



Clinical trial results:

Does Glucagon-like Peptide 1 (GLP-1) receptor stimulation reduce alcohol intake in patients with alcohol dependence?

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2016-003343-11 |
| Trial protocol | DK |
| Global end of trial date | 06 October 2020 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 13 May 2022 |
| First version publication date | 13 May 2022 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | GLP1ALCOHOL |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03232112 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Psychiatric Centre Copenhagen |
| Sponsor organisation address | Edel Sauntés Allé 10, 2100 København Ø, Copenhagen, Denmark, 2100 |
| Public contact | Professor Anders Fink-Jensen, Professor Anders Fink-Jensen, +45 22755843, Anders.Fink-Jensen@regionh.dk |
| Scientific contact | Professor Anders Fink-Jensen, Professor Anders Fink-Jensen, +45 22755843, Anders.Fink-Jensen@regionh.dk |

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 | 10 February 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 October 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to investigate the effects of the GLP-1 receptor agonist Bydureon® on total number of heavy drinking days from baseline to follow up after 26 weeks of treatment in patients with alcohol dependence in a 26-weeks double-blinded, randomized placebo-controlled clinical trial.)). Furthermore, patients will be approached 26 weeks after end participation, in order to evaluate whether or not there is a long-term effect of the intervention on the TLFB questionnaire.

Protection of trial subjects:

The patients could call a phoneline 24/7, if needed due to side-effects or illness

Background therapy:

All patients included recieved standardized cognitive behavioral therapy while included

Evidence for comparator: -

| | |
|---|-------------------------------|
| Actual start date of recruitment | 07 August 2017 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Scientific research |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Denmark: 152 |
| Worldwide total number of subjects | 152 |
| EEA total number of subjects | 152 |

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) | 135 |

| | |
|---------------------|----|
| From 65 to 84 years | 17 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from 7th of August 2017 to 1st of October 2019. All patients were recruited from four outpatient alcohol treatment facilities in the suburbs of Copenhagen or through a project webpage. The 25 healthy controls were recruited via the project webpage.

Pre-assignment

Screening details:

In total 156 patients were screened for eligibility. 29 were excluded due to other substance disorder, paraclinic above upper limit, withdrawal symptoms, AUDIt score below 15, a medical record of alcohol-related withdrawal seizures/pancreatitis, less than 5 heavy drinking days or absent from first injection.

Period 1

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

Blinding implementation details:

All patients were blindfolded when receiving the assigned treatment by an unblinded nurse. The unblinded nurses, were not involved in any other trial related activity.

Arms

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

Arm description:

Bydureon once weekly, 2 mg sc

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bydureon 2 mg powder and solvent for prolonged-release suspension for injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for prolonged-release suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

2 mg sc

| | |
|------------------|---------|
| Arm title | placebo |
|------------------|---------|

Arm description:

saline 2 ml sc

| | |
|--|---|
| Arm type | Placebo |
| Investigational medicinal product name | Saline |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection/infusion |
| Routes of administration | Cutaneous use |

Dosage and administration details:

2 ml were given sc

| Number of subjects in period 1[1] | Intervention | placebo |
|--------------------------------------|--------------|---------|
| | | |
| Started | 62 | 65 |
| Completed | 26 | 32 |
| Not completed | 36 | 33 |
| Consent withdrawn by subject | 5 | 11 |
| Adverse event, non-fatal | 14 | 2 |
| Lost to follow-up | 7 | 8 |
| Lack of efficacy | 10 | 12 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Of the people included, 25 individuals were healthy controls for the fMRI brain imaging. They are not included in the baseline data.

Baseline characteristics

Reporting groups

| | |
|---|--------------|
| Reporting group title | Intervention |
| Reporting group description: Bydureon once weekly, 2 mg sc | |
| Reporting group title | placebo |
| Reporting group description: saline 2 ml sc | |

| Reporting group values | Intervention | placebo | Total |
|------------------------------------|--------------|---------|-------|
| Number of subjects | 62 | 65 | 127 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----------------|----|
| Age continuous Units: years arithmetic mean standard deviation | 52.1 ± 10.8 | 52.5 ± 10.0 | - |
| Gender categorical Units: Subjects | | | |
| Female | 25 | 26 | 51 |
| Male | 37 | 39 | 76 |

End points

End points reporting groups

| | |
|---|--------------|
| Reporting group title | Intervention |
| Reporting group description: Bydureon once weekly, 2 mg sc | |
| Reporting group title | placebo |
| Reporting group description: saline 2 ml sc | |

Primary: Change in heavy drinking days

| | |
|---|-------------------------------|
| End point title | Change in heavy drinking days |
| End point description: A heavy drinking day is defined as days with an excess intake of 60/48 grams of alcohol per day (men and women, respectively). Self-reported with the TLFB-method. | |
| End point type | Primary |
| End point timeframe: week 0 - week 26 | |

| End point values | Intervention | placebo | | |
|---|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: percentage points | | | | |
| arithmetic mean (confidence interval 95%) | -19.6 (-27.4 to -11.8) | -26.8 (-34.4 to -19.2) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
| Statistical analysis description: All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed. | |
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | = 0.37 |
| Method | ANOVA |

Notes:

[1] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Total alcohol consumption

| | |
|-----------------|---------------------------|
| End point title | Total alcohol consumption |
|-----------------|---------------------------|

End point description:

Self-reported with the TLFB-method

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

End point timeframe:

week 0- week 26

| End point values | Intervention | placebo | | |
|---|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: g/30 days | | | | |
| arithmetic mean (confidence interval 95%) | -1304 (-1584 to -1024) | -1313 (-1586 to -1039) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|-----------------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|-------------------|------------------------|
| Comparison groups | Intervention v placebo |
|-------------------|------------------------|

| | |
|---|-----|
| Number of subjects included in analysis | 127 |
|---|-----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|----------------------|
| Analysis type | other ^[2] |
|---------------|----------------------|

| | |
|---------|--------|
| P-value | = 0.86 |
|---------|--------|

| | |
|--------|-------|
| Method | ANOVA |
|--------|-------|

Notes:

[2] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Days without alcohol consumption

| | |
|-----------------|----------------------------------|
| End point title | Days without alcohol consumption |
|-----------------|----------------------------------|

End point description:

Self-reported with the TLFB-method

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

End point timeframe:

week 0 - week 26

| End point values | Intervention | placebo | | |
|---|--------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: percentage points | | | | |
| arithmetic mean (confidence interval 95%) | 11.3 (3.6 to 18.9) | 20.6 (13.1 to 28.1) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[3] |
| P-value | = 0.11 |
| Method | ANOVA |

Notes:

[3] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in PACS score

| | |
|-----------------|----------------------|
| End point title | Change in PACS score |
|-----------------|----------------------|

End point description:

Penn Alcohol Craving Scale (PACS)

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

End point timeframe:

week 0 - week 26

| End point values | Intervention | placebo | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: points | | | | |
| arithmetic mean (confidence interval 95%) | -5.4 (-7.0 to -3.9) | -7.3 (-8.8 to -5.8) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R

software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[4] |
| P-value | = 0.42 |
| Method | ANOVA |

Notes:

[4] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in AUDIT score

| | |
|---|-----------------------|
| End point title | Change in AUDIT score |
| End point description: Alcohol Use Disorders Identification Test (AUDIT) | |
| End point type | Secondary |
| End point timeframe: Week 0 - week 26 | |

| End point values | Intervention | placebo | | |
|---|---------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: points | | | | |
| arithmetic mean (confidence interval 95%) | -7.0 (-8.8 to -5.1) | -8.2 (-10.0 to -6.5) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
| Statistical analysis description: All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed. | |
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[5] |
| P-value | = 0.59 |
| Method | ANOVA |

Notes:

[5] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in DUDIT score

| | |
|-----------------|-----------------------|
| End point title | Change in DUDIT score |
|-----------------|-----------------------|

| | |
|--|-----------|
| End point description: | |
| Drug Use Disorders Identification Test (DUDIT) score | |
| End point type | Secondary |
| End point timeframe: | |
| week 0 - week 26 | |

| End point values | Intervention | placebo | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: points | | | | |
| arithmetic mean (confidence interval 95%) | -7.3 (-7.7 to -6.9) | -8.3 (-8.9 to -7.8) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|-----------------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[6] |
| P-value | > 0.001 |
| Method | ANOVA |

Notes:

[6] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in GGT

| | |
|--|---------------|
| End point title | Change in GGT |
| End point description: | |
| Liverparameter gamma-glutamyltransferase (GGT) | |
| End point type | Secondary |
| End point timeframe: | |
| week 0 - week 26 | |

| End point values | Intervention | placebo | | |
|---|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: U/L | | | | |
| arithmetic mean (confidence interval 95%) | -13.6 (-42.8 to 15.6) | -16.5 (-45.0 to 12.0) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[7] |
| P-value | = 0.84 |
| Method | ANOVA |

Notes:

[7] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in ALAT

| | |
|-----------------|----------------|
| End point title | Change in ALAT |
|-----------------|----------------|

End point description:

Liverparameter alanine aminotransferase (ALAT)

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

End point timeframe:

week 0 - week 26

| End point values | Intervention | placebo | | |
|---|--------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: U/L | | | | |
| arithmetic mean (confidence interval 95%) | -3.7 (-9.7 to 2.2) | -7.9 (-13.7 to -2.1) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R

software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[8] |
| P-value | = 0.68 |
| Method | ANOVA |

Notes:

[8] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in phosphatidyl-ethanol (PEth)

| | |
|------------------------|---------------------------------------|
| End point title | Change in phosphatidyl-ethanol (PEth) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Week 0 – week 26 | |

| End point values | Intervention | placebo | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: µmol/l | | | | |
| arithmetic mean (confidence interval 95%) | -0.09 (-0.3 to 0.2) | -0.03 (-0.3 to 0.2) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
| Statistical analysis description: | |
| All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed. | |
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[9] |
| P-value | = 0.64 |
| Method | ANOVA |

Notes:

[9] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Pancreas type Amylase

| | |
|-----------------|-----------------------|
| End point title | Pancreas type Amylase |
|-----------------|-----------------------|

| | |
|------------------------|-----------|
| End point description: | |
| Safety measurement | |
| End point type | Secondary |
| End point timeframe: | |
| Week 0 – week 26 | |

| End point values | Intervention | placebo | | |
|---|------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: U/L | | | | |
| arithmetic mean (confidence interval 95%) | 4.1 (2.0 to 6.3) | -0.4 (-2.5 to 1.6) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|-----------------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[10] |
| P-value | = 0.054 |
| Method | ANOVA |

Notes:

[10] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in mean cell volume (MCV)

| | |
|-----------------|----------------------------------|
| End point title | Change in mean cell volume (MCV) |
|-----------------|----------------------------------|

End point description:

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 0 – week 26 | |

| End point values | Intervention | placebo | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: fL | | | | |
| arithmetic mean (confidence interval 95%) | -1.8 (-2.6 to -1.0) | -1.3 (-2.1 to -0.5) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[11] |
| P-value | = 0.45 |
| Method | ANOVA |

Notes:

[11] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Changes in body weight

| | |
|-----------------|------------------------|
| End point title | Changes in body weight |
|-----------------|------------------------|

End point description:

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

End point timeframe:

Week 0 – week 26

| End point values | Intervention | placebo | | |
|---|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: kg | | | | |
| arithmetic mean (confidence interval 95%) | -2.9 (-4.3 to 9.4) | -0.5 (-1.8 to 0.9) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R

software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[12] |
| P-value | = 0.07 |
| Method | ANOVA |

Notes:

[12] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in Systolic blood pressure

| | |
|------------------------|-----------------------------------|
| End point title | Change in Systolic blood pressure |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Week 0 – week 26 | |

| End point values | Intervention | placebo | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: mm Hg | | | | |
| arithmetic mean (confidence interval 95%) | -4.3 (-7.7 to -0.8) | -4.2 (-7.6 to -0.9) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
| Statistical analysis description: | |
| All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed. | |
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[13] |
| P-value | = 0.93 |
| Method | ANOVA |

Notes:

[13] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in diastolic blood pressure

| | |
|-----------------|------------------------------------|
| End point title | Change in diastolic blood pressure |
|-----------------|------------------------------------|

End point description:

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

End point timeframe:

Week 0 – week 26

| End point values | Intervention | placebo | | |
|---|---------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: mm Hg | | | | |
| arithmetic mean (confidence interval 95%) | -1.9 (-4.39 to 0.6) | 0.2 (-2.2 to 2.6) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|-----------------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[14] |
| P-value | = 0.32 |
| Method | ANOVA |

Notes:

[14] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in pulse

| | |
|-----------------|-----------------|
| End point title | Change in pulse |
|-----------------|-----------------|

End point description:

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

End point timeframe:

Week 0 – week 26

| End point values | Intervention | placebo | | |
|---|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: p | | | | |
| arithmetic mean (confidence interval 95%) | 5.0 (2.6 to 7.4) | 2.4 (0.1 to 4.7) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.36 ^[15] |
| Method | ANOVA |

Notes:

[15] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in HbA1c

| | |
|-----------------|-----------------|
| End point title | Change in HbA1c |
|-----------------|-----------------|

End point description:

overall glycaemic control parameters (HbA1c)

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

End point timeframe:

Week 0 – week 26

| End point values | Intervention | placebo | | |
|---|---------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: mmol/mol | | | | |
| arithmetic mean (confidence interval 95%) | -0.7 (-1.3 to -0.1) | 1.4 (0.8 to 2.0) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R

software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[16] |
| P-value | = 0.011 |
| Method | ANOVA |

Notes:

[16] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Change in SF-36 score

| | |
|---|-----------------------|
| End point title | Change in SF-36 score |
| End point description: | |
| Measures of health (Short Form Health Survey (SF-36)) | |
| End point type | Secondary |
| End point timeframe: | |
| Week 0 – week 26 | |

| End point values | Intervention | placebo | | |
|---|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: points | | | | |
| arithmetic mean (confidence interval 95%) | 7.9 (4.9 to 10.9) | 12.3 (9.3 to 15.2) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
| Statistical analysis description: | |
| All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed. | |
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[17] |
| P-value | = 0.48 |
| Method | ANOVA |

Notes:

[17] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Changes in Symptom Checklist (SCL-92)

| | |
|-----------------|---------------------------------------|
| End point title | Changes in Symptom Checklist (SCL-92) |
|-----------------|---------------------------------------|

| | |
|---|-----------|
| End point description: life quality measurement - Symptom Checklist (SCL-92) | |
| End point type | Secondary |
| End point timeframe: Week 0 – week 26 | |

| End point values | Intervention | placebo | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 65 | | |
| Units: points | | | | |
| arithmetic mean (confidence interval 95%) | -0.2 (-0.3 to -0.1) | -0.4 (-0.5 to -0.3) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|-----------------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[18] |
| P-value | = 0.38 |
| Method | ANOVA |

Notes:

[18] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Secondary: Heavy drinking days 6 months after end of trial

| | |
|--|---|
| End point title | Heavy drinking days 6 months after end of trial |
| End point description: Longterm effects of the intervention | |
| End point type | Secondary |
| End point timeframe: week 26 to 6 months followup | |

| End point values | Intervention | placebo | | |
|---|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 26 | | |
| Units: percentage points | | | | |
| arithmetic mean (confidence interval 95%) | -3.2 (-5.9 to -0.5) | -5.6 (-8.4 to -2.7) | | |

Statistical analyses

| Statistical analysis title | ANOVA from baseline to last observation endpoint |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

All continuous outcomes were analyzed with an ANOVA adjusted for baseline until the last observational endpoint, and missing data were imputed with the use of multiple imputations in the mice package in R software version 3.6.0, method = "pmm" (predictive mean matching), and the number of imputed datasets = 100. No adjustment for covariates was performed.

| | |
|---|------------------------|
| Comparison groups | Intervention v placebo |
| Number of subjects included in analysis | 55 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[19] |
| P-value | = 0.18 |
| Method | ANOVA |

Notes:

[19] - No superiority, equivalence, or noninferiority hypothesis testing framework were performed

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events were assessed at the week 4, week 12, week 20, and week 26 session. Patients were encouraged to make contact with the investigators at any time, and not wait for the assessments, if they experienced adverse events.

Adverse event reporting additional description:

Patients were asked if they had experienced any adverse events since the last meeting.

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

Dictionary used

| | |
|-----------------|------|
| Dictionary name | None |
|-----------------|------|

| | |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Intervention |
|-----------------------|--------------|

Reporting group description:

Bydureon

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

Reporting group description: -

| Serious adverse events | Intervention | Placebo | |
|---|--|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 62 (17.74%) | 8 / 65 (12.31%) | |
| number of deaths (all causes) | 1 | 1 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Alcohol withdrawal syndrome | Additional description: Number of hospitalizations (4 patients in each group, some admitted twice) | | |
| subjects affected / exposed | 9 / 62 (14.52%) | 6 / 65 (9.23%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Death | Additional description: No known cause of the death | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | 1 / 65 (1.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Gastrointestinal disorders | | | |
| Appendicitis | | | |

| | | | |
|---|---|----------------|--|
| subjects affected / exposed | 1 / 62 (1.61%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicide | Additional description: 7 weeks after the end of participation in the trial | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Suicidal behaviour | | | |
| subjects affected / exposed | 0 / 62 (0.00%) | 1 / 65 (1.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Intervention | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 60 / 62 (96.77%) | 60 / 65 (92.31%) | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | 2 / 65 (3.08%) | |
| occurrences (all) | 3 | 2 | |
| Headache | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | 4 / 65 (6.15%) | |
| occurrences (all) | 1 | 4 | |
| General disorders and administration site conditions | | | |
| Weight gain | | | |
| subjects affected / exposed | 12 / 62 (19.35%) | 31 / 65 (47.69%) | |
| occurrences (all) | 12 | 31 | |
| Weight loss overall | | | |
| subjects affected / exposed | 42 / 62 (67.74%) | 26 / 65 (40.00%) | |
| occurrences (all) | 42 | 26 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|------------------|------------------|--|
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 62 (1.61%) | 3 / 65 (4.62%) | |
| occurrences (all) | 1 | 3 | |
| Reflux gastritis | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | 2 / 65 (3.08%) | |
| occurrences (all) | 3 | 2 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | 3 / 65 (4.62%) | |
| occurrences (all) | 3 | 3 | |
| stool pattern changes | | | |
| subjects affected / exposed | 3 / 62 (4.84%) | 5 / 65 (7.69%) | |
| occurrences (all) | 3 | 5 | |
| Vomiting | | | |
| subjects affected / exposed | 14 / 62 (22.58%) | 5 / 65 (7.69%) | |
| occurrences (all) | 14 | 5 | |
| loss of appetite | | | |
| subjects affected / exposed | 15 / 62 (24.19%) | 6 / 65 (9.23%) | |
| occurrences (all) | 15 | 6 | |
| Nausea | | | |
| subjects affected / exposed | 23 / 62 (37.10%) | 10 / 65 (15.38%) | |
| occurrences (all) | 23 | 10 | |
| Hepatobiliary disorders | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 5 / 62 (8.06%) | 8 / 65 (12.31%) | |
| occurrences (all) | 5 | 8 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 8 / 62 (12.90%) | 9 / 65 (13.85%) | |
| occurrences (all) | 8 | 9 | |
| Skin and subcutaneous tissue disorders | | | |
| generalized itching | | | |
| subjects affected / exposed | 2 / 62 (3.23%) | 7 / 65 (10.77%) | |
| occurrences (all) | 9 | 9 | |
| injection site reactions | | | |
| subjects affected / exposed | 26 / 62 (41.94%) | 0 / 65 (0.00%) | |
| occurrences (all) | 26 | 0 | |

| | | | |
|---|--|---|--|
| Musculoskeletal and connective tissue disorders Fatigue subjects affected / exposed occurrences (all) muscle weakness subjects affected / exposed occurrences (all) | 8 / 62 (12.90%) 8 2 / 62 (3.23%) 2 | 3 / 65 (4.62%) 3 1 / 65 (1.54%) 1 | |
| Metabolism and nutrition disorders Weightloss 0-2 kg subjects affected / exposed occurrences (all) Weightloss 2-4 kg subjects affected / exposed occurrences (all) Weightloss > 4 kg subjects affected / exposed occurrences (all) | 17 / 62 (27.42%) 30 7 / 62 (11.29%) 7 18 / 62 (29.03%) 18 | 13 / 65 (20.00%) 30 10 / 65 (15.38%) 10 3 / 65 (4.62%) 3 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|--|
| It is not possible to repport the findings from the fMRI brain imaging, and DAT SPECT scans, in this format. |
|--|

Notes: