ClinicalTrials.gov PRS
Protocol Registration and Results System

ID: 12023A Efficacy of Nalmefene in Patients With Alcohol Dependence NCT00812461

Protocol Registration and Results Preview

Close

Efficacy of Nalmefene in Patients With Alcohol Dependence (ESENSE2)

This study has been completed.

Sponsor:	H. Lundbeck A/S
Collaborators:	
Information provided by (Responsible Party):	H. Lundbeck A/S
ClinicalTrials.gov Identifier:	NCT00812461

Purpose

The purpose of the study is to evaluate the efficacy, safety and tolerability of nalmefene in the treatment of alcohol dependence.

Condition	Intervention	Phase
Alcohol Dependence	Drug: Placebo Drug: Nalmefene	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Efficacy Study

Official Title: Nalmefene Efficacy Study II: Randomised, Double-blind, Placebo-controlled, Parallel-group, Efficacy Study of 20 mg Nalmefene, as Needed Use, in Patients With Alcohol Dependence

Further study details as provided by H. Lundbeck A/S:

Primary Outcome Measure:

- Change From Baseline in the Monthly Number of Heavy Drinking Days (HDDs) [Time Frame: Baseline and Month 6] [Designated as safety issue: No]
  Number of HDDs over a month (28 days), where one HDD was defined as a day with alcohol consumption ≥60 grams (g) for men and ≥40 g for women.

- Change From Baseline in the Monthly Total Alcohol Consumption (TAC) [Time Frame: Baseline and Month 6] [Designated as safety issue: No]
  TAC was defined as mean daily alcohol consumption in g/day over a month (28 days).

Secondary Outcome Measures:

- Drinking Risk Level (RSDRL) Response [Time Frame: Month 6] [Designated as safety issue: No]

RSDRL response was defined as a downward shift from baseline in Drinking Risk Level (DRL); for patients at very high risk at Baseline: a shift to medium risk or below, and for patients at high or medium risk at Baseline: a shift to low risk or below.

- Change From Baseline in Clinical Status Using CGI-S [Time Frame: Baseline and Week 24] [Designated as safety issue: No]
  The Clinical Global Impression - Severity of Illness (CGI-S) provides the clinician's impression of the patient's current state of mental illness. The clinician uses his or her clinical experience of this patient population to rate the severity of the patient's current mental illness on a 7-point scale ranging from 1 (Normal - not at all ill) to 7 (among the most extremely ill patients).

- Change in Clinical Status Using the CGI-I [Time Frame: Week 24] [Designated as safety issue: No]
  The Clinical Global Impression - Global Improvement (CGI-I) provides the clinician's impression of the patient's improvement (or worsening). The clinician assesses the patient's condition relative to a baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse).

- Liver Function Test Gamma-glutamyl Transferase (GGT) [Time Frame: Week 24] [Designated as safety issue: No]
  GGT values

- Liver Function Test Alanine Aminotransferase (ALAT) [Time Frame: Week 24] [Designated as safety issue: No]
  ALAT values

Enrollment: 678
Study Start Date: March 2009
Study Completion Date: April 2011
Primary Completion Date: March 2011

Arms	Assigned Interventions
Placebo Comparator: Placebo	Drug: Placebo as-needed use, tablets, orally, 6 months
Experimental: Nalmefene	Drug: Nalmefene 18.06 mg, as-needed use, tablets, orally, 6 months. 18.06 mg nalmefene equals 20 mg nalmefene hydrochloride. Other Names: • Selincro™

Alcohol dependence is a maladaptive pattern of alcohol use, leading to clinically significant impairment or distress, as manifested by at least three of a number of criteria such as tolerance, withdrawal symptoms, frequent use of alcohol in larger amounts or over longer periods than was intended, and others. Excessive intake of alcohol reduces the life span by a decade, and alcohol drinking is strongly related to mortality from liver cirrhosis, chronic pancreatitis, certain cancers, hypertension, accidents and violence. This study is planned to evaluate the efficacy and safety of as needed use of nalmefene 18.06 mg versus placebo in decreasing monthly Heavy Drinking

Days (HDDs) and decreasing the total consumption during a period of 24 weeks in adult patients with alcohol dependence.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Inclusion Criteria:

In- and outpatients who:

- had a primary diagnosis of alcohol dependence according to Diagnostic and Statistical Manual of Mental Disorders - text revision (DSM-IV-TR) criteria
- had had ≥6 HDDs in the 4 weeks preceding the Screening Visit
- had had an average alcohol consumption at WHO medium risk level or above in the 4 weeks preceding the Screening Visit

Exclusion Criteria:

The patient:

- had a DSM-IV Axis I disorder other than alcohol dependence or nicotine dependence
- had an antisocial personality disorder
- had risk of suicide evaluated by the suicidality module of the Mini-International Neuropsychiatric Interview (MINI)
- had a history of delirium tremens or alcohol withdrawal seizures
- reported current or recent (within 3 months preceding screening) treatment with disulfiram, acamprosate, topiramate, naltrexone or carbimide, or with any opioid antagonists
- reported current or recent treatment with antipsychotics or antidepressants
- was pregnant or breast-feeding

Other protocol-defined inclusion and exclusion criteria may apply.

Contacts and Locations

Locations

Belgium

BE002
Assebroek, Belgium, 8310
BE007
Brugge, Belgium, 8000
BE006
Charleroi, Belgium, 6000
BE005
Kortenberg, Belgium, 3070
BE001
Liège, Belgium, 4000
BE003
Mechelen, Belgium, 2800
BE004
Oostende, Belgium, 8400

Czech Republic

CZ001
Litomerice, Czech Republic, 41201
CZ002
Praha 10, Czech Republic, 100 00
CZ003
Praha 6, Czech Republic, 160 00

France

FR008
Angers, France, 4933
FR004
Bully les Mines, France, 62160
FR009
Clichy Cedex 92, France, 92110
FR012
Elancourt, France, 78990
FR021
La Rochelle, France, 17022
FR011
Le Pecq, France, 78230
FR019
Lille, France, 59037
FR016
Lyon, France, 69005
FR014
Nancy, France, 54000
FR015
Nimes, France, 30029
FR002
Rennes, France, 35000
FR001
Sartrouville, France, 78500
FR007
Strasbourg, France, 67000
FR005
Toulouse, France, 31000
FR006
Toulouse, France, 31200
FR003
Villejuif, France, 94804

Italy

IT017
Bologna, Italy, 40123
IT013

Bologna, Italy, 44042

IT008

Cento, Italy, 44042

IT006

Firenze, Italy, 50134

IT002

Parma, Italy, 43100

IT004

Rome, Italy, RM 00186

IT011

Rome, Italy, RM 00168

IT001

Rome, Italy, 00163

IT007

Rome, Italy, 00123

IT018

Soverato, Italy, CZ 88068

Poland

PL005

Gdansk, Poland, 80-952

PL004

Leszno, Poland, 64-100

PL006

Lublin, Poland, 20-109

PL007

Lublin, Poland, 20-442

PL002

Piekary Slaskie, Poland, 41940

PL003

Skorzewo, Poland, 60-185

PL001

Szczecin, Poland, 71-460

Portugal

PT003

Angra do Heroismo, Portugal, 9700-161

PT001

Lisboa, Portugal, 1649-035

PT002

Lisboa, Portugal, 1350-179

PT006

Mem Martins, Portugal, 2725

Spain

ES005
Alicante, Spain, 3550
ES004
Barcelona, Spain, 8028
ES006
Barcelona, Spain, 8003
ES008
Barcelona, Spain, 8025
ES014
Burgos, Spain, 9006
ES010
Madrid, Spain, 28034
ES001
Mallorca, Spain, 7193
ES002
Oviedo, Spain, 33011
ES003
Valencia, Spain, 46010
ES011
Zamora, Spain, 49021

Investigators

Study Director:	Email contact via H. Lundbeck A/S	LundbeckClinicalTrials@lundbeck.com

More Information

Results Publications:

Gual A, He Y, Torup L, van den Brink W, Mann K; ESENSE 2 Study Group. A randomised, double-blind, placebo-controlled, efficacy study of nalmefene, as-needed use, in patients with alcohol dependence. Eur Neuropsychopharmacol. 2013 Nov;23(11):1432-42. doi: 10.1016/j.euroneuro.2013.02.006. Epub 2013 Apr 3.

Responsible Party: H. Lundbeck A/S
Study ID Numbers: 12023A
2007-002563-27 [EudraCT Number]
Health Authority: Belgium: Federal Agency for Medicinal Products and Health Products
Czech Republic: State Institute for Drug Control
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Italy: The Italian Medicines Agency
Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
Portugal: National Pharmacy and Medicines Institute
Spain: Spanish Agency of Medicines

Study Results

Participant Flow

Recruitment Details	
Pre-Assignment Details	

Arm/Group Title	Placebo	Nalmefene 18.06 mg	Total (Not public)
▼ Arm/Group Description	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months	
Period Title: **All Randomised Patients**			
Started	360	358	718
Completed	337	341	678
Not Completed	23	17	40
Reason Not Completed			
Did not receive placebo/nalmefene	23	17	40
(Not Public)	Not Completed = 23 Total from all reasons = 23	Not Completed = 17 Total from all reasons = 17	
Period Title: **All Treated Patients**			
Started	337	341	678
Completed	205 [1]	194 [2]	399
Not Completed	132	147	279
Reason Not Completed			
Adverse Event	8	15	23
Lack of Efficacy	13	7	20
Non-compliance	6	9	15
Protocol Violation	36	27	63
Withdrawal by Subject	45	54	99
Lost to Follow-up	11	14	25
Other Reason	13	21	34
(Not Public)	Not Completed = 132 Total from all reasons = 132	Not Completed = 147 Total from all reasons = 147	

[1] Patients who had the final visit of the study protocol

[2] Patients who had the final visit of the study protocol

Baseline Characteristics

Arm/Group Title	Placebo	Nalmefene 18.06 mg	Total
▼ Arm/Group Description	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months	

Overall Number of Baseline Participants	360	358	**718**
▼ Baseline Analysis Population Description [Not specified]			
Age, Continuous [1] Mean (Standard Deviation) Units: years	44.4 (10.7)	45.1 (10.7)	44.8 (10.7)
	[1] All-patients-randomised set (APRS).		
Gender, Male/Female [1] Measure Type: Number Units: participants NOTE : Baseline Measure Description is shorter than the Baseline Measure Title.			
Female	104	92	196
Male	256	266	522
	[1] APRS.		
Previously Treated for Alcohol Dependence [1] Measure Type: Number Units: participants NOTE : Baseline Measure Description is shorter than the Baseline Measure Title.			
NO	213	215	428
YES	147	142	289
UNKNOWN	0	1	1
	[1] APRS		
Previously Treated for Alcohol Withdrawal Symptoms] [1] Measure Type: Number Units: participants NOTE : Baseline Measure Description is shorter than the Baseline Measure Title.			
NO	292	300	592
YES	68	57	125
UNKNOWN	0	1	1
	[1] APRS.		
Total Monthly Heavy			

Drinking Days (HDD) [1] Mean (Standard Deviation) Units: days	18.37 (7.03)	19.71 (6.96)	19.04 (7.03)
	[1] APRS. Based on Timeline Followback (TLFB) data from the month preceding the screening visit.		
Total Alcohol Consumption (TAC) g Alcohol/Day [1] Mean (Standard Deviation) Units: g	88.76 (48.15)	92.22 (46.87)	90.49 (47.52)
	[1] APRS. Based on TLFB data from the month preceding the screening visit.		
Drinking Risk Level (DRL) [1] Measure Type: Number Units: participants NOTE : Baseline Measure Description is shorter than the Baseline Measure Title.			
Low	6	5	11
Medium	82	68	150
High	134	129	263
Very High	138	156	294
	[1] APRS.		
Clinical Global Impression - Severity of Illness (CGI-S) [1] Mean (Standard Deviation) Units: units on a scale	3.99 (1.42)	4.05 (1.45)	4.02 (1.44)
	[1] APRS. The Clinical Global Impression - Severity of Illness (CGI-S) provides the clinician's impression of the patient's current state of mental illness. The clinician uses his or her clinical experience of this patient population to rate the severity of the patient's current mental illness on a 7-point scale ranging from 1 (Normal - not at all ill) to 7 (among the most extremely ill patients).		
Gamma-glutamyl Transferase (GGT) [1] Mean (Standard Deviation) Units: international units per liter (IU/L) NOTE : Baseline Measure Description is shorter than the Baseline Measure Title.	97.39 (165.12)	91.98 (153.01)	94.69 (159.09)
	[1] APRS.		
Alanine Aminotransferase			

(ALAT) [1] Mean (Standard Deviation) Units: IU/L NOTE : Baseline Measure Description is shorter than the Baseline Measure Title.	34.32 (26.06)	34.20 (22.70)	34.26 (24.42)
	[1] APRS.		

Outcome Measures

1. Primary Outcome

Title:	Change From Baseline in the Monthly Number of Heavy Drinking Days (HDDs)
Description:	Number of HDDs over a month (28 days), where one HDD was defined as a day with alcohol consumption ≥60 grams (g) for men and ≥40 g for women.
Time Frame:	Baseline and Month 6
Safety Issue?	No

Outcome Measure Data

Analysis Population Description

Full-analysis set (FAS) - all patients in the all-patients-treated set (APTS) who had at least one valid post-baseline assessment in the main treatment period of both co-primary efficacy variables (HDD and TAC) and had an average alcohol consumption at medium Drinking Risk Level (DRL) or above according to WHO criteria at Baseline.

Arm/Group Title	Placebo	Nalmefene 18.06 mg
Arm/Group Description:	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months
Number of Participants Analyzed	229	212
Mean (Standard Error) Units: days	-10.58 (0.52)	-12.30 (0.54)

Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Placebo, Nalmefene 18.06 mg
	Comments	The primary hypothesis concerned the treatment effect at Month 6. The null hypothesis of no difference in treatment

		effect was tested against the alternative hypothesis that there was a difference in treatment effect. MMRM model with the Baseline score as a covariate; site, sex, time in months (Month 1-6); and treatment as fixed effects. The Baseline score-by-time and treatment-by-time interactions were also included in the model. An unstructured covariance matrix was used.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.012
	Comments	[Not specified]
	Method	Other [Adjusted change from Baseline to Month 6]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.72
	Confidence Interval	(2-Sided) 95% -3.07 to -0.38
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.68
	Estimation Comments	The Number of Participants Analyzed is participants with efficacy measurement available at this endpoint, that is, 229 participants in the placebo group and 212 participants in the nalmefene group.

2. Primary Outcome

Title:	Change From Baseline in the Monthly Total Alcohol Consumption (TAC)
▼ Description:	TAC was defined as mean daily alcohol consumption in g/day over a month (28 days).

Time Frame:	Baseline and Month 6
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

FAS

Arm/Group Title	Placebo	Nalmefene 18.06 mg
▼ Arm/Group Description:	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months
Number of Participants Analyzed	229	212
Mean (Standard Error) Units: g	-54.06 (2.23)	-59.01 (2.29)

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Placebo, Nalmefene 18.06 mg
	Comments	The primary hypothesis concerned the treatment effect at Month 6. The null hypothesis of no difference in treatment effect was tested against the alternative hypothesis that there was a difference in treatment effect. MMRM model with the Baseline score as a covariate; site, sex, time in months (Month 1-6); and treatment as fixed effects. The Baseline score-by-time and treatment-by-time interactions were also included in the model. An unstructured covariance matrix was used.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.088
	Comments	[Not specified]
	Method	Other [Adjusted change from Baseline to Month 6]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-4.95
	Confidence Interval	(2-Sided) 95% -10.63 to 0.73
	Parameter Dispersion	Type: Standard Error of the mean Value: 2.89
	Estimation Comments	The Number of Participants Analyzed is participants with efficacy measurement available at this endpoint, that is, 229 participants in the placebo group and 212 participants in the nalmefene group.

3. Secondary Outcome

Title:	Drinking Risk Level (RSDRL) Response
▼ Description:	RSDRL response was defined as a downward shift from baseline in Drinking Risk Level (DRL); for patients at very high risk at Baseline: a shift to medium risk or below, and for patients at high or medium risk at Baseline: a shift to low risk or below.
Time Frame:	Month 6
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
FAS

Arm/Group Title	Placebo	Nalmefene 18.06 mg
▼ Arm/Group Description:	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months
Number of Participants Analyzed	326	329
Measure Type: Number Units: percentage of participants	47.9	45.6

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Nalmefene 18.06 mg
	Comments	The analysis of RSDRL used a logistic regression (LREG) model, with country, sex, Baseline DRL, and treatment as fixed effects, and missing values were imputed using individual-patient predicted values of TAC derived from the MMRM model.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.630
	Comments	[Not specified]
	Method	Other [Adjusted Odds Ratio (OR) response]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	0.92
	Confidence Interval	(2-Sided) 95% 0.67 to 1.27
	Estimation Comments	[Not specified]

4. Secondary Outcome

Title:	Change From Baseline in Clinical Status Using CGI-S
▼ Description:	The Clinical Global Impression - Severity of Illness (CGI-S) provides the clinician's impression of the patient's current state of mental illness. The clinician uses his or her clinical experience of this patient population to rate the severity of the patient's current mental illness on a 7-point scale ranging from 1 (Normal - not at all ill) to 7 (among the most extremely ill patients).
Time Frame:	Baseline and Week 24
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description
FAS

Arm/Group Title	Placebo	Nalmefene 18.06 mg
▼ Arm/Group Description:	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months
Number of Participants Analyzed	225	203
Mean (Standard Error) Units: units on a scale	-1.04 (0.08)	-1.27 (0.08)

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Placebo, Nalmefene 18.06 mg
	Comments	MMRM model with the Baseline score as a covariate, and site, sex, time in weeks, and treatment as fixed effects. The Baseline score-by-time and treatment-by-time interactions were also included in the model; an unstructured covariance matrix was used.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.029
	Comments	[Not specified]
	Method	Other [Adjusted change from Baseline to Week 24]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.23
	Confidence Interval	(2-Sided) 95% -0.44 to -0.02
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.11
	Estimation Comments	The Number of Participants Analyzed is participants with efficacy measurement available at this endpoint, that is, 225 participants in the placebo group and 203 participants in the nalmefene group.

5. Secondary Outcome

Title:	Change in Clinical Status Using the CGI-I
▼ Description:	The Clinical Global Impression - Global Improvement (CGI-I) provides the clinician's impression of the patient's improvement (or worsening). The clinician assesses the patient's condition relative to a baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse).
Time Frame:	Week 24
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

FAS

Arm/Group Title	Placebo	Nalmefene 18.06 mg
▼ Arm/Group Description:	as-needed use, tablets,	as-needed use, tablets, orally,

	orally, 6 months	6 months
Number of Participants Analyzed	225	203
Mean (Standard Error) Units: units on a scale	2.68 (0.08)	2.51 (0.08)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Nalmefene 18.06 mg
	Comments	MMRM model with the Baseline CGI-S score as a covariate, and site, sex, time in weeks, and treatment as fixed effects. The Baseline CGI-S score-by-time and treatment-by-time interactions were also included in the model. An unstructured covariance matrix was used.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.111
	Comments	[Not specified]
	Method	Other [Adjusted change from Baseline to Week 24]

	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-0.17
	Confidence Interval	(2-Sided) 95% -0.38 to 0.04
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.11
	Estimation Comments	The Number of Participants Analyzed is participants with efficacy measurement available at this endpoint, that is, 225 participants in the placebo group and 203 participants in the nalmefene group.

6. Secondary Outcome

Title:	Liver Function Test Gamma-glutamyl Transferase (GGT)
▼ Description:	GGT values NOTE : Outcome Measure Description is shorter than the Outcome Measure Title.
Time Frame:	Week 24
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description
FAS

Arm/Group Title	Placebo	Nalmefene 18.06 mg
▼ Arm/Group Description:	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months
Number of Participants Analyzed	224	207
Geometric Mean (Geometric Coefficient of Variation) Units: IU/L	44.9 (75.7%)	43.3 (75.2%)

▼ Statistical Analysis 1 ✓

Statistical Analysis	Comparison Groups	Placebo, Nalmefene 18.06 mg
	Comments	Log-transformed GGT values

Overview		were analysed using an MMRM model with the log-transformed Baseline value as a covariate, and site, sex, time in weeks, and treatment as fixed effects. Logtransformed Baseline value-by-time interaction and treatment-by-time interaction were included in the model. An unstructured covariance matrix was used.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.529
	Comments	[Not specified]
	Method	Other [[Adjusted values]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[Ratio to placebo]
	Estimated Value	0.96
	Confidence Interval	(2-Sided) 95% 0.86 to 1.08
	Estimation Comments	The Number of Participants Analyzed is participants with efficacy measurement available at this endpoint, that is, 224 participants in the placebo group and 207 participants in the nalmefene group.

7. Secondary Outcome

Title:	Liver Function Test Alanine Aminotransferase (ALAT)
▼ Description:	ALAT values NOTE : Outcome Measure Description is shorter than the Outcome Measure Title.
Time Frame:	Week 24
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

FAS

Arm/Group Title	Placebo	Nalmefene 18.06 mg
▼ Arm/Group Description:	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months
Number of Participants Analyzed	222	205
Geometric Mean (Geometric Coefficient of Variation) Units: IU/L	27.2 (56.3%)	25.0 (55.7%)

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Placebo, Nalmefene 18.06 mg
	Comments	Log-transformed ALAT values were analysed using an MMRM model with the log-transformed Baseline value as a covariate, and site, sex, time in weeks, and treatment as fixed effects. Logtransformed Baseline value-by-time and treatment-by-time interactions were included in the model. An unstructured covariance matrix was used.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.049
	Comments	[Not specified]
	Method	Other [[Adjusted values]

	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[Ratio to placebo]
	Estimated Value	0.92
	Confidence Interval	(2-Sided) 95% 0.84 to 1.00
	Estimation Comments	The Number of Participants Analyzed is participants with efficacy measurement available at this endpoint, that is, 222 participants in the placebo group and 205 participants in the nalmefene group.

Adverse Events

Time Frame	Serious Adverse Events: 24 weeks, a 4-week run-out period, and a safety follow-up (visit/telephone call) scheduled for 4 weeks after completion of the study or after withdrawal from the study. Other Adverse Events: 24 weeks and a 4-week run-out period.
Additional Description	
Source Vocabulary Name	[Not specified]
Assessment Type	[Not specified] NOTE : An Assessment Type for Table Default has not been specified.

Arm/Group Title	Placebo	Nalmefene 18.06 mg
Arm/Group Description	as-needed use, tablets, orally, 6 months	as-needed use, tablets, orally, 6 months

Serious Adverse Events

	Placebo	Nalmefene 18.06 mg
	Affected / at Risk (%)	Affected / at Risk (%)
Total	14/337 (4.15%)	7/341 (2.05%)
Cardiac disorders		
Myocardial infarction [A]	0/337 (0%)	1/341 (0.29%)
Gastrointestinal disorders		
Pancreatitis acute [A]	1/337 (0.3%)	0/341 (0%)
Rectal haemorrhage [A]	1/337 (0.3%)	0/341 (0%)
General disorders		

Sudden death	A	0/337 (0%)	1/341 (0.29%)
Infections and infestations			
Pneumonia	A	1/337 (0.3%)	0/341 (0%)
Pyothorax	A	1/337 (0.3%)	0/341 (0%)
Subcutaneous abscess	A	1/337 (0.3%)	0/341 (0%)
Injury, poisoning and procedural complications			
Accidental overdose	A	1/337 (0.3%)	0/341 (0%)
Alcohol poisoning	A	1/337 (0.3%)	0/341 (0%)
Drug toxicity	A	1/337 (0.3%)	0/341 (0%)
Fall	A	0/337 (0%)	1/341 (0.29%)
Fibula fracture	A	1/337 (0.3%)	0/341 (0%)
Head injury	A	0/337 (0%)	1/341 (0.29%)
Intentional overdose	A	3/337 (0.89%)	0/341 (0%)
Tendon rupture	A	0/337 (0%)	1/341 (0.29%)
Tibia fracture	A	1/337 (0.3%)	0/341 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bile duct cancer	A	1/337 (0.3%)	0/341 (0%)
Nervous system disorders			
Dizziness	A	1/337 (0.3%)	0/341 (0%)
Epilepsy	A	1/337 (0.3%)	0/341 (0%)
Subarachnoid haemorrhage	A	0/337 (0%)	1/341 (0.29%)
Psychiatric disorders			
Alcoholism	A	0/337 (0%)	2/341 (0.59%)
Suicidal behaviour	A	1/337 (0.3%)	0/341 (0%)
Vascular disorders			
Arteritis	A	1/337 (0.3%)	0/341 (0%)
Hypotension	A	1/337 (0.3%)	0/341 (0%)

Indicates events were collected by non-systematic methods.

A Term from vocabulary, Meddra 13.0

▼ Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%

	Placebo	**Nalmefene 18.06 mg**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	102/337 (30.27%)	157/341 (46.04%)
Gastrointestinal disorders		

Diarrhoea	A	18/337 (5.34%)	8/341 (2.35%)
Nausea	A	20/337 (5.93%)	59/341 (17.3%)
Vomiting	A	8/337 (2.37%)	19/341 (5.57%)
Infections and infestations			
Nasopharyngitis	A	20/337 (5.93%)	22/341 (6.45%)
Nervous system disorders			
Dizziness	A	14/337 (4.15%)	52/341 (15.25%)
Headache	A	26/337 (7.72%)	43/341 (12.61%)
Psychiatric disorders			
Anxiety	A	17/337 (5.04%)	11/341 (3.23%)
Insomnia	A	23/337 (6.82%)	49/341 (14.37%)

Indicates events were collected by non-systematic methods.

A Term from vocabulary, Meddra 13.0

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The main publication has to be published before any sub publication. The investigators shall obtain Lundbeck's written approval before publishing any publication relating to nalmefene, the Study, the Protocol and/or the results recorded during the Study.

Results Point of Contact

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