ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 03/19/2015

ClinicalTrials.gov ID: NCT00707746

Study Identification

Unique Protocol ID:	301012-CS19
Brief Title:	Safety and Efficacy Study of ISIS 301012 (Mipomersen) Administration in High Risk Statin Intolerant Subjects (ASSIST)
Official Title:	A Randomized, Double-Blind, Placebo-Controlled Study to Assess Safety and Efficacy of ISIS 301012 Administration in High Risk Statin Intolerant Subjects
Secondary IDs:	2007-005140-24 [EudraCT Number]

Study Status

Record Verification:	March 2015
Overall Status:	Completed
Study Start:	October 2008
Primary Completion:	August 2010 [Actual]
Study Completion:	January 2011 [Actual]

Sponsor/Collaborators

Sponsor:	Genzyme, a Sanofi Company
Responsible Party:	Sponsor
Collaborators:	Isis Pharmaceuticals

Oversight

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

Review Board:	Approval Status: Approved Approval Number: 27052008 Board Name: Central Committee on Research Involving Human Subjects Board Affiliation: Central Committee on Research Involving Human Subjects Phone: +31 70 340 6700 Email: ccmo@ccmo.nl
Data Monitoring?:	No
Oversight Authorities:	Netherlands: Ministry of Health, Welfare and Sport

Study Description

Brief Summary:	The purpose of this study is to determine safety and efficacy of mipomersen (ISIS 301012) in the reduction of total cholesterol, low density lipoprotein cholesterol (LDL-C), and apolipoprotein B (apoB) in high risk subjects intolerant to statins.
Detailed Description:	In humans, apoB is the principal apolipoprotein of the atherogenic lipoproteins, comprising very low-density lipoprotein (VLDL), intermediate density lipoprotein (IDL) and low density lipoprotein (LDL). ApoB messenger ribonucleic acid (mRNA) is abundantly present in the liver. Within the endoplasmatic reticulum, apoB requires lipidation by microsomal triglyceride transfer protein, which allows apoB to be incorporated in the VLDL particle within the lumen of the endoplasmatic reticulum. Non-lipidated apoB is readily degraded via ubiquitination. Notably, apoB within the VLDL particle is obligatory for hepatic secretion of VLDL. ApoB remains present within the VLDL-metabolism pathway, from secretion to clearance of the end product LDL by the liver LDL receptor. As a consequence, apoB reliably reflects the total burden of atherogenic lipoproteins. Thus, apoB carries strong prognostic value for cardiovascular events, which exceeds the predictive value of LDL-C. Conversely, decreased levels of apoB (e.g. in familial hypobetalipoproteinemia) have been associated with reduced levels of atherosclerosis. These genetic observations have prompted interest in pharmacologic inhibition of apoB synthesis. Mipomersen (ISIS 301012) is an antisense drug targeted to human apoB, the principal apolipoprotein of LDL and its metabolic precursor, VLDL. Mipomersen (ISIS 301012) is complementary to the coding region of the mRNA for apoB, binding by Watson and Crick base pairing. The hybridization (binding) of mipomersen (ISIS 301012) to the cognate mRNA results in Ribonuclease (RNase) H-mediated degradation of the cognate mRNA, thus inhibiting translation of the apoB protein. This was a randomized, double-blind, placebo-controlled Phase 2 study to assess the safety and efficacy of mipomersen administration in high-risk statin-intolerant patients with hypercholesterolemia. This study consisted of a ≤3-week screening period, 26 weeks of treatment, and a 24-week post-treatment follow-up period. Eligible patients were randomized in a 2:1 ratio to receive mipomersen 200 mg or matching volume placebo subcutaneous (SC) injections weekly. Following the screening visit, eligible patients returned to the study center for clinical evaluation every week for study drug administration and assessments.

Conditions

Conditions:	Metabolic Diseases Hyperlipidemias

Metabolic Disorder
Hypercholesterolemia
Dyslipidemias
Lipid Metabolism Disorders

Keywords: statin intolerant
hypercholesterolemia

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 2

Intervention Model: Parallel Assignment

Number of Arms: 2

Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 34 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Placebo Comparator: Placebo 1 mL placebo saline, weekly subcutaneous injections for 26 weeks	Drug: placebo Other Names: • placebo saline
Experimental: Mipomersen 200 mg (1 mL), weekly subcutaneous injections for 26 weeks	Drug: mipomersen Other Names: • ISIS 301012 • mipomersen sodium • Kynamro™

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Diagnosis of statin intolerance
- Diagnosis of Coronary Artery Disease (CAD)
- Diagnosis of hypercholesterolemia
- Stable weight for > 6 weeks

Exclusion Criteria:

- Significant health problems in the recent past (≤24 weeks) including heart attack, heart surgery, heart failure, uncontrolled hypothyroidism, blood disorders, digestive problems, disease of central nervous system, cancer, liver or renal disease

Contacts/Locations

Study Officials: Medical Monitor
Genzyme Corporation

Locations: Netherlands
Amsterdam, Netherlands, 1105AZ

References

Citations:

Links:

Participant Flow

Pre-Assignment Details	42 patients were screened, 34 participants were randomized, and 33 participants were treated: 21 participants to mipomersen and 12 participants to placebo.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Treatment Period

	Placebo	Mipomersen
Started	12	22
Full Analysis Set (FAS) and Safety Set	12 [1]	21 [1]
Completed	10	17
Not Completed	2	5
Adverse Event	2	4
Ineligibility	0	1

[1] FAS: Treated patients with a valid baseline & post-baseline LDL-C measurement

Follow-up Period

	Placebo	Mipomersen
Started	12	21
Completed	12	21
Not Completed	0	0

Baseline Characteristics

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Baseline Measures

	Placebo	Mipomersen	Total
Number of Participants	12	21	33
Age, Continuous [units: years] Mean (Standard Deviation)	51.7 (8.7)	55.6 (6.8)	54.2 (7.6)
Gender, Male/Female [units: participants]			
Female	8	10	18
Male	4	11	15
Ethnicity (NIH/OMB) [units: participants]			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	12	21	33
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized [units: participants]			
White	12	20	32
Black	0	1	1
Body Mass Index (BMI) [units: kg/m^2] Mean (Standard Deviation)	26.06 (2.49)	26.46 (3.25)	26.31 (2.96)
Waist/hip Ratio [units: ratio] Mean (Standard Deviation)	0.92 (0.09)	0.93 (0.08)	0.93 (0.08)

	Placebo	Mipomersen	Total
Metabolic syndrome [1] [units: participants]			
No	4	12	16
Yes	8	9	17
Tobacco Use [units: participants]			
Current	2	6	8
Non-current	5	9	14
Never	5	6	11
Alcohol use [units: participants]			
Current	8	16	24
Non-current	2	3	5
Never	2	2	4

[1] A participant was classified as having metabolic syndrome if any 3 of the following risk factors existed: 1) Waist circumference ≥102 cm (men) or ≥88 cm (women); 2) Triglycerides ≥150 mg/dl *; 3) High density lipoprotein cholesterol <40 mg/dl (men) or <50 mg/dl (women)*; 4) Systolic blood pressure ≥130 or diastolic ≥85 mmHg *; 5) Fasting glucose ≥100 mg/dl *.

* = or on medication for the specified risk factor.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at the Primary Efficacy Time Point
Measure Description	LDL-C was measured in mg/dL. Samples were taken following an overnight fast. For patients with triglycerides <400 mg/dL, LDL-C was obtained using Friedewald's calculation; and for patients with triglycerides ≥400 mg/dL, LDL-C was directly measured by the central laboratory using ultracentrifugation. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at the Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	-2.0 (8.40)	-47.3 (18.43)

Statistical Analysis 1 for Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	It was estimated that the standard deviation of the percent change in LDL-C was 20%. A sample size of 30 patients was planned for this study: 20 patients in the mipomersen group and 10 patients in the placebo group. A 2-sided t-test with an alpha level of 0.05 was expected to provide ≥90% power to detect a 30% difference in LDL-C percent reduction between the 2 groups (35% reduction for the mipomersen group and 5% reduction for the placebo group).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Statistical significance was concluded if p ≤ 0.05.
	Method	t-test, 2 sided
	Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Low-density Lipoprotein Cholesterol at Baseline and the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Low-density Lipoprotein Cholesterol at Baseline and the Primary Efficacy Time Point [units: mg/dL] Mean (Standard Deviation)		
Baseline	243.7 (65.6)	241.9 (90.8)
Primary efficacy time point	236.3 (52.8)	128.3 (74.2)

3. Primary Outcome Measure:

Measure Title	Summary of Participants With Adverse Events

Measure Description	The on-treatment time frame spanned the time during which the study drug was administered until the later of the primary efficacy time point and 14 days beyond the last study drug date. Adverse events (AEs) were considered related if assessed by the Investigator as possibly, probably or definitely related to study drug. Severity was assessed as: • Mild-symptom barely noticeable to the patient or do not make the patient uncomfortable; • Moderate-symptom makes the patient uncomfortable, affects performance of daily activities; • Severe-symptom causes the patient severe discomfort, may cause cessation of treatment with the study drug. Serious AEs (SAEs) are those that resulted in death, were life-threatening, required or prolonged inpatient hospitalization, resulted in persistent or significant disability/incapacity, congenital anomaly, or resulted in an important medical event that may have jeopardized the patient or required medical or surgical intervention.
Time Frame	Pre-treatment (prior to first dose), On-treatment (Day 1 to week 28), Post-treatment (Week 28-52)
Safety Issue?	Yes

Analysis Population Description

Safety set of all randomized participants who received at least one injection of study drug.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Summary of Participants With Adverse Events [units: participants]		
Pre-treatment adverse events (AEs)	3	7
Post-treatment AEs	9	20
On-treatment AEs	12	21
On-treatment AEs-related	12	21
On-treatment AEs-mild	6	5
On-treatment AEs-moderate	5	16
On-treatment AEs-severe	1	0

	Placebo	Mipomersen
On-treatment AEs-leading to trt discontinuation	2	4
On-treatment Serious Adverse Events (SAEs)	1	0
On-treatment SAEs-related	1	0
On-treatment SAEs-mild	0	0
On-treatment SAEs-moderate	0	0
On-treatment SAEs-severe	1	0
On-treatment SAEs-leading to trt discontinuation	1	0
Deaths	0	0

4. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Apolipoprotein B at the Primary Efficacy Time Point
Measure Description	Apolipoprotein B was measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in Apolipoprotein B at the Primary Efficacy Time Point	-4.0 (-8.8 to 0.5)	-45.8 (-57.5 to -34.4)

	Placebo	Mipomersen
[units: percentage of baseline] Median (Inter-Quartile Range)		

Statistical Analysis 1 for Percent Change From Baseline in Apolipoprotein B at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Inflation of type 1 error was controlled by specifying a small number of secondary parameters and a sequential inferential approach in which inferential conclusions about each successive parameter required statistical significance of the prior one.
	Method	Other [Wilcoxon signed rank sum]
	Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Apolipoprotein B at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Apolipoprotein B at Baseline and at the Primary Efficacy Time Point [units: mg/dL] Median (Inter-Quartile Range)		
Baseline	180 (145 to 196)	177 (142 to 205)
Primary efficacy time point	173 (143 to 187)	96 (66 to 110)

6. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Total Cholesterol at the Primary Efficacy Time Point
Measure Description	Total cholesterol was measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in Total Cholesterol at the Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	-1.7 (6.46)	-36.9 (14.66)

Statistical Analysis 1 for Percent Change From Baseline in Total Cholesterol at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Inflation of type 1 error was controlled by specifying a small number of secondary parameters and a sequential inferential approach in which inferential conclusions about each successive parameter required statistical significance of the prior one.
	Method	t-test, 2 sided
	Comments	[Not specified]

7. Secondary Outcome Measure:

Measure Title	Total Cholesterol at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21

	Placebo	Mipomersen
Total Cholesterol at Baseline and at the Primary Efficacy Time Point [units: mg/dL] Mean (Standard Deviation)		
Baseline	322.3 (66.2)	318.9 (91.8)
Primary efficacy time point	314.5 (53.0)	200.1 (77.6)

8. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Non-High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point
Measure Description	Non-high-density lipoprotein cholesterol was measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in Non-High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	-1.9 (7.06)	-45.6 (18.22)

Statistical Analysis 1 for Percent Change From Baseline in Non-High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Inflation of type 1 error was controlled by specifying a small number of secondary parameters and a sequential inferential approach in which inferential conclusions about each successive parameter required statistical significance of the prior one.
	Method	t-test, 2 sided
	Comments	[Not specified]

9. Secondary Outcome Measure:

Measure Title	Non-High-Density Lipoprotein Cholesterol at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21

	Placebo	Mipomersen
Non-High-Density Lipoprotein Cholesterol at Baseline and at the Primary Efficacy Time Point [units: mg/dL] Mean (Standard Deviation)		
Baseline	273.5 (65.3)	270.1 (92.9)
Primary efficacy time point	266.0 (53.0)	147.7 (81.1)

10. Other Pre-specified Outcome Measure:

Measure Title	Percent Change From Baseline in Triglycerides at the Primary Efficacy Time Point
Measure Description	Triglycerides were measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in Triglycerides at the Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	5.0 (26.81)	-27.0 (30.21)

Statistical Analysis 1 for Percent Change From Baseline in Triglycerides at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.005
	Comments	Statistical significance was concluded if p ≤0.05. No further adjustments were made for tertiary parameters.
	Method	t-test, 2 sided
	Comments	[Not specified]

11. Other Pre-specified Outcome Measure:

Measure Title	Triglycerides at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Triglycerides at Baseline and at the Primary Efficacy Time Point [units: mg/dL]		

	Placebo	Mipomersen
Mean (Standard Deviation)		
Baseline	149.0 (63.9)	141.4 (50.9)
Primary efficacy time point	149.3 (62.4)	97.3 (47.3)

12. Other Pre-specified Outcome Measure:

Measure Title	Percent Change From Baseline in Lipoprotein (a) at the Primary Efficacy Time Point
Measure Description	Lipoprotein (a) was measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in Lipoprotein (a) at the Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	0.0 (8.65)	-27.1 (31.19)

Statistical Analysis 1 for Percent Change From Baseline in Lipoprotein (a) at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Statistical significance was concluded if p ≤0.05. No further adjustments were made for tertiary parameters.
	Method	t-test, 2 sided
	Comments	[Not specified]

13. Other Pre-specified Outcome Measure:

Measure Title	Lipoprotein (a) at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Lipoprotein (a) at Baseline and at the Primary Efficacy Time Point [units: mg/dL]		

	Placebo	Mipomersen
Mean (Standard Deviation)		
Baseline	37.3 (76.3)	53.5 (45.8)
Primary efficacy time point	41.3 (90.1)	42.3 (48.2)

14. Other Pre-specified Outcome Measure:

Measure Title	Percent Change From Baseline in Very Low Density Lipoprotein Cholesterol at the Primary Efficacy Time Point
Measure Description	Very low density lipoprotein cholesterol was measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in Very Low Density Lipoprotein Cholesterol at the Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	4.6 (26.53)	-27.1 (30.79)

Statistical Analysis 1 for Percent Change From Baseline in Very Low Density Lipoprotein Cholesterol at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.006
	Comments	Statistical significance was concluded if p ≤0.05. No further adjustments were made for tertiary parameters.
	Method	t-test, 2 sided
	Comments	[Not specified]

15. Other Pre-specified Outcome Measure:

Measure Title	Very Low Density Lipoprotein Cholesterol at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Very Low Density Lipoprotein Cholesterol at Baseline and at the Primary Efficacy Time Point [units: mg/dL]		

	Placebo	Mipomersen
Mean (Standard Deviation)		
Baseline	29.8 (12.7)	28.3 (10.2)
Primary efficacy time point	29.8 (12.5)	19.4 (9.5)

16. Other Pre-specified Outcome Measure:

Measure Title	Percent Change From Baseline in the Ratio of Low-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point
Measure Description	The ratio of low-density lipoprotein (LDL) cholesterol to high-density lipoprotein (HDL) cholesterol was measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in the Ratio of Low-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	1.4 (12.84)	-49.2 (22.16)

Statistical Analysis 1 for Percent Change From Baseline in the Ratio of Low-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Statistical significance was concluded if p ≤0.05. No further adjustments were made for tertiary parameters.
	Method	t-test, 2 sided
	Comments	[Not specified]

17. Other Pre-specified Outcome Measure:

Measure Title	Ratio of Low-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Ratio of Low-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol at Baseline and at the Primary Efficacy Time Point [units: ratio] Mean (Standard Deviation)		
Baseline	5.3 (2.18)	5.2 (2.38)
Primary efficacy time point	5.4 (2.27)	2.7 (2.21)

18. Other Pre-specified Outcome Measure:

Measure Title	Percent Change From Baseline in Apolipoprotein A1 at the Primary Efficacy Time Point
Measure Description	Apolipoprotein A1 was measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in Apolipoprotein A1 at the Primary Efficacy Time Point [units: percentage of baseline]	-1.2 (11.11)	-0.0 (12.45)

	Placebo	Mipomersen
Mean (Standard Deviation)		

Statistical Analysis 1 for Percent Change From Baseline in Apolipoprotein A1 at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.784
	Comments	Statistical significance was concluded if p ≤0.05. No further adjustments were made for tertiary parameters.
	Method	t-test, 2 sided
	Comments	[Not specified]

19. Other Pre-specified Outcome Measure:

Measure Title	Apolipoprotein A1 at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Apolipoprotein A1 at Baseline and at the Primary Efficacy Time Point [units: mg/dL] Mean (Standard Deviation)		
Baseline	150.0 (24.8)	150.3 (25.6)
Primary efficacy time point	148.9 (33.2)	149.1 (24.0)

20. Other Pre-specified Outcome Measure:

Measure Title	Percent Change From Baseline in High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point
Measure Description	High-density lipoprotein cholesterol (HDL-C) was measured in mg/dL. Samples were taken following an overnight fast. The primary efficacy time point was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

The Full Analysis Set, which consisted of all randomized patients who received at least 1 injection of study drug (mipomersen or placebo) and with a valid baseline and at least 1 post-baseline LDL-C measurement.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
Percent Change From Baseline in High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point [units: percentage of baseline]	-2.3 (12.72)	8.1 (17.15)

	Placebo	Mipomersen
Mean (Standard Deviation)		

Statistical Analysis 1 for Percent Change From Baseline in High-Density Lipoprotein Cholesterol at the Primary Efficacy Time Point

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.079
	Comments	Statistical significance was concluded if p ≤0.05. No further adjustments were made for tertiary parameters.
	Method	t-test, 2 sided
	Comments	[Not specified]

21. Other Pre-specified Outcome Measure:

Measure Title	High-Density Lipoprotein Cholesterol at Baseline and at the Primary Efficacy Time Point
Measure Description	The primary efficacy time point (PET) was the post-baseline visit closest to 14 days after the last dose of study treatment.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET; Week 28 or the post-baseline visit closest to 14 days after the last dose).
Safety Issue?	No

Analysis Population Description

Full analysis set

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	12	21
High-Density Lipoprotein Cholesterol at Baseline and at the Primary Efficacy Time Point [units: mg/dL] Mean (Standard Deviation)		
Baseline	48.8 (12.4)	48.8 (9.9)
Primary efficacy time point	48.5 (16.9)	52.4 (12.4)

Reported Adverse Events

Time Frame	Day 1 to week 28. On-treatment AEs started on/after the first study drug dose and on/before the end of the treatment period. The treatment period was the time study drug was administered until the later of the PET or 14 days after last study drug dose.
Additional Description	The Safety Set includes all randomized patients who receive at least 1 injection of the study treatment. In the event a single participant has experienced both a serious and a non-serious form of the same adverse event term, the individual has been included in the numerator ("number of affected participants") of both adverse event tables.

Reporting Groups

	Description
Placebo	1 mL placebo saline, weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg (1 mL) of mipomersen, weekly subcutaneous injections for 26 weeks

Serious Adverse Events

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/12 (8.33%)	0/21 (0%)
Cardiac disorders		
Acute myocardial infarction [A] †	1/12 (8.33%)	0/21 (0%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA 13.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Total	12/12 (100%)	21/21 (100%)
Blood and lymphatic system disorders		
Haemorrhagic diathesis [A] †	0/12 (0%)	1/21 (4.76%)
Cardiac disorders		
Angina pectoris [A] †	1/12 (8.33%)	0/21 (0%)
Left ventricular hypertrophy [A] †	0/12 (0%)	1/21 (4.76%)
Palpitations [A] †	0/12 (0%)	2/21 (9.52%)
Ear and labyrinth disorders		
Deafness unilateral [A] †	1/12 (8.33%)	0/21 (0%)
Eye disorders		
Eye allergy [A] †	0/12 (0%)	1/21 (4.76%)
Eye inflammation [A] †	0/12 (0%)	1/21 (4.76%)
Eye pruritus [A] †	0/12 (0%)	1/21 (4.76%)
Panophthalmitis [A] †	0/12 (0%)	1/21 (4.76%)
Gastrointestinal disorders		
Abdominal discomfort [A] †	1/12 (8.33%)	0/21 (0%)
Abdominal distension [A] †	1/12 (8.33%)	0/21 (0%)
Abdominal pain [A] †	1/12 (8.33%)	3/21 (14.29%)
Abdominal pain lower [A] †	1/12 (8.33%)	1/21 (4.76%)
Abdominal pain upper [A] †	1/12 (8.33%)	4/21 (19.05%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Abnormal faeces [A] †	0/12 (0%)	1/21 (4.76%)
Change of bowel habit [A] †	1/12 (8.33%)	0/21 (0%)
Constipation [A] †	1/12 (8.33%)	1/21 (4.76%)
Diarrhoea [A] †	3/12 (25%)	8/21 (38.1%)
Dyspepsia [A] †	1/12 (8.33%)	1/21 (4.76%)
Faeces discoloured [A] †	0/12 (0%)	2/21 (9.52%)
Faeces hard [A] †	1/12 (8.33%)	0/21 (0%)
Flatulence [A] †	0/12 (0%)	2/21 (9.52%)
Food poisoning [A] †	0/12 (0%)	1/21 (4.76%)
Frequent bowel movements [A] †	1/12 (8.33%)	0/21 (0%)
Gastrointestinal pain [A] †	2/12 (16.67%)	0/21 (0%)
Gingivitis [A] †	0/12 (0%)	1/21 (4.76%)
Haemorrhoids [A] †	0/12 (0%)	2/21 (9.52%)
Intestinal functional disorder [A] †	0/12 (0%)	1/21 (4.76%)
Nausea [A] †	4/12 (33.33%)	6/21 (28.57%)
Tooth disorder [A] †	1/12 (8.33%)	2/21 (9.52%)
Toothache [A] †	0/12 (0%)	1/21 (4.76%)
Vomiting [A] †	0/12 (0%)	1/21 (4.76%)
General disorders		
Asthenia [A] †	1/12 (8.33%)	2/21 (9.52%)
Chest discomfort [A] †	0/12 (0%)	1/21 (4.76%)
Chest pain [A] †	0/12 (0%)	1/21 (4.76%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Fatigue [A] †	2/12 (16.67%)	8/21 (38.1%)
Feeling abnormal [A] †	1/12 (8.33%)	1/21 (4.76%)
Feeling cold [A] †	0/12 (0%)	1/21 (4.76%)
Impaired healing [A] †	0/12 (0%)	1/21 (4.76%)
Influenza like illness [A] †	6/12 (50%)	10/21 (47.62%)
Injection site discolouration [A] †	0/12 (0%)	13/21 (61.9%)
Injection site discomfort [A] †	1/12 (8.33%)	6/21 (28.57%)
Injection site erythema [A] †	0/12 (0%)	18/21 (85.71%)
Injection site exfoliation [A] †	0/12 (0%)	1/21 (4.76%)
Injection site haematoma [A] †	7/12 (58.33%)	12/21 (57.14%)
Injection site induration [A] †	1/12 (8.33%)	11/21 (52.38%)
Injection site inflammation [A] †	0/12 (0%)	4/21 (19.05%)
Injection site nodule [A] †	0/12 (0%)	3/21 (14.29%)
Injection site pain [A] †	2/12 (16.67%)	14/21 (66.67%)
Injection site pallor [A] †	0/12 (0%)	1/21 (4.76%)
Injection site pruritus [A] †	0/12 (0%)	10/21 (47.62%)
Injection site reaction [A] †	0/12 (0%)	2/21 (9.52%)
Injection site swelling [A] †	0/12 (0%)	9/21 (42.86%)
Injection site vesicles [A] †	0/12 (0%)	1/21 (4.76%)
Injection site warmth [A] †	0/12 (0%)	1/21 (4.76%)
Malaise [A] †	0/12 (0%)	2/21 (9.52%)
Non-cardiac chest pain [A] †	1/12 (8.33%)	0/21 (0%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Pyrexia [A] †	0/12 (0%)	2/21 (9.52%)
Sensation of pressure [A] †	1/12 (8.33%)	0/21 (0%)
Tenderness [A] †	0/12 (0%)	1/21 (4.76%)
Vessel puncture site haematoma [A] †	0/12 (0%)	2/21 (9.52%)
Vessel puncture site reaction [A] †	0/12 (0%)	1/21 (4.76%)
Hepatobiliary disorders		
Hepatic steatosis [A] †	1/12 (8.33%)	11/21 (52.38%)
Infections and infestations		
Eye infection [A] †	0/12 (0%)	1/21 (4.76%)
Herpes zoster [A] †	0/12 (0%)	1/21 (4.76%)
Influenza [A] †	3/12 (25%)	1/21 (4.76%)
Injection site cellulitis [A] †	0/12 (0%)	1/21 (4.76%)
Nasopharyngitis [A] †	4/12 (33.33%)	8/21 (38.1%)
Oral herpes [A] †	0/12 (0%)	1/21 (4.76%)
Sinusitis [A] †	1/12 (8.33%)	1/21 (4.76%)
Urinary tract infection [A] †	0/12 (0%)	3/21 (14.29%)
Injury, poisoning and procedural complications		
Contusion [A] †	1/12 (8.33%)	0/21 (0%)
Fall [A] †	0/12 (0%)	1/21 (4.76%)
Limb injury [A] †	1/12 (8.33%)	0/21 (0%)
Post procedural complication [A] †	0/12 (0%)	1/21 (4.76%)
Procedural pain [A] †	0/12 (0%)	1/21 (4.76%)
Investigations		

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Activated partial thromboplastin time [A] †	0/12 (0%)	1/21 (4.76%)
Activated partial thromboplastin time prolonged [A] †	2/12 (16.67%)	1/21 (4.76%)
Alanine aminotransferase increased [A] †	0/12 (0%)	6/21 (28.57%)
Albumin urine present [A] †	0/12 (0%)	1/21 (4.76%)
Aspartate aminotransferase increased [A] †	0/12 (0%)	6/21 (28.57%)
Blood alkaline phosphatase increased [A] †	0/12 (0%)	1/21 (4.76%)
Blood calcium decreased [A] †	0/12 (0%)	1/21 (4.76%)
Blood phosphorus decreased [A] †	1/12 (8.33%)	2/21 (9.52%)
Blood potassium increased [A] †	1/12 (8.33%)	0/21 (0%)
Body temperature decreased [A] †	0/12 (0%)	3/21 (14.29%)
Body temperature increased [A] †	0/12 (0%)	1/21 (4.76%)
C-reactive protein increased [A] †	1/12 (8.33%)	1/21 (4.76%)
Coagulation test abnormal [A] †	0/12 (0%)	1/21 (4.76%)
Electrocardiogram poor R-wave progression [A] †	0/12 (0%)	1/21 (4.76%)
Gastric pH decreased [A] †	0/12 (0%)	1/21 (4.76%)
Globulins decreased [A] †	0/12 (0%)	1/21 (4.76%)
Hepatic enzyme increased [A] †	0/12 (0%)	1/21 (4.76%)
International normalised ratio increased [A] †	0/12 (0%)	1/21 (4.76%)
Liver function test abnormal [A] †	0/12 (0%)	1/21 (4.76%)
Platelet count decreased [A] †	0/12 (0%)	1/21 (4.76%)
Protein urine present [A] †	0/12 (0%)	1/21 (4.76%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Prothrombin time prolonged [A] †	0/12 (0%)	1/21 (4.76%)
Sputum abnormal [A] †	0/12 (0%)	1/21 (4.76%)
Urine albumin/creatinine ratio increased [A] †	1/12 (8.33%)	4/21 (19.05%)
Metabolism and nutrition disorders		
Decreased appetite [A] †	0/12 (0%)	2/21 (9.52%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	1/12 (8.33%)	1/21 (4.76%)
Back pain [A] †	3/12 (25%)	5/21 (23.81%)
Bone disorder [A] †	0/12 (0%)	1/21 (4.76%)
Bursitis [A] †	1/12 (8.33%)	0/21 (0%)
Groin pain [A] †	0/12 (0%)	2/21 (9.52%)
Muscle spasms [A] †	4/12 (33.33%)	3/21 (14.29%)
Musculoskeletal disorder [A] †	0/12 (0%)	1/21 (4.76%)
Musculoskeletal pain [A] †	0/12 (0%)	2/21 (9.52%)
Musculoskeletal stiffness [A] †	1/12 (8.33%)	2/21 (9.52%)
Myalgia [A] †	5/12 (41.67%)	9/21 (42.86%)
Myosclerosis [A] †	0/12 (0%)	1/21 (4.76%)
Pain in extremity [A] †	1/12 (8.33%)	4/21 (19.05%)
Pain in jaw [A] †	0/12 (0%)	1/21 (4.76%)
Sensation of heaviness [A] †	1/12 (8.33%)	1/21 (4.76%)
Tendon pain [A] †	3/12 (25%)	0/21 (0%)
Nervous system disorders		

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Aphonia [A] †	0/12 (0%)	1/21 (4.76%)
Dizziness [A] †	3/12 (25%)	3/21 (14.29%)
Dizziness postural [A] †	0/12 (0%)	1/21 (4.76%)
Headache [A] †	3/12 (25%)	9/21 (42.86%)
Migraine with aura [A] †	0/12 (0%)	1/21 (4.76%)
Paraesthesia [A] †	2/12 (16.67%)	2/21 (9.52%)
Poor quality sleep [A] †	1/12 (8.33%)	0/21 (0%)
Syncope [A] †	1/12 (8.33%)	0/21 (0%)
Psychiatric disorders		
Depressed mood [A] †	0/12 (0%)	1/21 (4.76%)
Initial insomnia [A] †	0/12 (0%)	1/21 (4.76%)
Listless [A] †	0/12 (0%)	2/21 (9.52%)
Tension [A] †	0/12 (0%)	2/21 (9.52%)
Renal and urinary disorders		
Pollakiuria [A] †	0/12 (0%)	1/21 (4.76%)
Proteinuria [A] †	0/12 (0%)	1/21 (4.76%)
Reproductive system and breast disorders		
Menstruation irregular [A] †	1/12 (8.33%)	0/21 (0%)
Postmenopausal haemorrhage [A] †	0/12 (0%)	1/21 (4.76%)
Respiratory, thoracic and mediastinal disorders		
Chronic obstructive pulmonary disease [A] †	0/12 (0%)	1/21 (4.76%)
Cough [A] †	2/12 (16.67%)	5/21 (23.81%)
Epistaxis [A] †	1/12 (8.33%)	0/21 (0%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Oropharyngeal pain [A] †	2/12 (16.67%)	4/21 (19.05%)
Rhinitis allergic [A] †	1/12 (8.33%)	0/21 (0%)
Rhinorrhoea [A] †	0/12 (0%)	1/21 (4.76%)
Skin and subcutaneous tissue disorders		
Eczema [A] †	1/12 (8.33%)	0/21 (0%)
Hyperkeratosis [A] †	0/12 (0%)	1/21 (4.76%)
Nail disorder [A] †	1/12 (8.33%)	0/21 (0%)
Nail growth abnormal [A] †	1/12 (8.33%)	0/21 (0%)
Pruritus generalised [A] †	0/12 (0%)	2/21 (9.52%)
Rash [A] †	0/12 (0%)	1/21 (4.76%)
Skin burning sensation [A] †	0/12 (0%)	1/21 (4.76%)
Vascular disorders		
Haematoma [A] †	0/12 (0%)	1/21 (4.76%)
Hot flush [A] †	0/12 (0%)	3/21 (14.29%)
Hypertension [A] †	0/12 (0%)	2/21 (9.52%)
Vasodilatation [A] †	1/12 (8.33%)	0/21 (0%)

† Indicates events were collected by systematic assessment.
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.

Institution will submit for review a proposed publication or presentation at least 90 days prior to submission date. Sponsor has the right to delay publication or presentation for not more than 6 months to address patent applications. Sponsor also has the right to demand in writing the deletion of confidential information. Investigator will not make public raw study data, detailed subject cases, or information identifying any subject.

Results Point of Contact:

Name/Official Title: Genzyme Medical Information
Organization: Genzyme Corporation
Phone: 617-252-7832
Email:

U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health & Human Services