



## Clinical trial results:

### Albiglutide versus Placebo in insulin-treated Subjects with new-onset type 1 diabetes mellitus

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-001825-33  |
| Trial protocol           | DE IT GB        |
| Global end of trial date | 18 October 2017 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v2 (current)    |
| This version publication date  | 06 April 2019   |
| First version publication date | 28 October 2018 |
| Version creation reason        |                 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 110933 |
|-----------------------|--------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                            |
|------------------------------|------------------------------------------------------------|
| Sponsor organisation name    | GlaxoSmithKline                                            |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact               | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |

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                       | 27 April 2018 |
| Is this the analysis of the primary completion data? | No            |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 18 October 2017 |
| Was the trial ended prematurely? | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

To determine the effect of albiglutide therapy versus placebo on endogenous insulin secretion over 52 weeks when added to standard of care in subjects with new onset type 1 diabetes mellitus (NOT1DM)

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 10 October 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 | France: 6          |
| Country: Number of subjects enrolled | Germany: 8         |
| Country: Number of subjects enrolled | Italy: 10          |
| Country: Number of subjects enrolled | Spain: 29          |
| Country: Number of subjects enrolled | United Kingdom: 14 |
| Worldwide total number of subjects   | 67                 |
| EEA total number of subjects         | 67                 |

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)                      | 67 |
| From 65 to 84 years                       | 0  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

This was a multicenter study conducted at 29 sites in Europe (Spain 10, United Kingdom (UK) 9, Germany 4, France 3 and Italy 3). A total of 67 participants with New-onset type 1 diabetes mellitus (NOT1DM) were randomized.

### Pre-assignment

Screening details:

Study was terminated early as part of the decision to withdraw albiglutide for commercial reasons. Study stopped after 67 participants were randomized instead of 68 as per protocol. Impact of early termination was minimal and did not affect the interpretation of results.

### Period 1

|                              |                                                               |
|------------------------------|---------------------------------------------------------------|
| Period 1 title               | Overall Study (overall period)                                |
| Is this the baseline period? | Yes                                                           |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind                                                  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Matching placebo was administered once weekly for 52 weeks by sc injection in the abdomen, thigh or upper arm region in addition to insulin.

|                                        |                                                                 |
|----------------------------------------|-----------------------------------------------------------------|
| Arm type                               | Placebo                                                         |
| Investigational medicinal product name | Placebo                                                         |
| Investigational medicinal product code |                                                                 |
| Other name                             |                                                                 |
| Pharmaceutical forms                   | Powder and solvent for solution for injection in pre-filled pen |
| Routes of administration               | Subcutaneous use                                                |

Dosage and administration details:

Placebo was administered once weekly by SC injection in the abdomen, thigh or upper arm region in addition to insulin

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

Arm description:

Albiglutide 30 mg was administered once weekly for 52 weeks by sc injection in the abdomen, thigh or upper arm region along with insulin (Dose increased to 50 mg once weekly at Week 6 if the 30 mg weekly dose was tolerated).

|                                        |                                                                 |
|----------------------------------------|-----------------------------------------------------------------|
| Arm type                               | Experimental                                                    |
| Investigational medicinal product name | Albiglutide                                                     |
| Investigational medicinal product code |                                                                 |
| Other name                             |                                                                 |
| Pharmaceutical forms                   | Powder and solvent for solution for injection in pre-filled pen |
| Routes of administration               | Subcutaneous use                                                |

Dosage and administration details:

Albiglutide 30 mg was administered once weekly by SC injection in the abdomen, thigh or upper arm region in addition to insulin (Dose increased to 50 mg once weekly at Week 6 if the 30 mg weekly dose was tolerated)

| <b>Number of subjects in period 1</b> | Placebo | Albiglutide |
|---------------------------------------|---------|-------------|
| Started                               | 17      | 50          |
| Completed                             | 11      | 40          |
| Not completed                         | 6       | 10          |
| Consent withdrawn by subject          | 2       | 5           |
| Physician decision                    | -       | 2           |
| Adverse event, non-fatal              | 3       | -           |
| Lost to follow-up                     | 1       | 3           |

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Matching placebo was administered once weekly for 52 weeks by sc injection in the abdomen, thigh or upper arm region in addition to insulin.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Albiglutide |
|-----------------------|-------------|

Reporting group description:

Albiglutide 30 mg was administered once weekly for 52 weeks by sc injection in the abdomen, thigh or upper arm region along with insulin (Dose increased to 50 mg once weekly at Week 6 if the 30 mg weekly dose was tolerated).

| Reporting group values             | Placebo | Albiglutide | Total |
|------------------------------------|---------|-------------|-------|
| Number of subjects                 | 17      | 50          | 67    |
| Age categorical<br>Units: Subjects |         |             |       |

|                                                                         |                |                |    |
|-------------------------------------------------------------------------|----------------|----------------|----|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 22.8<br>± 3.83 | 22.7<br>± 3.72 | -  |
| Gender categorical<br>Units: Subjects                                   |                |                |    |
| Female                                                                  | 7              | 21             | 28 |
| Male                                                                    | 10             | 29             | 39 |
| Race/Ethnicity, Customized<br>Units: Subjects                           |                |                |    |
| Black or African American                                               | 0              | 1              | 1  |
| White                                                                   | 17             | 49             | 66 |
| Multi Racial                                                            | 0              | 0              | 0  |

### Subject analysis sets

|                            |                  |
|----------------------------|------------------|
| Subject analysis set title | defend-1 placebo |
|----------------------------|------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Historical placebo data from the DEFEND-1 (NCT00678886) study was used as prior knowledge.

|                                    |                  |  |  |
|------------------------------------|------------------|--|--|
| Reporting group values             | defend-1 placebo |  |  |
| Number of subjects                 | 53               |  |  |
| Age categorical<br>Units: Subjects |                  |  |  |

|                                                                         |                |  |  |
|-------------------------------------------------------------------------|----------------|--|--|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 22.7<br>± 4.00 |  |  |
|-------------------------------------------------------------------------|----------------|--|--|

|                            |    |  |  |
|----------------------------|----|--|--|
| Gender categorical         |    |  |  |
| Units: Subjects            |    |  |  |
| Female                     | 20 |  |  |
| Male                       | 33 |  |  |
| Race/Ethnicity, Customized |    |  |  |
| Units: Subjects            |    |  |  |
| Black or African American  | 2  |  |  |
| White                      | 49 |  |  |
| Multi Racial               | 2  |  |  |

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## End points

### End points reporting groups

|                                                                                                                                                                                                                                  |                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| Reporting group title                                                                                                                                                                                                            | Placebo            |
| Reporting group description:                                                                                                                                                                                                     |                    |
| Matching placebo was administered once weekly for 52 weeks by sc injection in the abdomen, thigh or upper arm region in addition to insulin.                                                                                     |                    |
| Reporting group title                                                                                                                                                                                                            | Albiglutide        |
| Reporting group description:                                                                                                                                                                                                     |                    |
| Albiglutide 30 mg was administered once weekly for 52 weeks by sc injection in the abdomen, thigh or upper arm region along with insulin (Dose increased to 50 mg once weekly at Week 6 if the 30 mg weekly dose was tolerated). |                    |
| Subject analysis set title                                                                                                                                                                                                       | defend-1 placebo   |
| Subject analysis set type                                                                                                                                                                                                        | Sub-group analysis |
| Subject analysis set description:                                                                                                                                                                                                |                    |
| Historical placebo data from the DEFEND-1 (NCT00678886) study was used as prior knowledge.                                                                                                                                       |                    |

### Primary: Mean change from Baseline in time normalized stimulated (from mixed meal tolerance test [MMTT]) 2-hour plasma C-peptide area under the curve (AUC) at Week 52

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Mean change from Baseline in time normalized stimulated (from mixed meal tolerance test [MMTT]) 2-hour plasma C-peptide area under the curve (AUC) at Week 52 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                               |
| Participants (parts) had a balanced diet consistent with dietitian's advice and made no major changes in exercise regimens. Evening before the MMTT, participants had a full meal then fasted from 9 post meridiem (pm) until MMTT was completed. Water, black coffee or tea without sugar or artificial sweeteners was allowed. Plasma glucose was measured prior to the finger-stick test and MMTT was performed only if in range > 3.9 millimoles per liter (mmol/L) [70 mg/deciliter (dL)] and ≤ 11.1 mmol/L (200 mg/dL). Baseline was defined as the last non-missing value with assessment date on or before the 1st day of study medication. Change from Baseline was calculated by subtracting Baseline value from Week 52 value. Intent-to-treat (ITT) Population comprised of all randomly assigned participants who received at least 1 dose of study medication with at least 1 post-Baseline assessment of the primary endpoint. |                                                                                                                                                               |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Primary                                                                                                                                                       |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                               |
| Baseline and Week 52                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                               |

| End point values                     | Placebo           | Albiglutide       | defend-1 placebo     |  |
|--------------------------------------|-------------------|-------------------|----------------------|--|
| Subject group type                   | Reporting group   | Reporting group   | Subject analysis set |  |
| Number of subjects analysed          | 11 <sup>[1]</sup> | 40 <sup>[2]</sup> | 53 <sup>[3]</sup>    |  |
| Units: Nanomoles per liter           |                   |                   |                      |  |
| arithmetic mean (standard deviation) |                   |                   |                      |  |
| Nanomoles per liter                  | -0.16 (± 0.366)   | -0.13 (± 0.244)   | -0.27 (± 0.314)      |  |

Notes:

[1] - Intent to treat (ITT) Population.

[2] - ITT Population.

[3] - ITT Population.

### Statistical analyses



|                                                                                                                                                                                                                                                                                                                                                                        |                                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                                                      | Statistical analysis 1         |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                      |                                |
| Analysis was performed using a Bayesian model incorporating historical placebo data using a robust mixture prior. Values above are 95% credible intervals. Probability of treatment difference (Albiglutide – Placebo) $\geq 0.2$ nmol/L = 0.097. Fifty one participants from current study and 53 participants from the DEFEND-1 study were included in the analysis. |                                |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                      | Albiglutide v Placebo          |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                                | 51                             |
| Analysis specification                                                                                                                                                                                                                                                                                                                                                 | Pre-specified                  |
| Analysis type                                                                                                                                                                                                                                                                                                                                                          | superiority                    |
| Parameter estimate                                                                                                                                                                                                                                                                                                                                                     | Mean difference (final values) |
| Point estimate                                                                                                                                                                                                                                                                                                                                                         | 0.12                           |
| Confidence interval                                                                                                                                                                                                                                                                                                                                                    |                                |
| level                                                                                                                                                                                                                                                                                                                                                                  | 95 %                           |
| sides                                                                                                                                                                                                                                                                                                                                                                  | 2-sided                        |
| lower limit                                                                                                                                                                                                                                                                                                                                                            | 0                              |
| upper limit                                                                                                                                                                                                                                                                                                                                                            | 0.24                           |

### Secondary: Mean change from Baseline in time normalized stimulated (from MMTT) 2 hour plasma C-peptide AUC at Week 16, 28 and Week 64

|                 |                                                                                                                            |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean change from Baseline in time normalized stimulated (from MMTT) 2 hour plasma C-peptide AUC at Week 16, 28 and Week 64 |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|

End point description:

Participants had a balanced diet consistent with dietitian's advice and made no major changes in exercise regimens. On the evening before the MMTT, participants had a full meal and then fasted from 9 pm until the MMTT was completed. Water, black coffee or tea without sugar or artificial sweeteners was allowed. Plasma glucose was measured prior to the test using a finger-stick test and MMTT was performed only if it was in range  $> 3.9$  mmol/L (70 mg/dL) and  $\leq 11.1$  mmol/L (200 mg/dL). Baseline was defined as the last non-missing value with an assessment date on or before the first day of study medication. Change from Baseline was calculated by subtracting Baseline value from the specified time point value.

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

End point timeframe:

Baseline and Weeks 16, 28 and 64

| End point values                     | Placebo              | Albiglutide          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed          | 15 <sup>[4]</sup>    | 46 <sup>[5]</sup>    |  |  |
| Units: Nanomoles per liter           |                      |                      |  |  |
| arithmetic mean (standard deviation) |                      |                      |  |  |
| Week 16, n=15,44                     | 0.00 ( $\pm$ 0.216)  | 0.07 ( $\pm$ 0.234)  |  |  |
| Week 28, n=13,41                     | -0.14 ( $\pm$ 0.177) | 0.01 ( $\pm$ 0.225)  |  |  |
| Week 64, n=11,36                     | -0.22 ( $\pm$ 0.277) | -0.22 ( $\pm$ 0.246) |  |  |

Notes:

[4] - ITT Population.

[5] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum stimulated plasma C-peptide (MMTT) at Baseline, Week 16, 28, 52 and 64

|                 |                                                                                |
|-----------------|--------------------------------------------------------------------------------|
| End point title | Maximum stimulated plasma C-peptide (MMTT) at Baseline, Week 16, 28, 52 and 64 |
|-----------------|--------------------------------------------------------------------------------|

End point description:

Maximum stimulated plasma C-peptide was the highest value at any time point during the 2 hour MMTT after the participant has ingested the mixed meal at Baseline, Week 16, Week 28, Week 52 and Week 64. Blood samples were taken to assess levels of C-peptide at: 10 minutes before Time 0 (-10 minutes), immediately before the participant starts drinking the nutritional drink (Time 0) and 15, 30, 60, 90, and 120 minutes after Time 0. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

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

End point timeframe:

Baseline and Weeks 16, 28, 52 and 64

| End point values                     | Placebo           | Albiglutide       |  |  |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed          | 15 <sup>[6]</sup> | 46 <sup>[7]</sup> |  |  |
| Units: Nanomoles per liter           |                   |                   |  |  |
| arithmetic mean (standard deviation) |                   |                   |  |  |
| Baseline, n=15,46                    | 0.86 (± 0.382)    | 0.82 (± 0.448)    |  |  |
| Week 16, n=15,45                     | 0.84 (± 0.481)    | 1.02 (± 0.558)    |  |  |
| Week 28, n=13,42                     | 0.68 (± 0.442)    | 0.91 (± 0.594)    |  |  |
| Week 52, n=11,41                     | 0.63 (± 0.516)    | 0.69 (± 0.479)    |  |  |
| Week 64, n=11,37                     | 0.58 (± 0.453)    | 0.48 (± 0.363)    |  |  |

Notes:

[6] - ITT Population

[7] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean change from Baseline in time normalized plasma glucagon AUC (from MMTT) at Week 16, 28, 52 and 64

|                 |                                                                                                        |
|-----------------|--------------------------------------------------------------------------------------------------------|
| End point title | Mean change from Baseline in time normalized plasma glucagon AUC (from MMTT) at Week 16, 28, 52 and 64 |
|-----------------|--------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were taken to assess levels of glucagon at: 10 minutes before Time 0 (-10 minutes), immediately before the participant started drinking the nutritional drink (Time 0) and 15, 30, 60, 90, and 120 minutes after Time 0. Mean change from Baseline in time normalized plasma glucagon AUC (from MMTT) at Week 16, 28, 52 and 64 was reported. Baseline was defined as the last non-missing value with an assessment date on or before the first day of study medication. Change from Baseline was calculated by subtracting Baseline value from the specified time point value.

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

End point timeframe:

Baseline and Weeks 16, 28, 52 and 64

| End point values                     | Placebo           | Albiglutide       |  |  |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed          | 15 <sup>[8]</sup> | 46 <sup>[9]</sup> |  |  |
| Units: Nanograms per liter           |                   |                   |  |  |
| arithmetic mean (standard deviation) |                   |                   |  |  |
| Week 16,n=15,45                      | -2.28 (± 11.221)  | -1.10 (± 4.496)   |  |  |
| Week 28,n=13,43                      | -2.97 (± 11.574)  | 3.91 (± 22.197)   |  |  |
| Week 52,n=11,40                      | -0.31 (± 15.989)  | 4.66 (± 13.628)   |  |  |
| Week 64,n=11,37                      | 3.19 (± 18.279)   | 8.82 (± 17.650)   |  |  |

Notes:

[8] - ITT Population.

[9] - ITT Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of responders at Baseline, Weeks 4, 8, 16, 28, 40, 52 and 64

|                 |                                                                         |
|-----------------|-------------------------------------------------------------------------|
| End point title | Percentage of responders at Baseline, Weeks 4, 8, 16, 28, 40, 52 and 64 |
|-----------------|-------------------------------------------------------------------------|

End point description:

Responders were defined as participants achieving glycosylated hemoglobin A1c (HbA1c) ≤ 7.0 percent and mean daily insulin use < 0.5 units per kilograms (kg) per day. Percentages are based on the number of participants with available HbA1c and insulin use data in each treatment group at that visit. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

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

End point timeframe:

Baseline and Weeks 4, 8, 16, 28, 40, 52 and 64

| End point values                  | Placebo            | Albiglutide        |  |  |
|-----------------------------------|--------------------|--------------------|--|--|
| Subject group type                | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed       | 15 <sup>[10]</sup> | 46 <sup>[11]</sup> |  |  |
| Units: Percentage of participants |                    |                    |  |  |
| number (not applicable)           |                    |                    |  |  |
| Baseline, n=15, 46                | 26.7               | 37.0               |  |  |
| Week 4,n=14,42                    | 71.4               | 78.6               |  |  |
| Week 8,n=14,46                    | 85.7               | 67.4               |  |  |
| Week 16,n=15,45                   | 86.7               | 73.3               |  |  |
| Week 28,n=12,42                   | 75.0               | 73.8               |  |  |
| Week 40,n=13,40                   | 76.9               | 62.5               |  |  |
| Week 52,n=12,41                   | 41.7               | 48.8               |  |  |
| Week 64,n=11,38                   | 36.4               | 34.2               |  |  |

Notes:

[10] - ITT Population.

[11] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants achieving partial remission status (insulin dose-adjusted hemoglobin A1c (IDAA1C) ≤ 9.0) at Baseline, Week 4, 8, 16, 28, 40, 52 and 64

|                 |                                                                                                                                                                   |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of participants achieving partial remission status (insulin dose-adjusted hemoglobin A1c (IDAA1C) ≤ 9.0) at Baseline, Week 4, 8, 16, 28, 40, 52 and 64 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Participant achieving partial remission status was defined as a participant with IDAA1C ≤ 9.0 . Percentages were based on the number of participants with available IDAA1c data in each treatment group at that visit. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

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

End point timeframe:

Baseline and Weeks 4, 8, 16, 28, 40, 52 and 64

| End point values                  | Placebo            | Albiglutide        |  |  |
|-----------------------------------|--------------------|--------------------|--|--|
| Subject group type                | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed       | 15 <sup>[12]</sup> | 46 <sup>[13]</sup> |  |  |
| Units: Percentage of participants |                    |                    |  |  |
| number (not applicable)           |                    |                    |  |  |
| Baseline, n= 15, 46               | 73.3               | 60.9               |  |  |
| Week 4, n=14, 42                  | 92.9               | 88.1               |  |  |
| Week 8, n=14, 46                  | 92.9               | 87.0               |  |  |
| Week 16, n=15, 45                 | 86.7               | 86.7               |  |  |
| Week 28, n=12, 42                 | 75.0               | 85.7               |  |  |
| Week 40, n=13, 40                 | 84.6               | 82.5               |  |  |
| Week 52, n=12, 41                 | 58.3               | 70.7               |  |  |
| Week 64, n=11, 38                 | 54.5               | 55.3               |  |  |

Notes:

[12] - ITT Population.

[13] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in percent HbA1c at Week 52

|                 |                                                  |
|-----------------|--------------------------------------------------|
| End point title | Change from Baseline in percent HbA1c at Week 52 |
|-----------------|--------------------------------------------------|

End point description:

Change from Baseline in percent HbA1c was reported. Baseline was defined as the last non-missing

value with an assessment date on or before the first day of study medication. Change from Baseline was calculated by subtracting Baseline value the Week 52 value. Only those participants with available data at the specified time points were analyzed.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline and Week 52 |           |

| End point values                     | Placebo            | Albiglutide        |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 12 <sup>[14]</sup> | 43 <sup>[15]</sup> |  |  |
| Units: Percentage of HbA1c           |                    |                    |  |  |
| arithmetic mean (standard deviation) |                    |                    |  |  |
| Percentage of HbA1c                  | -0.73 (± 1.033)    | -0.59 (± 1.649)    |  |  |

Notes:

[14] - ITT Population.

[15] - ITT Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent HbA1c over time (at Weeks 4, 8, 16, 28, 40, 52 and 64)

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Percent HbA1c over time (at Weeks 4, 8, 16, 28, 40, 52 and 64) |
|-----------------|----------------------------------------------------------------|

End point description:

Blood samples were collected from participants for analysis of HbA1c at indicated time points and percentage of HbA1c has been calculated for Weeks 4, 8, 16, 28, 40, 52 and 64. Only those participants with data available at the specified time points were analyzed (represented by n=x in the category titles).

|                                   |           |
|-----------------------------------|-----------|
| End point type                    | Secondary |
| End point timeframe:              |           |
| Weeks 4, 8, 16, 28, 40, 52 and 64 |           |

| End point values                     | Placebo            | Albiglutide        |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 15 <sup>[16]</sup> | 46 <sup>[17]</sup> |  |  |
| Units: Percentage of HbA1c           |                    |                    |  |  |
| arithmetic mean (standard deviation) |                    |                    |  |  |
| Week 4,n=15,43                       | 6.29 (± 0.688)     | 6.10 (± 0.725)     |  |  |
| Week 8,n=15,46                       | 5.91 (± 0.689)     | 5.82 (± 0.725)     |  |  |
| Week 16,n=15,46                      | 5.97 (± 0.801)     | 5.78 (± 0.733)     |  |  |
| Week 28,n=13,43                      | 6.03 (± 0.747)     | 6.00 (± 0.824)     |  |  |
| Week 40,n=13,42                      | 6.22 (± 0.860)     | 6.20 (± 0.894)     |  |  |
| Week 52,n=12,43                      | 6.56 (± 0.950)     | 6.58 (± 1.512)     |  |  |
| Week 64,n=12,40                      | 7.12 (± 1.335)     | 6.92 (± 1.176)     |  |  |

Notes:

[16] - ITT Population.

[17] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in mean daily insulin use at Week 4, 8, 16, 28, 40, 52 and 64

|                 |                                                                                    |
|-----------------|------------------------------------------------------------------------------------|
| End point title | Change from Baseline in mean daily insulin use at Week 4, 8, 16, 28, 40, 52 and 64 |
|-----------------|------------------------------------------------------------------------------------|

End point description:

The mean daily insulin use value was calculated, in units per kg per day (units/kg/day) as the sum of average prandial insulin doses and average of basal insulin doses for each participant recorded daily for the 3 days prior to the specified visits, divided by the participant's body weight in kg. Baseline was defined as the last non-missing value with an assessment date on or before the first day of study medication. Change from Baseline was calculated by subtracting Baseline value from the specified time point value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

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

End point timeframe:

Baseline and Weeks 4, 8, 16, 28, 40, 52 and 64

| End point values                     | Placebo            | Albiglutide        |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 15 <sup>[18]</sup> | 46 <sup>[19]</sup> |  |  |
| Units: Units/kg/day                  |                    |                    |  |  |
| arithmetic mean (standard deviation) |                    |                    |  |  |
| Week 4,n=14,43                       | -0.02 (± 0.076)    | -0.03 (± 0.093)    |  |  |
| Week 8,n=14,46                       | -0.04 (± 0.105)    | -0.02 (± 0.123)    |  |  |
| Week 16,n=15,45                      | -0.05 (± 0.100)    | -0.01 (± 0.148)    |  |  |
| Week 28,n=12,42                      | -0.01 (± 0.139)    | 0.03 (± 0.145)     |  |  |
| Week 40,n=13,40                      | -0.01 (± 0.151)    | 0.03 (± 0.145)     |  |  |
| Week 52,n=12,41                      | 0.04 (± 0.119)     | 0.11 (± 0.215)     |  |  |
| Week 64,n=11,38                      | 0.04 (± 0.140)     | 0.10 (± 0.187)     |  |  |

Notes:

[18] - ITT Population

[19] - ITT Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of events of participant-reported significant hypoglycemia,

**occurring > Week 24 and <= Week 52**

|                 |                                                                                                       |
|-----------------|-------------------------------------------------------------------------------------------------------|
| End point title | Number of events of participant-reported significant hypoglycemia, occurring > Week 24 and <= Week 52 |
|-----------------|-------------------------------------------------------------------------------------------------------|

## End point description:

Significant hypoglycemia was defined as an event with plasma glucose level  $\leq 3.9$  mmol/L ( $\leq 70$  mg/dL) and/or requiring third party intervention. This corresponds to American Diabetes Association (ADA) category definitions of severe, documented symptomatic, and asymptomatic hypoglycemia. The time period was defined as: > Week 24 to  $\leq$  Week 52 = Day 169 to Day 364. Number of Events were defined as the total number of significant hypoglycemic events at each level of summarization. Number of events of hypoglycemia with confirmed self plasma glucose monitoring  $\leq 3.9$  mmol/L and/or requiring third party intervention (i.e., severe, documented symptomatic and asymptomatic hypoglycemic events) occurring >Week 24 and  $\leq$ Week 52 are presented. Only those participants with available data at specified time points were analyzed.

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

## End point timeframe:

Week 24 to 52

| End point values                    | Placebo            | Albiglutide        |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 13 <sup>[20]</sup> | 45 <sup>[21]</sup> |  |  |
| Units: Hypoglycemic events          |                    |                    |  |  |
| Any Significant Hypoglycemia        | 472                | 1592               |  |  |
| Severe Hypoglycemia                 | 0                  | 0                  |  |  |
| Documented Symptomatic Hypoglycemia | 241                | 996                |  |  |
| Asymptomatic Hypoglycemia           | 231                | 596                |  |  |

## Notes:

[20] - ITT Population

[21] - ITT Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Time Spent with Plasma Glucose Level  $\leq 3.9$ , > 3.9 to  $\leq 10.0$ , and > 10.0 measured by 72 hour Continuous Glucose Monitoring (CGM) at Baseline, Week 28 and 52**

|                 |                                                                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Time Spent with Plasma Glucose Level $\leq 3.9$ , > 3.9 to $\leq 10.0$ , and > 10.0 measured by 72 hour Continuous Glucose Monitoring (CGM) at Baseline, Week 28 and 52 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## End point description:

Three days before the visit, the participants made an additional visit to the study site to have the CGM fitted/inserted. It was worn for 3 consecutive days and was removed at the scheduled study visit. Whilst wearing the CGM, participants continued to monitor their plasma glucose at least 4 times a day and on one of the days, conducted 7-point glucose profile (Before breakfast, 2 hours after breakfast, Before lunch, 2 hours after lunch, Before dinner, 2 hours after dinner, At bedtime). Time spent with a plasma glucose  $\leq 3.9$  millimoles per liter (mmol/L), between >3.9 and 10.0 mmol/L, and >10.0 mmol/L, respectively as performed by 72-hour CGM at Baseline, Week 28 and Week 52 was reported. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

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

## End point timeframe:

Baseline and Weeks 28 and 52

| End point values                         | Placebo            | Albiglutide        |  |  |
|------------------------------------------|--------------------|--------------------|--|--|
| Subject group type                       | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed              | 15 <sup>[22]</sup> | 46 <sup>[23]</sup> |  |  |
| Units: hours per day                     |                    |                    |  |  |
| arithmetic mean (standard deviation)     |                    |                    |  |  |
| <= 3.9 mmol/L, Baseline,n=14,42          | 0.80 (± 1.251)     | 0.98 (± 1.400)     |  |  |
| <= 3.9 mmol/L, Week 28,n=12,36           | 1.72 (± 1.248)     | 1.38 (± 1.808)     |  |  |
| <= 3.9 mmol/L, Week 52,n=10,31           | 1.60 (± 2.142)     | 1.36 (± 2.405)     |  |  |
| > 3.9 to <= 10.0 mmol/L,Baseline,n=14,42 | 20.14 (± 3.675)    | 19.11 (± 3.732)    |  |  |
| > 3.9 to <= 10.0 mmol/L,Week 28,n=12,36  | 18.93 (± 3.452)    | 18.83 (± 4.009)    |  |  |
| > 3.9 to <= 10.0 mmol/L,Week 52,n=10,31  | 17.98 (± 4.491)    | 18.19 (± 4.772)    |  |  |
| > 10.0 mmol/L, Baseline,n=14,42          | 3.06 (± 3.560)     | 3.90 (± 3.727)     |  |  |
| > 10.0 mmol/L,Week 28,n=12,36            | 3.35 (± 3.115)     | 3.79 (± 3.782)     |  |  |
| > 10.0 mmol/L,Week 52,n=10,31            | 4.42 (± 4.597)     | 4.45 (± 4.781)     |  |  |

Notes:

[22] - ITT Population.

[23] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Hypoglycemic Excursions for each participant from 7-Point Glucose Profile at Baseline, Week 28 and 52

|                 |                                                                                                                 |
|-----------------|-----------------------------------------------------------------------------------------------------------------|
| End point title | Number of Hypoglycemic Excursions for each participant from 7-Point Glucose Profile at Baseline, Week 28 and 52 |
|-----------------|-----------------------------------------------------------------------------------------------------------------|

End point description:

A hypoglycemic excursion was defined as an occurrence where the plasma glucose level was <=3.9 mmol/L (<=70 mg/dL). At each visit, only evaluable participants, defined as those with >= 4 non-missing glucose values or >= 1 hypoglycemic excursions were included. Number of Hypoglycemic Excursions for each participant from 7-Point Glucose Profile (Before breakfast, 2 hours after breakfast, Before lunch, 2 hours after lunch, Before dinner, 2 hours after dinner, At bedtime) were reported. Baseline was defined as the last non-missing value with an assessment date on or before the first day of study medication. Only evaluable participants, as defined above were analyzed (represented by n=X in the category titles).

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

End point timeframe:

Baseline and Weeks 28 and 52

| End point values                     | Placebo            | Albiglutide        |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 15 <sup>[24]</sup> | 46 <sup>[25]</sup> |  |  |
| Units: Hypoglycemic excursions       |                    |                    |  |  |
| arithmetic mean (standard deviation) |                    |                    |  |  |
| Bseline,n=15,42                      | 0.40 (± 0.632)     | 0.36 (± 0.656)     |  |  |



|                 |                |                |  |  |
|-----------------|----------------|----------------|--|--|
| Week 28,n=13,40 | 0.31 (± 0.630) | 0.28 (± 0.554) |  |  |
| Week 52,n=12,40 | 0.25 (± 0.452) | 0.40 (± 0.672) |  |  |

Notes:

[24] - ITT Population.

[25] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Greatest magnitude of Hypoglycemic Excursions for each participant from 7-Point Glucose Profile at Baseline, Week 28 and 52

|                 |                                                                                                                             |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|
| End point title | Greatest magnitude of Hypoglycemic Excursions for each participant from 7-Point Glucose Profile at Baseline, Week 28 and 52 |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|

End point description:

A hypoglycemic excursion was defined as an occurrence where the plasma glucose level was  $\leq 3.9$  mmol/L ( $\leq 70$  mg/dL). At each visit, only evaluable participants, defined as those with  $\geq 4$  non-missing glucose values or  $\geq 1$  hypoglycemic excursions were included. Greatest hypoglycemic excursion was calculated as 3.9 mmol/L minus the lowest recorded glucose level during the 7-point glucose profile (Before breakfast, 2 hours after breakfast, Before lunch, 2 hours after lunch, Before dinner, 2 hours after dinner, At bedtime). If a participant had data recorded at that visit, but did not have a value  $\leq 3.9$  mmol/L, their greatest hypoglycemic excursion were 0 mmol/L for that visit. Baseline was defined as the last non-missing value with an assessment date on or before the first day of study medication. Only evaluable participants, as defined above were analyzed (represented by n=X in the category titles).

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

End point timeframe:

Baseline and Weeks 28 and 52

| End point values                     | Placebo            | Albiglutide        |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 15 <sup>[26]</sup> | 46 <sup>[27]</sup> |  |  |
| Units: mmol/L                        |                    |                    |  |  |
| arithmetic mean (standard deviation) |                    |                    |  |  |
| Baseline,n=15,42                     | 0.24 (± 0.470)     | 0.22 (± 0.597)     |  |  |
| Week 28,n=13,40                      | 0.18 (± 0.359)     | 0.08 (± 0.231)     |  |  |
| Week 52,n=12,40                      | 0.22 (± 0.484)     | 0.17 (± 0.393)     |  |  |

Notes:

[26] - ITT Population.

[27] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Hyperglycemic Excursions for each participant from 7-Point Glucose Profile at Baseline, Week 28 and 52

|                 |                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Hyperglycemic Excursions for each participant from 7-Point Glucose Profile at Baseline, Week 28 and 52 |
|-----------------|------------------------------------------------------------------------------------------------------------------|

End point description:

A hyperglycemic excursion was defined as an occurrence where the plasma glucose level was  $> 10.0$

mmol/L (> 180 mg/dL). At each visit, only evaluable participants, defined as those with  $\geq 4$  non-missing glucose values or  $\geq 1$  hyperglycemic excursions were included. Number of Hyperglycemic Excursions for each participant from 7-Point Glucose Profile (Before breakfast, 2 hours after breakfast, Before lunch, 2 hours after lunch, Before dinner, 2 hours after dinner, At bedtime) were reported. Baseline was defined as the last non-missing value with an assessment date on or before the first day of study medication. Only evaluable participants, as defined above were analyzed (represented by n=X in the category titles)

|                              |           |
|------------------------------|-----------|
| End point type               | Secondary |
| End point timeframe:         |           |
| Baseline and Weeks 28 and 52 |           |

| End point values                     | Placebo             | Albiglutide         |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed          | 15 <sup>[28]</sup>  | 46 <sup>[29]</sup>  |  |  |
| Units: Hyperglycemic excursions      |                     |                     |  |  |
| arithmetic mean (standard deviation) |                     |                     |  |  |
| Baseline, n=15,43                    | 0.80 ( $\pm$ 1.014) | 1.53 ( $\pm$ 1.502) |  |  |
| Week 28, n=13,40                     | 1.23 ( $\pm$ 1.301) | 0.73 ( $\pm$ 0.933) |  |  |
| Week 52, n=12,40                     | 1.17 ( $\pm$ 1.115) | 1.30 ( $\pm$ 1.522) |  |  |

Notes:

[28] - ITT Population.

[29] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Greatest magnitude of Hyperglycemic Excursions for each participant from 7-Point Glucose Profile at Baseline, Week 28 and 52

|                 |                                                                                                                              |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|
| End point title | Greatest magnitude of Hyperglycemic Excursions for each participant from 7-Point Glucose Profile at Baseline, Week 28 and 52 |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|

End point description:

A hyperglycemic excursion is defined as an occurrence where the plasma glucose level > 10.0 mmol/L (> 180 mg/dL). At each visit, only evaluable participants, defined as those with  $\geq 4$  non-missing glucose values or  $\geq 1$  hyperglycemic excursions were included. Greatest hyperglycemic excursion was calculated as the largest recorded glucose level during the 7-point glucose profile (before breakfast, 2 hours after breakfast, before lunch, 2 hours after lunch, before dinner, 2 hours after dinner) minus 10.0 mmol/L. If a participant had data recorded at that visit, but did not have a value >10.0 mmol/L, their greatest hyperglycemic excursion would be 0 mmol/L for that visit. Baseline was defined as the last non-missing value with an assessment date on or before the first day of study medication. Only evaluable participants, as defined above were analyzed (represented by n=X in the category titles).

|                              |           |
|------------------------------|-----------|
| End point type               | Secondary |
| End point timeframe:         |           |
| Baseline and Weeks 28 and 52 |           |

| End point values                     | Placebo            | Albiglutide        |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 15 <sup>[30]</sup> | 46 <sup>[31]</sup> |  |  |
| Units: mmol/L                        |                    |                    |  |  |
| arithmetic mean (standard deviation) |                    |                    |  |  |
| Baseline,n=15,43                     | 0.94 (± 1.805)     | 2.72 (± 3.466)     |  |  |
| Week 28,n=13,40                      | 2.05 (± 2.154)     | 1.52 (± 2.493)     |  |  |
| Week 52,n=12,40                      | 2.19 (± 2.823)     | 2.42 (± 3.042)     |  |  |

Notes:

[30] - ITT Population.

[31] - ITT Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in body weight (kilograms) at Week 52

|                                                                                                                                                                                                                                                                                                                                                                           |                                                            |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                           | Change from Baseline in body weight (kilograms) at Week 52 |
| End point description:                                                                                                                                                                                                                                                                                                                                                    |                                                            |
| Change from Baseline in body weight of participants was reported. Baseline was defined as the last non-missing value with an assessment date on or before the first day of study medication. Change from Baseline was calculated by subtracting Baseline value the Week 52 value. Only those participants with available data at the specified time points were analyzed. |                                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                            | Secondary                                                  |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                      |                                                            |
| Baseline and Week 52                                                                                                                                                                                                                                                                                                                                                      |                                                            |

| End point values                     | Placebo         | Albiglutide     |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 12              | 43              |  |  |
| Units: Kilograms                     |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Kilograms                            | 0.26 (± 2.738)  | 0.77 (± 3.504)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Weight over time (at Weeks 2, 4, 6, 8, 16, 28, 40, 52 and 64)

|                                                                                                                                                                                                                      |                                                               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| End point title                                                                                                                                                                                                      | Weight over time (at Weeks 2, 4, 6, 8, 16, 28, 40, 52 and 64) |
| End point description:                                                                                                                                                                                               |                                                               |
| Body weight was measured in kilograms for participants at indicated time points. Only those participants with data available at the specified time points were analyzed (represented by n=x in the category titles). |                                                               |
| End point type                                                                                                                                                                                                       | Secondary                                                     |
| End point timeframe:                                                                                                                                                                                                 |                                                               |
| Weeks 2, 4, 6, 8, 16, 28, 40, 52 and 64                                                                                                                                                                              |                                                               |

| End point values                     | Placebo            | Albiglutide        |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 15 <sup>[32]</sup> | 46 <sup>[33]</sup> |  |  |
| Units: kilograms                     |                    |                    |  |  |
| arithmetic mean (standard deviation) |                    |                    |  |  |
| Week 2,n=15, 43                      | 70.16 (± 14.087)   | 66.16 (± 11.944)   |  |  |
| Week 4,n=15, 44                      | 69.87 (± 14.409)   | 66.39 (± 11.952)   |  |  |
| Week 6,n=15, 46                      | 69.83 (± 14.013)   | 65.65 (± 12.559)   |  |  |
| Week 8,n=15, 46                      | 70.08 (± 14.121)   | 65.32 (± 12.825)   |  |  |
| Week 16,n=15, 46                     | 69.40 (± 15.191)   | 65.41 (± 12.824)   |  |  |
| Week 28,n=13, 43                     | 66.08 (± 11.767)   | 65.32 (± 13.252)   |  |  |
| Week 40,n=13, 42                     | 66.08 (± 11.266)   | 66.20 (± 13.146)   |  |  |
| Week 52,n=12, 43                     | 66.86 (± 12.401)   | 66.80 (± 12.696)   |  |  |
| Week 64,n=12, 40                     | 68.29 (± 11.511)   | 68.13 (± 12.649)   |  |  |

Notes:

[32] - ITT Population

[33] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Population estimates of Pharmacokinetic (PK) parameters: apparent clearance [CL/F]

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Population estimates of Pharmacokinetic (PK) parameters: apparent clearance [CL/F] <sup>[34]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

PK of Albiglutide was evaluated in participants using CL/F using PK samples collected on Weeks 4, 6, 8, 16. CL/F was evaluated by population PK methods and mean and standard error from the final model has been tabulated. Estimates have been presented from the final model centered to mean bodyweights of 67 kilograms, and electronic glomerular filtration rate (eGFR) of 123 milliliters per minute. PK population comprised of participants in Safety Population for whom a PK sample was obtained and analyzed. Only participants who received albiglutide were included in PK Population.

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

End point timeframe:

48 hours after the most recent dose at Week 4, 6, 8 and 16

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this endpoint.

| End point values                 | Albiglutide        |  |  |  |
|----------------------------------|--------------------|--|--|--|
| Subject group type               | Reporting group    |  |  |  |
| Number of subjects analysed      | 49 <sup>[35]</sup> |  |  |  |
| Units: Milliliters per hour      |                    |  |  |  |
| arithmetic mean (standard error) |                    |  |  |  |
| Milliliters per hour             | 45.1 (± 2.56)      |  |  |  |

Notes:

[35] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Population estimates of PK parameters: apparent volume of distribution [V/F]

|                 |                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------|
| End point title | Population estimates of PK parameters: apparent volume of distribution [V/F] <sup>[36]</sup> |
|-----------------|----------------------------------------------------------------------------------------------|

End point description:

PK of Albiglutide was evaluated in participants using V/F using PK samples collected on Weeks 4, 6, 8, 16. V/F was evaluated by population PK methods and mean and standard error from the final model has been tabulated. Estimates have been presented from the final model centered to mean body weights of 67 kilograms, and eGFR of 123 milliliters per minute.

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

End point timeframe:

48 hours after the most recent dose at Week 4, 6, 8 and 16

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this endpoint.

| End point values                 | Albiglutide        |  |  |  |
|----------------------------------|--------------------|--|--|--|
| Subject group type               | Reporting group    |  |  |  |
| Number of subjects analysed      | 49 <sup>[37]</sup> |  |  |  |
| Units: Milliliters               |                    |  |  |  |
| arithmetic mean (standard error) |                    |  |  |  |
| Milliliters                      | 4830 (± 677)       |  |  |  |

Notes:

[37] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Population estimates of PK parameters: first-order absorption rate constant [Ka]

|                 |                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | Population estimates of PK parameters: first-order absorption rate constant [Ka] <sup>[38]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------|

End point description:

PK of Albiglutide was evaluated in participants using Ka using PK samples collected on Weeks 4, 6, 8, 16. Ka was evaluated by population PK methods and mean and standard error from the final model has been tabulated. Estimates have been presented from the final model centered to mean body weights of 67 kilograms, and eGFR of 123 milliliters per minute.

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

End point timeframe:

48 hours after the most recent dose at Week 4, 6, 8 and 16

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this endpoint.

|                                  |                    |  |  |  |
|----------------------------------|--------------------|--|--|--|
| <b>End point values</b>          | Albiglutide        |  |  |  |
| Subject group type               | Reporting group    |  |  |  |
| Number of subjects analysed      | 49 <sup>[39]</sup> |  |  |  |
| Units: Per hour                  |                    |  |  |  |
| arithmetic mean (standard error) |                    |  |  |  |
| 1/hour                           | 0.0122 (± 0.0022)  |  |  |  |

Notes:

[39] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

On-therapy AEs and SAEs were collected from start of study treatment up to 52-weeks

Adverse event reporting additional description:

AEs and SAEs were summarized in Safety Population. Safety Population comprised of all participants who received at least one dose of study treatment.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Albiglutide |
|-----------------------|-------------|

Reporting group description:

Albiglutide 30 mg was administered once weekly for 52 weeks by sc injection in the abdomen, thigh or upper arm region along with insulin (Dose increased to 50 mg once weekly at Week 6 if the 30 mg weekly dose was tolerated).

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Matching placebo was administered once weekly for 52 weeks by sc injection in the abdomen, thigh or upper arm region in addition to insulin.

| Serious adverse events                                              | Albiglutide    | Placebo         |  |
|---------------------------------------------------------------------|----------------|-----------------|--|
| Total subjects affected by serious adverse events                   |                |                 |  |
| subjects affected / exposed                                         | 1 / 50 (2.00%) | 2 / 17 (11.76%) |  |
| number of deaths (all causes)                                       | 0              | 0               |  |
| number of deaths resulting from adverse events                      |                |                 |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                 |  |
| Uterine leiomyoma                                                   |                |                 |  |
| subjects affected / exposed                                         | 1 / 50 (2.00%) | 0 / 17 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0           |  |
| Skin and subcutaneous tissue disorders                              |                |                 |  |
| Urticaria                                                           |                |                 |  |
| subjects affected / exposed                                         | 0 / 50 (0.00%) | 1 / 17 (5.88%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0           |  |
| Psychiatric disorders                                               |                |                 |  |
| Suicidal ideation                                                   |                |                 |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 17 (5.88%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Albiglutide      | Placebo          |  |
|-------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 37 / 50 (74.00%) | 13 / 17 (76.47%) |  |
| Nervous system disorders                              |                  |                  |  |
| Headache                                              |                  |                  |  |
| subjects affected / exposed                           | 4 / 50 (8.00%)   | 5 / 17 (29.41%)  |  |
| occurrences (all)                                     | 12               | 22               |  |
| Carpal tunnel syndrome                                |                  |                  |  |
| subjects affected / exposed                           | 0 / 50 (0.00%)   | 1 / 17 (5.88%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| Dizziness                                             |                  |                  |  |
| subjects affected / exposed                           | 0 / 50 (0.00%)   | 1 / 17 (5.88%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| Hypoaesthesia                                         |                  |                  |  |
| subjects affected / exposed                           | 0 / 50 (0.00%)   | 1 / 17 (5.88%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| Somnolence                                            |                  |                  |  |
| subjects affected / exposed                           | 0 / 50 (0.00%)   | 1 / 17 (5.88%)   |  |
| occurrences (all)                                     | 0                | 1                |  |
| General disorders and administration site conditions  |                  |                  |  |
| Asthenia                                              |                  |                  |  |
| subjects affected / exposed                           | 1 / 50 (2.00%)   | 2 / 17 (11.76%)  |  |
| occurrences (all)                                     | 2                | 2                |  |
| Injection site erythema                               |                  |                  |  |
| subjects affected / exposed                           | 3 / 50 (6.00%)   | 0 / 17 (0.00%)   |  |
| occurrences (all)                                     | 18               | 0                |  |
| Malaise                                               |                  |                  |  |
| subjects affected / exposed                           | 3 / 50 (6.00%)   | 0 / 17 (0.00%)   |  |
| occurrences (all)                                     | 8                | 0                |  |
| Pyrexia                                               |                  |                  |  |



|                                                                                                     |                        |                      |  |
|-----------------------------------------------------------------------------------------------------|------------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                    | 1 / 50 (2.00%)<br>1    | 1 / 17 (5.88%)<br>1  |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 3 / 50 (6.00%)<br>3    | 1 / 17 (5.88%)<br>1  |  |
| Gastrointestinal disorders<br>Nausea<br>subjects affected / exposed<br>occurrences (all)            | 19 / 50 (38.00%)<br>41 | 5 / 17 (29.41%)<br>7 |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                       | 13 / 50 (26.00%)<br>32 | 2 / 17 (11.76%)<br>2 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                        | 10 / 50 (20.00%)<br>23 | 4 / 17 (23.53%)<br>7 |  |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)                            | 7 / 50 (14.00%)<br>9   | 0 / 17 (0.00%)<br>0  |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                  | 7 / 50 (14.00%)<br>22  | 0 / 17 (0.00%)<br>0  |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                            | 4 / 50 (8.00%)<br>8    | 3 / 17 (17.65%)<br>6 |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)                                       | 3 / 50 (6.00%)<br>3    | 0 / 17 (0.00%)<br>0  |  |
| Flatulence<br>subjects affected / exposed<br>occurrences (all)                                      | 2 / 50 (4.00%)<br>4    | 1 / 17 (5.88%)<br>1  |  |
| Gastrointestinal pain<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 50 (2.00%)<br>1    | 1 / 17 (5.88%)<br>5  |  |
| Reproductive system and breast disorders                                                            |                        |                      |  |

|                                                                                                                                                                                                                                                                |                                                                           |                                                                           |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------|--|
| Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                              | 0 / 50 (0.00%)<br>0                                                       | 1 / 17 (5.88%)<br>1                                                       |  |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Wheezing<br>subjects affected / exposed<br>occurrences (all) | 3 / 50 (6.00%)<br>3<br><br>0 / 50 (0.00%)<br>0<br><br>0 / 50 (0.00%)<br>0 | 0 / 17 (0.00%)<br>0<br><br>1 / 17 (5.88%)<br>1<br><br>1 / 17 (5.88%)<br>1 |  |
| Skin and subcutaneous tissue disorders<br>Eczema<br>subjects affected / exposed<br>occurrences (all)<br><br>Lipodystrophy acquired<br>subjects affected / exposed<br>occurrences (all)                                                                         | 1 / 50 (2.00%)<br>1<br><br>0 / 50 (0.00%)<br>0                            | 1 / 17 (5.88%)<br>1<br><br>2 / 17 (11.76%)<br>2                           |  |
| Psychiatric disorders<br>Depression<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                        | 0 / 50 (0.00%)<br>0                                                       | 1 / 17 (5.88%)<br>1                                                       |  |
| Musculoskeletal and connective tissue disorders<br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                       | 0 / 50 (0.00%)<br>0                                                       | 1 / 17 (5.88%)<br>1                                                       |  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Influenza<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastroenteritis                                                                 | 13 / 50 (26.00%)<br>20<br><br>4 / 50 (8.00%)<br>5                         | 5 / 17 (29.41%)<br>5<br><br>0 / 17 (0.00%)<br>0                           |  |

|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed        | 3 / 50 (6.00%)  | 0 / 17 (0.00%)  |  |
| occurrences (all)                  | 3               | 0               |  |
| Urinary tract infection            |                 |                 |  |
| subjects affected / exposed        | 2 / 50 (4.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 2               | 1               |  |
| Folliculitis                       |                 |                 |  |
| subjects affected / exposed        | 0 / 50 (0.00%)  | 2 / 17 (11.76%) |  |
| occurrences (all)                  | 0               | 2               |  |
| Sinusitis                          |                 |                 |  |
| subjects affected / exposed        | 1 / 50 (2.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 1               | 1               |  |
| Bronchitis                         |                 |                 |  |
| subjects affected / exposed        | 0 / 50 (0.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Candida infection                  |                 |                 |  |
| subjects affected / exposed        | 0 / 50 (0.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Laryngitis                         |                 |                 |  |
| subjects affected / exposed        | 0 / 50 (0.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Paronychia                         |                 |                 |  |
| subjects affected / exposed        | 0 / 50 (0.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Pharyngitis                        |                 |                 |  |
| subjects affected / exposed        | 0 / 50 (0.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Tooth infection                    |                 |                 |  |
| subjects affected / exposed        | 0 / 50 (0.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Varicella                          |                 |                 |  |
| subjects affected / exposed        | 0 / 50 (0.00%)  | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Metabolism and nutrition disorders |                 |                 |  |
| Decreased appetite                 |                 |                 |  |
| subjects affected / exposed        | 6 / 50 (12.00%) | 1 / 17 (5.88%)  |  |
| occurrences (all)                  | 8               | 1               |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                  |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 12 September 2014 | Amendment No. 1: Clarification added to wording in the treatment compliance section regarding Week 2. Clarification added regarding the collection of daily insulin use prior to Baseline and correction of typographical errors was made. |
| 24 September 2014 | Amendment No. 2: Change to the acceptable contraceptive methods for United Kingdom (UK) sites only at the request of the Medicines & Healthcare products Regulatory Agency (MHRA).                                                         |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported