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 Sauntes 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
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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 ilness

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 hevy 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 recieving 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	52.1	52.5	
standard deviation	± 10.8	± 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 o - 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 controlparameters (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 assesed 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	8 / 62 (12.90%)	3 / 65 (4.62%)	
occurrences (all)	8	3	
muscle weakness			
subjects affected / exposed	2 / 62 (3.23%)	1 / 65 (1.54%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
Weightloss 0-2 kg			
subjects affected / exposed	17 / 62 (27.42%)	13 / 65 (20.00%)	
occurrences (all)	30	30	
Weightloss 2-4 kg			
subjects affected / exposed	7 / 62 (11.29%)	10 / 65 (15.38%)	
occurrences (all)	7	10	
Weightloss > 4 kg			
subjects affected / exposed	18 / 62 (29.03%)	3 / 65 (4.62%)	
occurrences (all)	18	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: