ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 06/17/2015

ClinicalTrials.gov ID: NCT01305577

Study Identification

Unique Protocol ID:	ATX-101-10-16
Brief Title:	Evaluation of Safety and Efficacy of Deoxycholic Acid Injection (ATX-101) in the Reduction of Submental Fat
Official Title:	Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study of ATX-101 (Sodium Deoxycholate Injection) Versus Placebo for the Reduction of Localized Subcutaneous Fat in the Submental Area
Secondary IDs:	2010-020690-17 [EudraCT Number]

Study Status

Record Verification:	June 2015
Overall Status:	Completed
Study Start:	December 2010
Primary Completion:	January 2012 [Actual]
Study Completion:	January 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Kythera Biopharmaceuticals
Responsible Party:	Sponsor
Collaborators:	Bayer

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: December 6 , 2010 Board Name: North West 3 Research Ethics Committee - Liverpool East Board Affiliation: Governance Arrangements for Research Ethics Committees Phone: 0161 6257835 Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United Kingdom: Medicines and Healthcare Products Regulatory Agency

Study Description

Brief Summary:	To evaluate the safety and efficacy of deoxycholic acid injection in the reduction of submental fat (fat below the chin).
Detailed Description:	

Conditions

Conditions:	Moderate or Severe Submental Fullness
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	3
Masking:	Double Blind (Subject, Investigator)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	363 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Placebo Comparator: Placebo Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.	Drug: Placebo Phosphate buffered saline placebo for injection
Experimental: Deoxycholic Acid Injection 1 mg/cm² Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.	Drug: Deoxycholic acid injection Other Names: • ATX-101
Experimental: Deoxycholic Acid Injection 2 mg/cm² Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.	Drug: Deoxycholic acid injection Other Names: • ATX-101

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 65 Years

Gender: Both

Accepts Healthy Volunteers?: Yes

Criteria: Inclusion Criteria:

1. Submental fat graded by the investigator as 2 or 3 using the Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) as determined on Visit 2.
2. Dissatisfaction with the submental area rated by the subject as 0, 1, 2, or 3 using the Subject Self Rating Scale (SSRS).
3. Males and nonpregnant, nonlactating females between 18 and 65 years of age, inclusive on the day of randomization. Females of childbearing potential must have a negative human chorionic gonadotropin (hCG) test result within 28 days before randomization and agree to practice medically acceptable birth control during the course of the study. Medically acceptable birth control includes: surgical sterilization, hormonal contraceptives, barrier methods or an intrauterine device (IUD).
4. History of stable body weight, in the judgment of the investigator, for at least 6 months before randomization. No significant change, in the judgment of the investigator, in diet or exercise practices for at least 6 months before randomization and agreement to not change diet or exercise practices during the course of the study.
5. Expected to comply with and understand the visit schedule and all protocol-specified tests and procedures.

6. Medically able to undergo the administration of study material determined by clinical evaluations made within 56 days before and laboratory tests obtained within 28 days before randomization for which the investigator identified no clinically significant abnormality.
7. Signed informed consent obtained before any study-specific procedure is performed.

Exclusion Criteria:

1. History of any intervention to treat submental fat (e.g., liposuction, surgery, or lipolytic agents) or trauma associated with the chin or neck areas, which in the judgment of the investigator may affect evaluation of safety or efficacy of treatment.
2. Loose skin in the neck or chin area for which reduction in submental fat may, in the judgment of the investigator, result in an aesthetically unacceptable outcome or a score of 4 on the Skin Laxity Rating Scale (SLRS).
3. Prominent platysmal bands at rest or other anatomical features that, in the judgment of the investigator, may interfere with the evaluation of submental fat or result in an aesthetically unacceptable outcome.
4. Evidence of any cause of enlargement in the submental area (e.g., thyroid enlargement or cervical adenopathy) other than localized submental fat.
5. Body mass index (BMI) greater than 30.
6. Currently on or considering starting a weight reduction regimen.
7. Any medical condition (e.g., respiratory, cardiovascular, hepatic, neurological disease, uncontrolled hypertension, or thyroid dysfunction) that would interfere with assessment of safety or efficacy or compromise the subject's ability to undergo study procedures or provide informed consent.
8. Treatment with radio frequency, laser procedures, chemical peels, or dermal fillers in the neck or chin area within 12 months before randomization, or botulinum toxin injections in the neck or chin area within 6 months before randomization.
9. History of sensitivity to any components of the study material or to topical or local anesthetics (e.g., lidocaine, benzocaine, or novocaine).
10. Previous randomization into this study or previous treatment with ATX-101.
11. Treatment with an investigational device or agent within 30 days of randomization.

Contacts/Locations

Study Officials: Frederick Beddingfield, MD, PhD
Study Director
Kythera Biopharmaceuticals, Inc.

Locations: United Kingdom
Investigational Site
Salford, Manchester, United Kingdom, M6 8HD

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Investigational Site
Plymouth, Plymouth, United Kingdom, PL6 8BX

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Barcelona, Spain, 08022

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Investigational Site
Barcelona, Spain, 08034

Investigational Site
Barcelona, Spain, 08028

Germany
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Darmstadt, Germany, 64297

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Potsdam, Germany, 14469

Investigational Site
Starnberg, Germany, 82319

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Northeim, Germany, D-37154

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Landau, Germany, 76829

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Ludwigshafen, Germany, 67061

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Frankfurt/Main, Germany, 60590

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Darmstadt, Germany, 64297

Investigational Site
Augsburg, Germany, 86179

Investigational Site
Augsburg, Germany, 86163

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München, Germany, 80337

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Paris, France, 75010

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References

Citations:

Links:

Study Results

Participant Flow

Recruitment Details	This study was conducted in 28 study centers in the European Union.
Pre-Assignment Details	The study consisted of a 12-week treatment period and a 12-week safety follow-up period.

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Overall Study

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Started	120	121	122
Received Treatment	119	121	122
Completed	107	110	112
Not Completed	13	11	10
Adverse Event	2	2	1
Withdrawal by Subject	7	5	6
Lost to Follow-up	4	3	2
Protocol Deviation	0	1	1

Baseline Characteristics

Analysis Population Description
Intent-to-treat population

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Baseline Measures

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo	Total
Number of Participants	120	121	122	363
Age, Continuous [units: years] Mean (Standard Deviation)	45.8 (10.94)	46.7 (9.78)	46.6 (10.17)	46.4 (10.28)
Age, Customized [units: participants]				
18 - 50 years	77	79	72	228
51 - 65 years	43	42	50	135
Gender, Male/Female [units: participants]				
Female	95	95	87	277
Male	25	26	35	86
Race/Ethnicity, Customized [units: participants]				
Asian	0	0	1	1
Black or African American	2	2	0	4
Hispanic or Latino	5	2	3	10

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo	Total
Native Hawaiian or Other Pacific Islander	1	0	0	1
White	111	116	117	344
Other	1	1	1	3
Weight [units: kg] Mean (Standard Deviation)	73.83 (11.518)	73.53 (12.413)	73.50 (12.126)	73.62 (11.994)
Body Mass Index (BMI) [units: kg/m²] Mean (Standard Deviation)	25.94 (2.724)	25.66 (3.063)	25.54 (2.758)	25.71 (2.850)
Fitzpatrick Skin Type [1] [units: participants]				
I-III	108	109	99	316
IV-VI	12	12	23	47

[1] Fitzpatrick Skin Type is a numerical classification schema for human skin color and typical response to ultraviolet (UV) light:

- Type I: Pale white skin, blue/hazel eyes, blond/red hair; Always burns, does not tan.
- Type II: Fair skin, blue eyes; Burns easily, tans poorly.
- Type III: Darker white skin; Tans after initial burn.
- Type IV: Light brown skin; Burns minimally, tans easily.
- Type V: Brown skin; Rarely burns, tans darkly easily.
- Type VI: Dark brown or black skin; Never burns, always tans darkly.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With a Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) 1-grade Response
Measure Description	A CR-SMFRS response is defined as at least a 1-point improvement (i.e. 1-point reduction) from Baseline 12 weeks after the last treatment. The CR-SMFRS score is based on the investigator's clinical evaluation of the participant, where submental fullness is scored on a 5-point ordinal scale (0-4) with 0 = absent, 1 = mild, 2 = moderate, 3 = severe, and 4 = extreme.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population, which consisted of all randomized participants who had at least one efficacy assessment (CR-SMFRS or Subject Self Rating Scale) at Baseline. Last observation carried forward (LOCF) method was used to impute missing data.

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Measured Values

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Number of Participants Analyzed	120	121	122
Percentage of Participants With a Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) 1-grade Response [units: percentage of participants]	59.2	65.3	23.0

Statistical Analysis 1 for Percentage of Participants With a Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) 1-grade Response

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 1 mg/cm², Placebo
	Comments	The null hypothesis was there was no difference between deoxycholic acid 1 mg/cm² and placebo. An adjustment for multiplicity was performed for the two co-primary endpoints. This was accounted for by using the larger of the two P-values in the Bonferroni-Holm scheme.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic

	Comments	Logistic regression analysis with treatment and Baseline CR-SMFRS value in the model.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	4.73
	Confidence Interval	(2-Sided) 95% 2.70 to 8.28
	Estimation Comments	The odds ratio was based on a logistic regression model adjusted for the Baseline score. Odds ratios >1 indicate a positive treatment effect.

Statistical Analysis 2 for Percentage of Participants With a Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) 1-grade Response

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 2 mg/cm², Placebo
	Comments	The null hypothesis was there was no difference between deoxycholic acid 2 mg/cm² and placebo. An adjustment for multiplicity was performed for the two co-primary endpoints. This was accounted for by using the larger of the two P-values in the Bonferroni-Holm scheme.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	Logistic regression analysis with treatment and Baseline CR-SMFRS value in the model.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	6.21
	Confidence Interval	(2-Sided) 95% 3.52 to 10.94
	Estimation Comments	The odds ratio was based on a logistic regression model adjusted for the Baseline score. Odds ratios >1 indicate a positive treatment effect.

2. Primary Outcome Measure:

Measure Title	Percentage of Participants With a Subject Self Rating Scale (SSRS) Response

Measure Description	A SSRS response is defined as an SSRS score that is 4 or greater 12 weeks after the last treatment. The SSRS assesses participant's satisfaction with their appearance in association with the face and chin on a 7-point scale from 0 to 6: where 0 = Extremely dissatisfied, 1 = Dissatisfied, 2 = Slightly dissatisfied, 3 = Neither satisfied nor dissatisfied, 4 = Slightly satisfied, 5 = Satisfied and 6 = Extremely satisfied.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population; LOCF method was used to impute missing data

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Measured Values

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Number of Participants Analyzed	120	121	122
Percentage of Participants With a Subject Self Rating Scale (SSRS) Response [units: percentage of participants]	53.3	66.1	28.7

Statistical Analysis 1 for Percentage of Participants With a Subject Self Rating Scale (SSRS) Response

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 1 mg/cm², Placebo
	Comments	The null hypothesis was there was no difference between deoxycholic acid 1 mg/cm² and placebo. An adjustment for multiplicity was performed for the two co-primary endpoints. This was accounted for by using the larger of the two P-values in the Bonferroni-Holm scheme.
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	Logistic regression analysis with treatment and Baseline SSRS value in the model

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	2.99
	Confidence Interval	(2-Sided) 95% 1.74 to 5.14
	Estimation Comments	Odds ratio was based on a logistic regression model adjusted for Baseline score. Odds ratios >1 indicate a positive treatment effect.

Statistical Analysis 2 for Percentage of Participants With a Subject Self Rating Scale (SSRS) Response

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 2 mg/cm², Placebo
	Comments	The null hypothesis was there was no difference between deoxycholic acid 2 mg/cm² and placebo. An adjustment for multiplicity was performed for the two co-primary endpoints. This was accounted for by using the larger of the two P-values in the Bonferroni-Holm scheme.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	Logistic regression analysis with treatment and baseline SSRS value in the model

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	5.22
	Confidence Interval	(2-Sided) 95% 2.99 to 9.11

	Estimation Comments	Odds ratio was based on a logistic regression model adjusted for Baseline score. Odds ratios >1 indicate a positive treatment effect.

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a CR-SMFRS 2-grade Response
Measure Description	A CR-SMFRS 2-grade response is defined as at least a 2-point improvement (i.e. 2-point reduction) from Baseline 12 weeks after the last treatment. The CR-SMFRS score is based on the investigator's clinical evaluation of the participant, where submental fullness is scored on a 5-point ordinal scale (0-4) with 0 = absent, 1 = mild, 2 = moderate, 3 = severe, and 4 = extreme.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population; LOCF method was used to impute missing data

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Measured Values

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Number of Participants Analyzed	120	121	122
Percentage of Participants With a CR-SMFRS 2-grade Response [units: percentage of participants]	9.2	17.4	1.6

Statistical Analysis 1 for Percentage of Participants With a CR-SMFRS 2-grade Response

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 1 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.028
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	Logistic regression analysis with treatment and Baseline CR-SMFRS value in the model.
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	5.58
	Confidence Interval	(2-Sided) 95% 1.20 to 25.87
	Estimation Comments	Odds ratio was based on a logistic regression model adjusted for the Baseline score. Odds ratios >1 indicate a positive treatment effect.

Statistical Analysis 2 for Percentage of Participants With a CR-SMFRS 2-grade Response

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 2 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Regression, Logistic
	Comments	Logistic regression analysis with treatment and Baseline CR-SMFRS value in the model.
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	12.05
	Confidence Interval	(2-Sided) 95%

		2.75 to 52.90
	Estimation Comments	Odds ratio was based on a logistic regression model adjusted for the Baseline score. Odds ratios >1 indicate a positive treatment effect.

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in CR-SMFRS Scores
Measure Description	The CR-SMFRS score is based on the investigator's clinical evaluation of the participant, where submental fullness is scored on a 5-point ordinal scale (0-4) with 0 = absent, 1 = mild, 2 = moderate, 3 = severe, and 4 = extreme. A negative change from Baseline indicates improvement.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population with available data

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Measured Values

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Number of Participants Analyzed	107	110	112
Change From Baseline in CR-SMFRS Scores [units: units on a scale] Mean (Standard Deviation)	-0.7 (0.65)	-0.9 (0.73)	-0.2 (0.55)

Statistical Analysis 1 for Change From Baseline in CR-SMFRS Scores

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 1 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Other [Mixed Models Repeated Measures]
	Comments	The model included the fixed effect factors visit and treatment, the visit*treatment interaction, and the baseline CR-SMFRS values as covariate.
Method of Estimation	Estimation Parameter	Other [LS Mean Difference]
	Estimated Value	-0.51
	Confidence Interval	(2-Sided) 95% -0.68 to -0.35
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Change From Baseline in CR-SMFRS Scores

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 2 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Other [Mixed Models Repeated Measures]
	Comments	The model included the fixed effect factors visit and treatment, the visit*treatment interaction, and the baseline CR-SMFRS values as covariate.
Method of Estimation	Estimation Parameter	Other [LS Mean Difference]
	Estimated Value	-0.67

	Confidence Interval	(2-Sided) 95% -0.84 to -0.50
	Estimation Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in SSRS Scores
Measure Description	The SSRS assesses participant's satisfaction with their appearance in association with the face and chin on a 7-point scale from 0 to 6: where 0 = Extremely dissatisfied, 1 = Dissatisfied, 2 = Slightly dissatisfied, 3 = Neither satisfied nor dissatisfied, 4 = Slightly satisfied, 5 = Satisfied and 6 = Extremely satisfied. A positive change from Baseline indicates improvement.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population with available data

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Measured Values

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Number of Participants Analyzed	106	108	111
Change From Baseline in SSRS Scores [units: units on a scale] Mean (Standard Deviation)	2.4 (1.74)	2.8 (1.72)	1.4 (1.60)

Statistical Analysis 1 for Change From Baseline in SSRS Scores

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 1 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	The model includes the fixed effect factor treatment and the Baseline values as covariate.
Method of Estimation	Estimation Parameter	Other [LS Mean Difference]
	Estimated Value	1.04
	Confidence Interval	(2-Sided) 95% 0.61 to 1.47
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Change From Baseline in SSRS Scores

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 2 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	The model includes the fixed effect factor treatment and the Baseline values as covariate.
Method of Estimation	Estimation Parameter	Other [LS Mean Difference]
	Estimated Value	1.41
	Confidence Interval	(2-Sided) 95% 0.99 to 1.84

	Estimation Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Submental Fat Thickness
Measure Description	Submental thickness was measured using caliper devices.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population with available data

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Measured Values

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Number of Participants Analyzed	107	110	112
Change From Baseline in Submental Fat Thickness [units: mm] Mean (Standard Deviation)	-3.8 (3.85)	-4.2 (3.90)	-1.7 (3.13)

Statistical Analysis 1 for Change From Baseline in Submental Fat Thickness

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 1 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Other [Mixed Models Repeated Measures]
	Comments	The model includes the fixed effect factors visit and treatment, the visit*treatment interaction, and the Baseline values as covariate.

Method of Estimation	Estimation Parameter	Other [LS mean Difference]
	Estimated Value	-1.68
	Confidence Interval	(2-Sided) 95% -2.50 to -0.87
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Change From Baseline in Submental Fat Thickness

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 2 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Other [Mixed Models Repeated Measures]
	Comments	The model includes the fixed effect factors visit and treatment, the visit*treatment interaction, and the baseline values as covariate.

Method of Estimation	Estimation Parameter	Other [LS Mean Difference]
	Estimated Value	-1.97
	Confidence Interval	(2-Sided) 95% -2.79 to -1.15
	Estimation Comments	[Not specified]

7. Secondary Outcome Measure:

Measure Title	Change From Baseline in Patient-reported Submental Fat Rating Scale (PR-SMFRS)

Measure Description	The PR-SMFRS is based on the participant's response to the question "How much fat do you currently have under your chin?" answered on a 5-point ordinal scale (0-4) with 0 = no chin fat at all, 1 = a slight amount of chin fat, 2 = a moderate amount of chin fat, 3 = a large amount of chin fat, and 4 = a very large amount of chin fat. Improvement is defined as any decrease in score and worsened as any increase in score.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population with available data

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Measured Values

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Number of Participants Analyzed	103	106	108
Change From Baseline in Patient-reported Submental Fat Rating Scale (PR-SMFRS) [units: percentage of participants]			
Improvement	67.0	73.6	32.4
No Change	32.0	22.6	59.3
Worsened	1.0	3.8	8.3

Statistical Analysis 1 for Change From Baseline in Patient-reported Submental Fat Rating Scale (PR-SMFRS)

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 1 mg/cm², Placebo
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Other [Pearson's chi-square test]
	Comments	[Not specified]

Statistical Analysis 2 for Change From Baseline in Patient-reported Submental Fat Rating Scale (PR-SMFRS)

Statistical Analysis Overview	Comparison Groups	Deoxycholic Acid Injection 2 mg/cm², Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Other [Pearson's chi-square test]
	Comments	[Not specified]

8. Secondary Outcome Measure:

Measure Title	Change From Baseline in Patient-Reported Submental Fat Impact Scale (PR-SMFIS)
Measure Description	The PR-SMFIS assesses the impact of submental fat on self-perception of 6 characteristics related to the appearance of submental fullness as evaluated by the participant. Each item is rated on an 11-point numeric scale from 0 to 10.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No
Anticipated Reporting Date	January 2016

Outcome Measure Data Not Reported

9. Secondary Outcome Measure:

Measure Title	Change From Baseline in Self-rating of Attractiveness

Measure Description	Self-rating of attractiveness assesses aspects of appearance from the participant's perspective by a series of 6 questions: How attractive do you think your overall appearance (chin/neck, eyes, nose, mouth, entire face) is/are?" Each question was answered on a scale from 1 to 9 where 1 = Not at all attractive, 5 = Neither attractive nor unattractive and 9 = Extremely attractive. A positive change from Baseline indicates improvement.
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population with available data

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Measured Values

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
Number of Participants Analyzed	101	104	105
Change From Baseline in Self-rating of Attractiveness [units: units on a scale] Mean (Standard Deviation)			
Overall Appearance	0.9 (1.58)	0.5 (1.44)	0.3 (1.28)
Chin/Neck	1.8 (2.05)	1.9 (2.21)	0.5 (1.90)
Eyes	0.8 (1.71)	0.1 (1.33)	0.3 (1.27)
Nose	0.3 (1.34)	0.0 (1.37)	0.2 (1.39)
Mouth	0.4 (1.63)	0.2 (1.50)	0.3 (1.28)
Entire Face	0.8 (1.25)	0.3 (1.31)	0.0 (1.19)

10. Secondary Outcome Measure:

Measure Title	Change From Baseline in Derriford Appearance Scale 24 (DAS24)
Measure Description	
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No
Anticipated Reporting Date	January 2016

Outcome Measure Data Not Reported

11. Secondary Outcome Measure:

Measure Title	Change From Baseline in Body Image Quality of Life Inventory (BIQLI)
Measure Description	
Time Frame	Baseline and 12 weeks after last treatment (up to 24 weeks after first dose)
Safety Issue?	No
Anticipated Reporting Date	January 2016

Outcome Measure Data Not Reported

Reported Adverse Events

Time Frame	From the first dose of study drug until 12 weeks after the last dose (up to 24 weeks after first treatment).
Additional Description	[Not specified]

Reporting Groups

	Description
Deoxycholic Acid Injection 1 mg/cm²	Participants received deoxycholic acid 1 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Deoxycholic Acid Injection 2 mg/cm²	Participants received deoxycholic acid 2 mg/cm² administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.
Placebo	Participants received placebo administered in 0.2 mL injections, up to 10 mL per treatment session at intervals of approximately 1 month for up to a maximum of 4 treatments.

Serious Adverse Events

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/119 (0.84%)	3/121 (2.48%)	2/122 (1.64%)
Gastrointestinal disorders			
Abdominal Adhesions [A] †	0/119 (0%)	1/121 (0.83%)	0/122 (0%)
Infections and infestations			
Chronic Tonsillitis [A] †	0/119 (0%)	0/121 (0%)	1/122 (0.82%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric Cancer [A] †	0/119 (0%)	1/121 (0.83%)	0/122 (0%)
Non-Hodgkin's Lymphoma [A] †	0/119 (0%)	0/121 (0%)	1/122 (0.82%)
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous [A] †	0/119 (0%)	1/121 (0.83%)	0/122 (0%)
Psychiatric disorders			
Depression [A] †	1/119 (0.84%)	0/121 (0%)	0/122 (0%)
Respiratory, thoracic and mediastinal disorders			
Sleep Apnoea Syndrome [A] †	0/119 (0%)	0/121 (0%)	1/122 (0.82%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA Version 14.1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	111/119 (93.28%)	115/121 (95.04%)	75/122 (61.48%)
General disorders			
Injection Site Anaesthesia [A] †	57/119 (47.9%)	62/121 (51.24%)	3/122 (2.46%)

	Deoxycholic Acid Injection 1 mg/cm²	Deoxycholic Acid Injection 2 mg/cm²	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Injection Site Erythema [A] †	46/119 (38.66%)	45/121 (37.19%)	28/122 (22.95%)
Injection Site Haematoma [A] †	65/119 (54.62%)	62/121 (51.24%)	48/122 (39.34%)
Injection Site Haemorrhage [A] †	6/119 (5.04%)	7/121 (5.79%)	6/122 (4.92%)
Injection Site Induration [A] †	22/119 (18.49%)	33/121 (27.27%)	3/122 (2.46%)
Injection Site Nodule [A] †	1/119 (0.84%)	9/121 (7.44%)	0/122 (0%)
Injection Site Oedema [A] †	21/119 (17.65%)	21/121 (17.36%)	12/122 (9.84%)
Injection Site Pain [A] †	92/119 (77.31%)	97/121 (80.17%)	31/122 (25.41%)
Injection Site Pruritus [A] †	11/119 (9.24%)	3/121 (2.48%)	1/122 (0.82%)
Injection Site Swelling [A] †	63/119 (52.94%)	63/121 (52.07%)	26/122 (21.31%)
Injection Site Warmth [A] †	6/119 (5.04%)	1/121 (0.83%)	1/122 (0.82%)
Nervous system disorders			
Headache [A] †	8/119 (6.72%)	7/121 (5.79%)	7/122 (5.74%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA Version 14.1

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 Clinical Study Agreement requires that the investigator or institution obtain written consent from Kythera prior to presenting and/or publishing results of this study.

Results Point of Contact:

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