



Clinical trial results:

A Multi-Center, Open-Label, Single-Arm, Multiple Dose Study With HOE901-U300 to Assess the Ease of Use And Safety of a New U300 Pen Injector in Insulin-Naive Patients With T2DM

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-001253-16 |
| Trial protocol | DE |
| Global end of trial date | 20 November 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 15 May 2016 |
| First version publication date | 15 May 2016 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | PDY14065 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02227212 |
| WHO universal trial number (UTN) | U1111-1155-7309 |

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 | 05 December 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 November 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the ease of use of the U300 pen injector in pen-naïve and insulin-naïve type 2 diabetes mellitus (T2DM) subjects in a 4-week once-daily dosing regimen with HOE901-U300.

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:

Subjects continued their background anti-hyperglycemic treatment during the study except sulfonylureas, glinides and other anti-hyperglycemic agents not approved in combination with Insulin.

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 22 August 2014 |
| 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 | Germany: 40 |
| Worldwide total number of subjects | 40 |
| EEA total number of subjects | 40 |

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) | 17 |
| From 65 to 84 years | 23 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 7 centres in Germany. A total of 51 subjects were screened between 22 August 2014 and 30 September 2014.

Pre-assignment

Screening details:

Of 51 screened subjects, 43 subjects were enrolled and 40 were treated.

Period 1

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

Arms

| | |
|------------------|-------------|
| Arm title | HOE901-U300 |
|------------------|-------------|

Arm description:

HOE901-U300 for 4 weeks using U300 pen injector.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Insulin Glargine U300 |
| Investigational medicinal product code | HOE901-U300 |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

HOE901-U300 (Insulin Glargine 300 U/ml) was self-administered once daily in evening. Subjects were individually up-titrated weekly from dose 0.2 U/kg seeking a fasting self-monitored plasma glucose (SMPG) in the range of 80 to 100 mg/dL/day (4.4 to 5.6 mmol/L). The injection time was fixed at the baseline visit and was maintained for the duration of the study with +/-1 hour window.

| | |
|---------------------------------------|-------------|
| Number of subjects in period 1 | HOE901-U300 |
| Started | 40 |
| Completed | 40 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | HOE901-U300 |
|-----------------------|-------------|

Reporting group description:

HOE901-U300 for 4 weeks using U300 pen injector.

| Reporting group values | HOE901-U300 | Total | |
|------------------------|-------------|-------|--|
| Number of subjects | 40 | 40 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 66.2 | | |
| standard deviation | ± 9.8 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 21 | 21 | |
| Male | 19 | 19 | |

End points

End points reporting groups

| | |
|--|-------------|
| Reporting group title | HOE901-U300 |
| Reporting group description: HOE901-U300 for 4 weeks using U300 pen injector. | |

Primary: Percentage of Subjects with an Excellent/Good Responses on Ease of Use/Ease of Learning Questionnaires

| | |
|-----------------|---|
| End point title | Percentage of Subjects with an Excellent/Good Responses on Ease of Use/Ease of Learning Questionnaires ^[1] |
|-----------------|---|

End point description:

The questionnaire consists of 8 questions to assess ease of use and 4 questions to assess ease of learning, ease of use in general, overall assessment of the pen, and does the subject recommend the pen. The responses for the first 11 questions were assessed on a 5-point Likert scale ranging from 1 (excellent) to 5 (very poor) about how easy it was to learn and use the pen device. The response of last question (Subject's recommendation of U300 pen injector) was evaluated in the form of 'Yes' or 'No' and % of subjects answering "yes" were reported. Analysis was performed on safety population, which included all enrolled subjects exposed to at least one dose of investigational medicinal product (IMP).

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

End point timeframe:

Baseline, Week 4

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: Data were descriptive in nature, hence statistical analysis could not be provided.

| End point values | HOE901-U300 | | | |
|---|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Ease of selecting the dose (Baseline) | 92.3 | | | |
| Ease of selecting the dose (Week 4) | 95 | | | |
| Ease of correcting a misdialled dose (Baseline) | 97.4 | | | |
| Ease of correcting a misdialled dose (Week 4) | 97.5 | | | |
| Ease of reading the insulin dose (Baseline) | 84.6 | | | |
| Ease of reading the insulin dose (Week 4) | 92.5 | | | |
| Ease of feeling/hearing dialing clicks (Baseline) | 76.9 | | | |
| Ease of feeling/hearing dialing clicks (Week 4) | 85 | | | |
| Force/effort needed to inject insulin (Baseline) | 89.7 | | | |
| Force/effort needed to inject insulin (Week 4) | 95 | | | |
| Smoothness/gentleness of injection (Baseline) | 89.7 | | | |
| Smoothness/gentleness of injection (Week 4) | 92.5 | | | |

| | | | | |
|--|------|--|--|--|
| Ease of knowing injection if complete (Baseline) | 74.4 | | | |
| Ease of knowing injection if complete (Week 4) | 85 | | | |
| Ease of reading remaining insulin (Baseline) | 59 | | | |
| Ease of reading remaining insulin (Week 4) | 90 | | | |
| Ease of learning (Baseline) | 89.7 | | | |
| Ease of learning (Week 4) | 95 | | | |
| General ease of use (Baseline) | 92.3 | | | |
| General ease of use (Week 4) | 97.5 | | | |
| Overall assessment (Baseline) | 89.7 | | | |
| Overall assessment (Week 4) | 95 | | | |
| Would you recommend U300 pen injector (Baseline) | 100 | | | |
| Would you recommend U300 pen injector (Week 4) | 97.5 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Treatment Satisfaction Score using Diabetes Treatment Satisfaction Questionnaire status (DTSQs)

| | |
|-----------------|---|
| End point title | Change from Baseline in Total Treatment Satisfaction Score using Diabetes Treatment Satisfaction Questionnaire status (DTSQs) |
|-----------------|---|

End point description:

DTSQs is a validated questionnaire designed to measure total diabetes treatment satisfaction and perceived frequency of hyper and hypoglycemia. It consists of 8 questions which are answered on a 7-point Likert scale with responses ranging from 0 (very dissatisfied) to 6 (very satisfied). A total treatment satisfaction score range between 0 and 36 was calculated as the sum of the following single items: Item 1 (current treatment), Item 4 (convenience), Item 5 (flexibility), Item 6 (understanding), Item 7 (recommend), and Item 8 (continue). Analysis was performed on safety population. Number of subjects analysed = subjects with DTSQs assessment at specified time-points.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 4 | |

| | | | | |
|--------------------------------------|-----------------|--|--|--|
| End point values | HOE901-U300 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 39 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | 1.13 (± 6.79) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Fasting Plasma Glucose (FPG) from Baseline to Week 4

| | |
|-----------------|--|
| End point title | Change in Fasting Plasma Glucose (FPG) from Baseline to Week 4 |
|-----------------|--|

End point description:

Subjects were self-monitored their FPG as usually done in the standard care after initiating an insulin treatment in insulin-naïve subjects. Analysis was performed on safety population. Number of subjects analysed = subjects with FPG assessment at specified time-points.

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

End point timeframe:

Baseline, Week 4

| | | | | |
|--------------------------------------|-----------------|--|--|--|
| End point values | HOE901-U300 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 38 | | | |
| Units: mmol/L | | | | |
| arithmetic mean (standard deviation) | -2.34 (± 2.54) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Product Technical Complaints (PTC)

| | |
|-----------------|--|
| End point title | Number of subjects with Product Technical Complaints (PTC) |
|-----------------|--|

End point description:

The incidences PTC with the new U300 pen injector were assessed using PTC forms. Any malfunction of the U300 pen injector whether or not associated with an AE, must have been reported to the monitoring team on a PTC form. Analysis was performed on safety population.

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

End point timeframe:

From Baseline to Week 4

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | HOE901-U300 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40 | | | |
| Units: Subjects | | | | |
| number (not applicable) | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Daily Insulin Dose to Week 4

| | |
|-----------------|--|
| End point title | Change from Baseline in Daily Insulin Dose to Week 4 |
|-----------------|--|

End point description:

Analysis was performed on safety population.

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

End point timeframe:

Baseline, Week 4

| | | | | |
|--------------------------------------|-----------------|--|--|--|
| End point values | HOE901-U300 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 39 | | | |
| Units: U/kg | | | | |
| arithmetic mean (standard deviation) | 0.15 (± 0.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Hypoglycemia Events

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Hypoglycemia Events |
|-----------------|---|

End point description:

Hypoglycemia events included: Severe (required assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions) ; Documented symptomatic (typical symptoms of hypoglycemia were accompanied by plasma glucose = <3.9 mmol/L) ; Asymptomatic (not accompanied by typical symptoms of hypoglycemia but with plasma glucose = <3.9 mmol/L) ; Probable symptomatic (symptoms of hypoglycemia were not accompanied by a plasma glucose determination, but was presumably caused by plasma glucose = <3.9 mmol/L) ; And Relative (subjects reported any of the typical symptoms of hypoglycemia, and interpreted the symptoms as indicative of hypoglycemia, but with plasma glucose >3.9 mmol/L). Analysis was performed on safety population.

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

End point timeframe:

From Baseline to Week 4

| | | | | |
|-------------------------------|-----------------|--|--|--|
| End point values | HOE901-U300 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Any hypoglycemia event | 17.5 | | | |
| Asymptomatic hypoglycemia | 7.5 | | | |
| Documented hypoglycemia | 10 | | | |

| | | | | |
|-----------------------|-----|--|--|--|
| Probable hypoglycemia | 0 | | | |
| Relative hypoglycemia | 2.5 | | | |
| Severe Hypoglycemia | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Week 6) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (the time from the first IMP administration until 2 days after the last dose of IMP).

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | HOE901-U300 |
|-----------------------|-------------|

Reporting group description:

HOE901-U300 for 4 weeks using U300 pen injector.

| Serious adverse events | HOE901-U300 | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | HOE901-U300 | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 40 (27.50%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Haemangioma Of Liver | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications Contusion | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |

| | | | |
|---|---|--|--|
| Mitral Valve Incompetence subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | | |
| General disorders and administration site conditions Injection Site Haematoma subjects affected / exposed occurrences (all) Injection Site Pain subjects affected / exposed occurrences (all) Peripheral Swelling subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 1 / 40 (2.50%) 1 1 / 40 (2.50%) 1 | | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | | |
| Immune system disorders Allergy To Arthropod Sting subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | | |
| Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary Tract Infection | 1 / 40 (2.50%) 1 4 / 40 (10.00%) 4 | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 40 (2.50%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported