insulin glargine 300 U/mL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 112 | | | |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| During hospitalization (n=112) | 28 | | | |
| Month 6 (n=93) | 55 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Re-hospitalisations or Emergency Visits at Month 6 After Discharge

| | |
|-----------------|--|
| End point title | Number of Re-hospitalisations or Emergency Visits at Month 6 After Discharge |
|-----------------|--|

End point description:

Analysis was performed on safety population. Here, subjects analysed signifies number of subjects with available data for this endpoint.

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

End point timeframe:

Month 6 (post discharge)

| | | | | |
|-----------------------------|------------------------------|--|--|--|
| End point values | Insulin glargine 300 U/mL | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45 | | | |
| Units: number of visits | | | | |
| number (not applicable) | | | | |
| Re-hospitalization | 46 | | | |
| Emergency visits | 64 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) were collected from signature of the informed consent form up to the final visit (Month 6) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs and deaths are treatment-emergent AEs that developed/worsened and deaths that occurred during the time from first study drug intake up to Month 6. Analysis was performed on safety population.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Insulin glargine 300 U/mL |
|-----------------------|---------------------------|

Reporting group description:

Subjects received Insulin glargine 300 U/mL once daily for 24 weeks. The dose was self-titrated every 3-4 days to achieve fasting self-measured plasma glucose (SMPG) in the target range of 80-110 mg/dL.

| Serious adverse events | Insulin glargine 300 U/mL | | |
|---|---------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 37 / 112 (33.04%) | | |
| number of deaths (all causes) | 6 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder Neoplasm | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Colon Cancer | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung Neoplasm | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vascular disorders | | | |

| | | | |
|---|-----------------|--|--|
| Peripheral Ischaemia | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pulmonary Embolism | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Varicose Ulceration | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 7 / 112 (6.25%) | | |
| occurrences causally related to treatment / all | 0 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary Mass | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Respiratory Failure | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory Tract Infection | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillar Hypertrophy | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Intervertebral Discitis | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute Myocardial Infarction | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Angina Pectoris | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac Failure | | | |
| subjects affected / exposed | 4 / 112 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac Failure Acute | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Cardiac Failure Chronic | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac Failure Congestive | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac Tamponade | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiogenic Shock | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Left Ventricular Failure | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial Ischaemia | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Brain Stem Stroke | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhagic Stroke | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoxic-Ischaemic Encephalopathy | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lacunar Infarction | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Plasma Cell Myeloma | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Gastrointestinal disorders | | | |
| Colitis Ischaemic | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enteritis Infectious | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Diabetic Ulcer | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Skin Ulcer | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Chronic Kidney Disease | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary Tract Infection Fungal | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral Discitis | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pelvic Fracture | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Klebsiella Sepsis | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Stoma Site Infection | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|---|---------------------------|--|--|
| Non-serious adverse events | Insulin glargine 300 U/mL | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 112 (28.57%) | | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 9 / 112 (8.04%) | | |
| occurrences (all) | 10 | | |
| Renal and urinary disorders | | | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 14 / 112 (12.50%) | | |
| occurrences (all) | 18 | | |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 11 / 112 (9.82%) | | |
| occurrences (all) | 16 | | |
| Vitamin D Deficiency | | | |
| subjects affected / exposed | 6 / 112 (5.36%) | | |
| occurrences (all) | 6 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 18 January 2016 | Following changes were made: Change in exclusion criteria: Following criteria added: - Subjects that required intensification with rapid-acting insulin at discharge. - Pregnant, lactating women or fertile women not using contraceptive methods during study. - Subjects unable or unwilling to sign informed consent. |
| 04 October 2016 | - Change in inclusion criteria: -Minimum expected hospitalization length moved from 7 to 5 days. - Criteria removed: Maximum age of 75 years. - Change in exclusion criteria:- Criteria added: subjects who were unable to titrate or manage correctly the insulin treatment due to their medical condition. - Non-allowed treatments: -Corticosteroid treatment limitations were clarified: Oral or parenteral corticosteroids were not allowed. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported