



Clinical trial results:

Long-Term, Follow-up Study of Subjects Who Completed Phase III Trials of ATX-101-10-16 or ATX-101-10-17 (Sodium Deoxycholate Injection) for the Reduction of Localized Subcutaneous Fat in the Submental Area

Summary

EudraCT number	2011-005026-21
Trial protocol	DE
Global end of trial date	13 December 2013

Results information

Result version number	v1 (current)
This version publication date	30 September 2018
First version publication date	30 September 2018

Trial information

Trial identification

Sponsor protocol code	1403740
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02052622
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan Pharmaceuticals International Limited
Sponsor organisation address	Clonsaugh Industrial Estate, Coolock, Dublin 17, Ireland, D17 E400
Public contact	Clinical Trials Registry Team, Allergan Pharmaceuticals International Limited, 001 8772778566, IR-CTRegistration@allergan.com
Scientific contact	Therapeutic Area Head, Allergan Pharmaceuticals International Limited, 001 877-277-8566, IR-CTRegistration@Allergan.com

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	13 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this non-treatment, placebo-controlled, observational, 24-month follow-up study was to evaluate the long-term efficacy and safety of subcutaneous (SC) injections of deoxycholic acid (ATX-101) in the submental area. No treatment was administered in this study. Participants who previously received deoxycholic acid injections in studies ATX-101-10-16 or ATX-101-10-17 were enrolled in this non-treatment observational follow-up study to further evaluate safety and efficacy.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 February 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 201
Worldwide total number of subjects	201
EEA total number of subjects	201

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)	199
From 65 to 84 years	2

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A subset of participants at selected centers who had successfully completed Phase 3 clinical studies ATX-101-10-16 or ATX-101-10-17 for the reduction of submental fat were enrolled in this non-treatment observational long-term follow-up (LTFU) study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Deoxycholic Acid Injection, 5 mg/mL

Arm description:

Non-treatment observational follow-up study: Participants were previously treated with deoxycholic acid injection, 5 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17.

Arm type	Experimental
Investigational medicinal product name	Deoxycholic acid Injection
Investigational medicinal product code	
Other name	Kybella
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Previously treated with deoxycholic acid injection, 5 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17

Arm title	Deoxycholic Acid Injection, 10 mg/mL
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Arm description:

Non-treatment observational follow-up study: Participants were previously treated with deoxycholic acid injection, 10 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17.

Arm type	Experimental
Investigational medicinal product name	Deoxycholic acid Injection
Investigational medicinal product code	
Other name	Kybella
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Previously treated with deoxycholic acid injection, 10 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17

Arm title	Placebo
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Arm description:

Non-treatment observational follow-up study: Participants were previously treated with placebo in studies ATX-101-10-16 or ATX-101-10-17.

Arm type	Placebo
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Investigational medicinal product name	Placebo, 10 mM sodium phosphate, 0.9% [w/v] sodium chloride in water for injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Previously treated with placebo in studies ATX-101-10-16 or ATX-101-10-17

Number of subjects in period 1	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo
Started	60	75	66
Completed	60	75	65
Not completed	0	0	1
Withdrawal by subject	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	Deoxycholic Acid Injection, 5 mg/mL
Reporting group description:	
Non-treatment observational follow-up study: Participants were previously treated with deoxycholic acid injection, 5 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17.	
Reporting group title	Deoxycholic Acid Injection, 10 mg/mL
Reporting group description:	
Non-treatment observational follow-up study: Participants were previously treated with deoxycholic acid injection, 10 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17.	
Reporting group title	Placebo
Reporting group description:	
Non-treatment observational follow-up study: Participants were previously treated with placebo in studies ATX-101-10-16 or ATX-101-10-17.	

Reporting group values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo
Number of subjects	60	75	66
Age Categorical			
Units: Subjects			
18-30 years	7	5	3
31-50 years	29	39	29
51-65 years	24	31	34
Age Continuous			
Units: years			
arithmetic mean	46.9	47.9	49.2
standard deviation	± 10.33	± 9.23	± 9.09
Gender Categorical			
Units: Subjects			
Female	49	59	44
Male	11	16	22

Reporting group values	Total		
Number of subjects	201		
Age Categorical			
Units: Subjects			
18-30 years	15		
31-50 years	97		
51-65 years	89		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	152		
Male	49		

End points

End points reporting groups

Reporting group title	Deoxycholic Acid Injection, 5 mg/mL
Reporting group description: Non-treatment observational follow-up study: Participants were previously treated with deoxycholic acid injection, 5 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17.	
Reporting group title	Deoxycholic Acid Injection, 10 mg/mL
Reporting group description: Non-treatment observational follow-up study: Participants were previously treated with deoxycholic acid injection, 10 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17.	
Reporting group title	Placebo
Reporting group description: Non-treatment observational follow-up study: Participants were previously treated with placebo in studies ATX-101-10-16 or ATX-101-10-17.	

Primary: Percentage of Participants Maintaining Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) 1-Grade Response During the 24 Months of Follow up, i.e. % of Participants who were CR-SMFRS 1-Grade Responders at both LTFU Baseline and at 24-Month Visit

End point title	Percentage of Participants Maintaining Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) 1-Grade Response During the 24 Months of Follow up, i.e. % of Participants who were CR-SMFRS 1-Grade Responders at both LTFU Baseline and at 24-Month Visit ^[1]
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End point description:

The CR-SMFRS was based on the investigator's clinical evaluation of the participant's chin and neck area using a 5-point ordinal scale (0 to 4) with 0=Absent Submental Convexity: no localized submental fat evident; 1=Mild Submental Convexity: minimal, localized submental fat; 2=Moderate Submental Convexity: prominent, localized submental fat; 3=Severe Submental Convexity; a marked amount of chin fat; and 4=Extreme Submental Convexity: marked, localized submental fat. 1-grade response=At least a 1-grade reduction from original study baseline in the CR-SMFRS assessment. The full analysis set included all participants who received a clearly identifiable treatment in the previous study and had at least one visit in the LTFU study. Participants were included in the analysis according to their randomized treatment assignment. Missing values at Month 24 were imputed using LOCF. Non-responders at LTFU baseline in each treatment group (including placebo) were not included in the analysis.

End point type	Primary
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End point timeframe:

LTFU Baseline (Month 0) to Month 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistical analyses were performed for this endpoint.

End point values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	54	22	
Units: percentage of participants				
number (not applicable)	90.0	87.0	90.9	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Maintenance of Response as Assessed by the Subject Satisfaction Rating Scale (SSRS) During the 24 Months of Follow up, i.e. % of Participants who were SSRS Responders at both LTFU Baseline and at 24-Month Visit

End point title	Percentage of Participants with Maintenance of Response as Assessed by the Subject Satisfaction Rating Scale (SSRS) During the 24 Months of Follow up, i.e. % of Participants who were SSRS Responders at both LTFU Baseline and at 24-Month Visit ^[2]
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End point description:

For the SSRS, the participant was asked to answer the question: "Considering your appearance in association with your face and chin, how satisfied do you feel with your appearance at the present time?" using a 7-point scale: 0=Extremely dissatisfied, 1=Dissatisfied, 2=Slightly dissatisfied, 3=neither satisfied nor dissatisfied, 4=Slightly satisfied, 5=Satisfied, and 6=Extremely satisfied. SSRS responder was a participant whose response was ≥ 4 . A positive change from Baseline indicates improvement. The full analysis set included all participants who received a clearly identifiable treatment in the previous study and had at least one visit in the LTFU study. Participants were included in the analysis according to their randomized treatment assignment. Missing values at Month 24 were imputed using last observation carried forward (LOCF). Non-responders at LTFU baseline in each treatment group (including placebo) were not included in the analysis.

End point type	Primary
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End point timeframe:

LTFU Baseline (Month 0) to Month 24

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistical analyses were performed for this endpoint.

End point values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	48	25	
Units: percentage of participants				
number (not applicable)	62.8	81.3	80.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Maintaining Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) 2-Grade Response During the 24 Months of Follow up, i.e. % of Participants who were CR-SMFRS 2-Grade Responders at both LTFU Baseline and at 24-Month Visit

End point title	Percentage of Participants Maintaining Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) 2-Grade Response During the 24 Months of Follow up, i.e. % of Participants who were CR-SMFRS 2-Grade Responders at both LTFU Baseline and at 24-Month Visit
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End point description:

The CR-SMFRS was based on the investigator's clinical evaluation of the participant's chin and neck area using a 5-point ordinal scale (0 to 4) with 0=Absent Submental Convexity: no localized submental fat evident; 1=Mild Submental Convexity: minimal, localized submental fat; 2=Moderate Submental Convexity: prominent, localized submental fat; 3=Severe Submental Convexity; a marked amount of chin fat; and 4=Extreme Submental Convexity: marked, localized submental fat. 2-grade response=At least a 2-grade reduction from original study baseline in the CR-SMFRS assessment. The full analysis set included all participants who received a clearly identifiable treatment in the previous study and had at least one visit in the LTFU study. Participants were included in the analysis according to their randomized treatment assignment. Missing values at Month 24 were imputed using LOCF. Non-responders at LTFU baseline in each treatment group (including placebo) were not included in the analysis.

End point type	Secondary
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End point timeframe:

LTFU Baseline (Month 0) to Month 24

End point values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	13	2	
Units: percentage of participants				
number (not applicable)	87.5	61.5	50.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Patient-Reported Submental Fat Impact Scale (PR-SMFIS)

End point title	Patient-Reported Submental Fat Impact Scale (PR-SMFIS)
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End point description:

The PR-SMFIS assessed the impact of submental fat on self-perception of 6 emotional and visual characteristics related to the appearance of submental fullness (unhappy, bothered, self-conscious, embarrassed, look older, and look overweight) as evaluated by the participant. Each item was rated on an 11-point numeric scale from 0 to 10. Scores for the 6 items were averaged to generate a PR-SMFIS total scale score ranging from 0 to 10 where low scores reflect a positive impact and high scores reflect a negative impact. The full analysis set included all participants who received a clearly identifiable treatment in the previous study and had at least one visit in the LTFU study. Participants were included in the analysis according to their randomized treatment assignment. Here, "n" represents the number of participants evaluated at specific time points.

End point type	Secondary
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End point timeframe:

LTFU Baseline (Month 0) to Month 24

End point values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	75	66	
Units: score on a scale				
median (full range (min-max))				
LTFU Baseline (n= 60, 74, 66)	-2.65 (-9.3 to 2.3)	-3.00 (-8.4 to 2.9)	-1.05 (-8.3 to 4.3)	
Month 24 (n= 60, 74, 65)	-2.50 (-9.5 to 3.1)	-3.25 (-9.0 to 3.5)	-1.50 (-8.3 to 3.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Maintaining Composite SMFRS 1-Grade Response During the 24 Months of Follow up, i.e. % of Participants who were Composite SMFRS 1-Grade Responders at both LTFU Baseline and at 24-Month Visit

End point title	Percentage of Participants Maintaining Composite SMFRS 1-Grade Response During the 24 Months of Follow up, i.e. % of Participants who were Composite SMFRS 1-Grade Responders at both LTFU Baseline and at 24-Month Visit
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End point description:

Participants who had at least a 1-grade reduction in both the CR-SMFRS and PR-SMFRS from the original baseline value in the predecessor study were defined as composite SMFRS-1 responders. The full analysis set included all participants who received a clearly identifiable treatment in the previous study and had at least one visit in the LTFU study. Participants were included in the analysis according to their randomized treatment assignment. Missing values at Month 24 were imputed using last observation carried forward (LOCF). Non-responders at LTFU baseline in each treatment group (including placebo) were not included in the analysis for this endpoint.

End point type	Secondary
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End point timeframe:

LTFU Baseline (Month 0) to Month 24

End point values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	43	16	
Units: percentage of participants				
number (not applicable)	69.0	81.4	81.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with at Least One Treatment-Emergent Adverse Event (TEAE)

End point title	Percentage of Participants with at Least One Treatment-Emergent Adverse Event (TEAE)
End point description: An adverse event was any undesirable medical occurrence or worsening of an existing condition, irrespective of whether the event was considered treatment-related. A treatment-emergent adverse event was defined as an adverse event with an onset that occurs after receiving treatment. The safety set included all participants who received a clearly identifiable treatment in the previous study. Participants were included in the analysis according to the actual treatments received.	
End point type	Secondary
End point timeframe: Up to approximately 24 months	

End point values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	75	66	
Units: percentage of participants				
number (not applicable)	10.0	12.0	1.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Treatment-emergent Adverse Events Associated with the Treatment Area (Drug-related)

End point title	Percentage of Participants with Treatment-emergent Adverse Events Associated with the Treatment Area (Drug-related)
End point description: An adverse event was any undesirable medical occurrence or worsening of an existing condition, irrespective of whether the event was considered treatment-related. A treatment-emergent adverse event was defined as an adverse event with an onset that occurs after receiving treatment. The safety set included all participants who received a clearly identifiable treatment in the previous study. Participants were included in the analysis according to the actual treatments received.	
End point type	Secondary
End point timeframe: Up to approximately 24 months	

End point values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	75	66	
Units: percentage of participants				
number (not applicable)	3.3	8.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Treatment-emergent Adverse Events of Special Interest (AESIs)

End point title	Percentage of Participants with Treatment-emergent Adverse Events of Special Interest (AESIs)
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End point description:

An adverse event was any undesirable medical occurrence or worsening of an existing condition, irrespective of whether the event was considered treatment-related. A treatment-emergent adverse event was defined as an adverse event with an onset that occurs after receiving treatment. AESIs for this study are common treatment reactions (consistently reported for overall AEs, treatment area-related AEs, or study-drug-related AEs) that were observed in earlier deoxycholic acid injection studies and identified as likely to be related to the injection procedure. The safety set included all participants who received a clearly identifiable treatment in the previous study. Participants were included in the analysis according to the actual treatments received.

End point type	Secondary
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End point timeframe:

Up to approximately 24 months

End point values	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	75	66	
Units: percentage of participants				
number (not applicable)	1.7	6.7	0.0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Approximately 24 months

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Deoxycholic Acid Injection, 5 mg/mL
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Reporting group description:

Non-treatment observational follow-up study: Participants were previously treated with deoxycholic acid injection, 5 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17.

Reporting group title	Deoxycholic Acid Injection, 10 mg/mL
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Reporting group description:

Non-treatment observational follow-up study: Participants were previously treated with deoxycholic acid injection, 10 mg/mL, in studies ATX-101-10-16 or ATX-101-10-17.

Reporting group title	Placebo
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Reporting group description:

Non-treatment observational follow-up study: Participants were previously treated with placebo in studies ATX-101-10-16 or ATX-101-10-17.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events occurred at the 5% threshold.

Serious adverse events	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 60 (5.00%)	2 / 75 (2.67%)	1 / 66 (1.52%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Parathyroid tumour benign			
subjects affected / exposed	1 / 60 (1.67%)	0 / 75 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 60 (0.00%)	1 / 75 (1.33%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			

subjects affected / exposed	0 / 60 (0.00%)	0 / 75 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 60 (0.00%)	1 / 75 (1.33%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Enterocolitis bacterial			
subjects affected / exposed	1 / 60 (1.67%)	0 / 75 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 75 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Deoxycholic Acid Injection, 5 mg/mL	Deoxycholic Acid Injection, 10 mg/mL	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)	0 / 75 (0.00%)	0 / 66 (0.00%)

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

None reported