ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 10/27/2014

ClinicalTrials.gov ID: NCT00794664

Study Identification

Unique Protocol ID: MIPO3500108

Brief Title: Safety and Efficacy of Mipomersen in Patients With Severe Hypercholesterolemia on a Maximally Tolerated Lipid-Lowering Regimen and Who Are Not on Apheresis

Official Title: A Prospective Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety and Efficacy of Mipomersen in Patients With Severe Hypercholesterolemia on a Maximally Tolerated Lipid-Lowering Regimen and Who Are Not on Apheresis

Secondary IDs: 2008-006020-53 [EudraCT Number]

Study Status

Record Verification: October 2014

Overall Status: Completed

Study Start: January 2009

Primary Completion: May 2010 [Actual]

Study Completion: October 2010 [Actual]

Sponsor/Collaborators

Sponsor: Genzyme, a Sanofi Company

Responsible Party: Sponsor

Collaborators: Isis Pharmaceuticals

Oversight

FDA Regulated?: Yes

IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 70,969 Serial Number: 0050 Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 11/26/2008 Board Name: Goodwyn IRB Board Affiliation: The Goodwyn Institutional Review Board, Ltd. Phone: 513-793-8900 Email: message@goodwynirb.com
Data Monitoring?:	Yes
Oversight Authorities:	United States: Food and Drug Administration Canada: Health Canada South Africa: Medicines Control Council Czech Republic: State Institute for Drug Control Germany: Federal Institute for Drugs and Medical Devices

Study Description

Brief Summary:	The purpose of the study is to evaluate the safety and efficacy of dosing with mipomersen for 26 weeks in treating severely hypercholesterolemic patients who are on a maximally tolerated lipid-lowering regimen and who are not on apheresis.
Detailed Description:	Hypercholesterolemia is characterized by markedly elevated low density lipoproteins (LDL). Elevated LDL is a major risk factor for coronary heart disease (CHD). Mipomersen is an antisense drug that reduces a protein in the liver cells called apolipoprotein B (Apo-B). Apo-B plays a role in producing low density lipoprotein cholesterol (LDL-C) (the "bad" cholesterol) and moving it from the liver to one's bloodstream. High LDL-C is an independent risk factor for the development of coronary heart disease (CHD) or other diseases of blood vessels. It has been shown that lowering LDL-C reduces the risk of heart attacks and other major adverse cardiovascular events. The purpose of this study is to determine whether mipomersen safely and effectively lowers LDL-C in severely hypercholesterolemic patients who are on a maximally tolerated lipid-lowering regimen and who are not on apheresis.

Conditions

Conditions:	Hypercholesterolemia Coronary Heart Disease
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	58 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Placebo Comparator: Placebo Weekly subcutaneous injections for 26 weeks	Drug: Placebo 1 mL weekly subcutaneous injections for 26 weeks Other Names: • placebo
Experimental: Mipomersen 200 mg weekly subcutaneous injections for 26 weeks	Drug: Mipomersen 200 mg (1 mL), weekly subcutaneous injections for 26 weeks 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:

- Fasting LDL-C ≥200 mg/dL (5.1 mmol/L) at screening and the presence of at least 1 of the following criteria:
  - Myocardial infarction (MI)
  - Percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG)
  - Coronary artery disease documented by angiography or any other accepted imaging technique
  - Positive exercise test (≥1 mm ST-depression at maximal exercise or test terminated because of angina) or a perfusion defect (e.g., thallium or single photon emission computed tomography)
  - Other clinical atherosclerotic diseases: peripheral artery disease, symptomatic carotid artery disease, abdominal aortic aneurysm
  - Or, if alternative above were not met, fasting LDL-C ≥300 mg/dL (7.8 mmol/L)
- On stable, maximally tolerated statin therapy for 8 weeks
- On stable, medication from an additional class of hypolipidemic agents for 8 weeks.
- On stable, low fat diet for 12 weeks
- Stable weight for 6 weeks

Exclusion Criteria:

- Significant health problems in the recent past including heart attack, stroke, coronary syndrome, unstable angina, heart failure, significant arrhythmia, hypertension, blood disorders, liver disease, cancer, digestive disorders, Type I diabetes, or uncontrolled Type II diabetes
- Apheresis within 3 months prior to Screening or expected to start apheresis during the treatment phase

Contacts/Locations

Study Officials: Medical Monitor
Genzyme Corporation

Locations: United States, Florida
Jupiter, Florida, United States, 33458

Winter Park, Florida, United States, 32792

United States, Georgia
Atlanta, Georgia, United States, 30338

United States, Kansas
Kansas City, Kansas, United States, 66160

United States, Massachusetts

Boston, Massachusetts, United States, 02114

United States, Missouri
St Louis, Missouri, United States, 63104

United States, New Hampshire
Concord, New Hampshire, United States, 03301

United States, Ohio
Cincinnati, Ohio, United States, 45212

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Chicoutimi, Quebec, Canada, G7H 5H6

Montreal, Quebec, Canada, H1T 1C8

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Pilsen, Czech Republic, 305 99

Praha, Czech Republic, 128 08

Uherske Hradiste, Czech Republic, 686 68

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Heidelberg, Germany, 69120

Koln (Lindenthal), Germany, 50937

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References

Citations: [Study Results] McGowan MP, Tardif J-C, Ceska R, Burgess LJ, Soran H, et al. (2012) Randomized, Placebo-Controlled Trial of Mipomersen in Patients with Severe Hypercholesterolemia Receiving Maximally Tolerated Lipid-Lowering Therapy. PLoS ONE 7(11): e49006. doi:10.1371/journal.pone.0049006

Links:

Study Results

Participant Flow

Pre-Assignment Details	One hundred and four patients were screened and 58 randomized in a 2:1 treatment arm ratio.

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Treatment Period

	Placebo	Mipomersen
Started	19	39
Completed	18 [1]	27 [2]
Not Completed	1	12
Withdrawal by Subject	0	2
Protocol non-compliance	0	1

	Placebo	Mipomersen
Not specified	0	1
Adverse Event	1	8

[1] 3 participants enrolled in open-label extension study NCT00694109
[2] 6 participants enrolled in open-label extension study NCT00694109

Follow-up Period

	Placebo	Mipomersen
Started	16 [1]	33 [1]
Completed	15	28
Not Completed	1	5
Not specified	1	2
Withdrawal by Subject	0	2
Protocol non-compliance	0	1

[1] Participants enrolled in the open-label extension (NCT00694109) or continued in the follow-up period

Baseline Characteristics

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Baseline Measures

	Placebo	Mipomersen	Total
Number of Participants	19	39	58
Age, Continuous [units: years] Mean (Standard Deviation)	47.9 (13.5)	51.8 (14.3)	50.5 (14.0)

	Placebo	Mipomersen	Total
Gender, Male/Female [units: participants]			
Female	12	21	33
Male	7	18	25
Race/Ethnicity, Customized [units: participants]			
White	16	33	49
Black	1	2	3
Asian	0	1	1
Multiple	2	1	3
Other	0	2	2
Ethnicity [units: participants]			
Not Hispanic or Latino	19	39	58
Hispanic or Latino	0	0	0
Body Mass Index [units: kg/m^2] Mean (Standard Deviation)	29.9 (4.10)	28.4 (5.35)	28.9 (4.98)
Waist/hip ratio [units: ratio] Mean (Standard Deviation)	0.94 (0.06)	0.92 (0.09)	0.93 (0.08)
Metabolic syndrome [1] [units: participants]			
No	10	25	35
Yes	9	14	23
Tobacco Use [units: participants]			
Current	5	4	9
Non-current	7	11	18
Never	7	24	31

	Placebo	Mipomersen	Total
Alcohol Use [units: participants]			
Current	7	27	34
Non-current	4	5	9
Never	8	7	15

[1] Yes if 3 or more risk factors are present: 1) Abdominal obesity 2) Triglycerides >=150 mg/dl * 3) High density lipoprotein cholesterol (men <40 mg/dl) (women <50 mg/dl) * 4) Systolic blood pressure >=130 or diastolic >=85 mmHg * 5) Fasting glucose >=100 mg/dl * * = or on medication for condition

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at 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. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description

Full analysis set (FAS). The FAS, which represents the practically-feasible intent-to-treat (ITT) population as delineated in ICH Guideline E9, consists of treated participants with a valid baseline and at least one post-baseline LDL-C measure.

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percent Change From Baseline in Low-density Lipoprotein Cholesterol (LDL-C) at Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	12.5 (46.87)	-35.9 (24.71)

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

Statistical Analysis Overview	Comparison Groups	Placebo, Mipomersen
	Comments	Based upon prior clinical study experience with mipomersen, it was estimated that the standard deviation of the percent change in LDL-C was approximately 22%. With 15 patients in the control group and 30 patients in the mipomersen-treated group, this study would have at least 80% power to detect a 20 percentage point difference between the 2 treatment groups. Enrollment was to be conducted such that at least 51 patients were randomized to allow for potential exclusions from an analysis set.
	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	LDL-C at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
LDL-C at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	249.4 (84.3)	276.1 (72.1)
PET	263.9 (102.0)	174.9 (82.8)

3. Secondary Outcome Measure:

Measure Title	Percent Change From Baseline in Apolipoprotein B (Apo-B) at Primary Efficacy Time Point
Measure Description	Apo-B was measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks

	Description
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percent Change From Baseline in Apolipoprotein B (Apo-B) at Primary Efficacy Time Point [units: percentage of baseline] Mean (Standard Deviation)	11.41 (36.80)	-35.88 (22.95)

Statistical Analysis 1 for Percent Change From Baseline in Apolipoprotein B (Apo-B) at 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]

4. Secondary Outcome Measure:

Measure Title	Apo-B at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Apo-B at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	182.8 (48.6)	202.1 (49.1)
PET	193.7 (54.2)	126.8 (49.6)

5. Secondary Outcome Measure:

Measure Title	Percentage Change From Baseline in Total Cholesterol at Primary Efficacy Time Point (PET)
Measure Description	Total cholesterol was measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks

	Description
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percentage Change From Baseline in Total Cholesterol at Primary Efficacy Time Point (PET) [units: percentage of baseline] Mean (Standard Deviation)	11.13 (34.74)	-28.31 (20.43)

Statistical Analysis 1 for Percentage Change From Baseline in Total Cholesterol at Primary Efficacy Time Point (PET)

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	Inferential conclusions about this parameter require statistical significance of the previous secondary outcome measure (i.e., percent change from baseline in Apo B at PET).
	Method	t-test, 2 sided
	Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	Total Cholesterol at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Total Cholesterol at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	320.6 (87.2)	356.8 (77.0)
PET	341.5 (100.5)	251.5 (82.2)

7. Secondary Outcome Measure:

Measure Title	Percentage Change From Baseline in Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) at Primary Efficacy Time Point (PET)
Measure Description	Non-HDL-C was measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percentage Change From Baseline in Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) at Primary Efficacy Time Point (PET) [units: percentage of baseline] Mean (Standard Deviation)	14.17 (47.75)	-33.95 (23.80)

Statistical Analysis 1 for Percentage Change From Baseline in Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) at Primary Efficacy Time Point (PET)

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	Inferential conclusions about this parameter require statistical significance of the previous secondary outcome measure (i.e., percent change from baseline in total cholesterol at PET).
	Method	t-test, 2 sided
	Comments	[Not specified]

8. Secondary Outcome Measure:

Measure Title	Non-HDL-C at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.

Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Non-HDL-C at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	277.5 (88.3)	305.6 (78.3)
PET	296.7 (103.8)	198.1 (85.3)

9. Other Pre-specified Outcome Measure:

Measure Title	Percentage Change From Baseline in Triglycerides at Primary Efficacy Time Point (PET)
Measure Description	Triglycerides were measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percentage Change From Baseline in Triglycerides at Primary Efficacy Time Point (PET) [units: percentage of baseline] Mean (Standard Deviation)	26.50 (60.61)	-8.71 (40.10)

Statistical Analysis 1 for Percentage Change From Baseline in Triglycerides at Primary Efficacy Time Point (PET)

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	0.034
	Comments	Statistical significance was concluded if p ≤0.05
	Method	t-test, 2 sided
	Comments	[Not specified]

10. Other Pre-specified Outcome Measure:

Measure Title	Triglycerides at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Triglycerides at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	140.3 (49.8)	142.2 (86.0)
PET	164.5 (61.2)	116.3 (63.3)

11. Other Pre-specified Outcome Measure:

Measure Title	Percentage Change From Baseline in Lipoprotein(a) at Primary Efficacy Time Point (PET)
Measure Description	Lipoprotein(a) was measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percentage Change From Baseline in Lipoprotein(a) at Primary Efficacy Time Point (PET) [units: percentage of baseline] Mean (Standard Deviation)	-1.46 (25.74)	-32.65 (32.98)

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

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
	Method	t-test, 2 sided
	Comments	[Not specified]

12. Other Pre-specified Outcome Measure:

Measure Title	Lipoprotein(a) at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Lipoprotein(a) at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	32.4 (28.5)	61.3 (68.4)
PET	32.1 (28.1)	43.3 (54.3)

13. Other Pre-specified Outcome Measure:

Measure Title	Percentage Change From Baseline in Very-Low-Density Lipoprotein Cholesterol (VLDL-C) at Primary Efficacy Time Point (PET)
Measure Description	VLDL-C was measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks

	Description
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percentage Change From Baseline in Very-Low-Density Lipoprotein Cholesterol (VLDL-C) at Primary Efficacy Time Point (PET) [units: percentage of baseline] Mean (Standard Deviation)	25.13 (58.66)	-9.36 (39.57)

Statistical Analysis 1 for Percentage Change From Baseline in Very-Low-Density Lipoprotein Cholesterol (VLDL-C) at Primary Efficacy Time Point (PET)

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	<0.032
	Comments	Statistical significance was concluded if p ≤0.05
	Method	t-test, 2 sided
	Comments	[Not specified]

14. Other Pre-specified Outcome Measure:

Measure Title	VLDL-C at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
VLDL-C at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	28.1 (9.9)	29.1 (20.0)
PET	32.8 (12.3)	23.2 (12.6)

15. Other Pre-specified Outcome Measure:

Measure Title	Change From Baseline in Ratio of Low-density Lipoprotein Cholesterol (LDL-C) to High-density Lipoprotein Cholesterol (HDL-C) at Primary Efficacy Time Point (PET)
Measure Description	LDL-C and HDL-C were measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Change From Baseline in Ratio of Low-density Lipoprotein Cholesterol (LDL-C) to High-density Lipoprotein Cholesterol (HDL-C) at Primary Efficacy Time Point (PET) [units: percentage of baseline] Median (Inter-Quartile Range)	1.9 (-14.3 to 18.0)	-41.8 (-57.4 to -16.4)

Statistical Analysis 1 for Change From Baseline in Ratio of Low-density Lipoprotein Cholesterol (LDL-C) to High-density Lipoprotein Cholesterol (HDL-C) at Primary Efficacy Time Point (PET)

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
	Method	Other [Wilcoxon rank sum test]
	Comments	[Not specified]

16. Other Pre-specified Outcome Measure:

Measure Title	Ratio of LDL-C to HDL-C at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.

Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Ratio of LDL-C to HDL-C at Baseline and the Primary Efficacy Time Point (PET) [units: ratio] Median (Inter-Quartile Range)		
Baseline	5.89 (3.89 to 6.58)	5.21 (4.13 to 6.97)
PET	5.85 (3.28 to 7.76)	3.05 (2.11 to 4.26)

17. Other Pre-specified Outcome Measure:

Measure Title	Percent Change From Baseline in Apolipoprotein A1 (Apo-A1) at Primary Efficacy Time Point (PET)
Measure Description	Apo-A1 was measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percent Change From Baseline in Apolipoprotein A1 (Apo-A1) at Primary Efficacy Time Point (PET) [units: percentage of baseline] Mean (Standard Deviation)	1.75 (14.33)	-3.04 (15.76)

Statistical Analysis 1 for Percent Change From Baseline in Apolipoprotein A1 (Apo-A1) at Primary Efficacy Time Point (PET)

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	0.278
	Comments	Statistical significance was concluded if p ≤0.05
	Method	t-test, 2 sided
	Comments	[Not specified]

18. Other Pre-specified Outcome Measure:

Measure Title	Apo-A1 at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Apo-A1 at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	139.2 (32.6)	154.9 (31.4)
PET	140.7 (34.2)	147.9 (27.0)

19. Other Pre-specified Outcome Measure:

Measure Title	Percentage Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) at Primary Efficacy Time Point (PET)
Measure Description	HDL-C was measured in mg/dL. Samples were taken following an overnight fast. Baseline was defined as the average of the screening and Study Day 1 (pre-treatment) assessments. An assessment was not included in this calculation if it was associated with a non-fasting blood draw or was drawn more than 4 weeks prior to Study Day 1. The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks

	Description
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
Percentage Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) at Primary Efficacy Time Point (PET) [units: percentage of baseline] Mean (Standard Deviation)	3.16 (16.50)	5.78 (21.25)

Statistical Analysis 1 for Percentage Change From Baseline in High-Density Lipoprotein Cholesterol (HDL-C) at Primary Efficacy Time Point (PET)

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	0.647
	Comments	Statistical significance was concluded if p ≤0.05
	Method	t-test, 2 sided
	Comments	[Not specified]

20. Other Pre-specified Outcome Measure:

Measure Title	HDL-C at Baseline and the Primary Efficacy Time Point (PET)
Measure Description	The PET was the post-baseline visit, for which LDL-C was assessed, closest to 14 days after the last dose of study drug.
Time Frame	Baseline (the average of the screening and Day 1 pre-treatment assessments) and the Primary Efficacy Time point (PET) up to week 28
Safety Issue?	No

Analysis Population Description
Full analysis set

Reporting Groups

	Description
Placebo	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Measured Values

	Placebo	Mipomersen
Number of Participants Analyzed	18	39
HDL-C at Baseline and the Primary Efficacy Time Point (PET) [units: mg/dL] Mean (Standard Deviation)		
Baseline	43.1 (11.6)	51.1 (15.1)
PET	44.8 (16.3)	53.4 (16.7)

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	Weekly subcutaneous injections for 26 weeks
Mipomersen	200 mg weekly subcutaneous injections for 26 weeks

Serious Adverse Events

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/19 (0%)	6/39 (15.38%)
Cardiac disorders		
Acute myocardial infarction [A] †	0/19 (0%)	1/39 (2.56%)
Angina pectoris [A] †	0/19 (0%)	1/39 (2.56%)
Angina unstable [A] †	0/19 (0%)	1/39 (2.56%)
Cardiac failure [A] †	0/19 (0%)	1/39 (2.56%)
Prinzmetal angina [A] †	0/19 (0%)	1/39 (2.56%)
General disorders		
Device malfunction [A] †	0/19 (0%)	1/39 (2.56%)
Hepatobiliary disorders		
Hepatic steatosis [A] †	0/19 (0%)	1/39 (2.56%)
Investigations		
Alanine aminotransferase increased [A] †	0/19 (0%)	1/39 (2.56%)
Aspartate aminotransferase increased [A] †	0/19 (0%)	1/39 (2.56%)

† 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	16/19 (84.21%)	39/39 (100%)
Cardiac disorders		
Angina pectoris [A] †	1/19 (5.26%)	1/39 (2.56%)
Coronary artery disease [A] †	0/19 (0%)	1/39 (2.56%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Supraventricular extrasystoles [A] †	0/19 (0%)	1/39 (2.56%)
Ear and labyrinth disorders		
Tinnitus [A] †	0/19 (0%)	1/39 (2.56%)
Eye disorders		
Eye swelling [A] †	0/19 (0%)	1/39 (2.56%)
Vitreous floaters [A] †	0/19 (0%)	1/39 (2.56%)
Gastrointestinal disorders		
Abdominal pain [A] †	0/19 (0%)	2/39 (5.13%)
Abdominal pain upper [A] †	1/19 (5.26%)	2/39 (5.13%)
Constipation [A] †	0/19 (0%)	1/39 (2.56%)
Diarrhoea [A] †	1/19 (5.26%)	1/39 (2.56%)
Gastritis [A] †	0/19 (0%)	1/39 (2.56%)
Gastrooesophageal reflux disease [A] †	0/19 (0%)	1/39 (2.56%)
Nausea [A] †	0/19 (0%)	5/39 (12.82%)
Rectal haemorrhage [A] †	0/19 (0%)	1/39 (2.56%)
Vomiting [A] †	0/19 (0%)	1/39 (2.56%)
General disorders		
Asthenia [A] †	0/19 (0%)	1/39 (2.56%)
Chest discomfort [A] †	1/19 (5.26%)	0/39 (0%)
Chills [A] †	0/19 (0%)	1/39 (2.56%)
Fatigue [A] †	2/19 (10.53%)	4/39 (10.26%)
Influenza like illness [A] †	0/19 (0%)	9/39 (23.08%)
Injection site discolouration [A] †	0/19 (0%)	3/39 (7.69%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Injection site erythema [A] †	2/19 (10.53%)	22/39 (56.41%)
Injection site haematoma [A] †	4/19 (21.05%)	9/39 (23.08%)
Injection site induration [A] †	0/19 (0%)	3/39 (7.69%)
Injection site inflammation [A] †	0/19 (0%)	3/39 (7.69%)
Injection site mass [A] †	0/19 (0%)	1/39 (2.56%)
Injection site nodule [A] †	0/19 (0%)	1/39 (2.56%)
Injection site oedema [A] †	0/19 (0%)	5/39 (12.82%)
Injection site pain [A] †	0/19 (0%)	23/39 (58.97%)
Injection site papule [A] †	0/19 (0%)	1/39 (2.56%)
Injection site pruritus [A] †	1/19 (5.26%)	13/39 (33.33%)
Injection site rash [A] †	0/19 (0%)	3/39 (7.69%)
Injection site reaction [A] †	0/19 (0%)	2/39 (5.13%)
Injection site recall reaction [A] †	0/19 (0%)	2/39 (5.13%)
Injection site swelling [A] †	0/19 (0%)	12/39 (30.77%)
Injection site urticaria [A] †	0/19 (0%)	1/39 (2.56%)
Injection site vesicles [A] †	0/19 (0%)	1/39 (2.56%)
Non-cardiac chest pain [A] †	0/19 (0%)	1/39 (2.56%)
Oedema peripheral [A] †	0/19 (0%)	2/39 (5.13%)
Pain [A] †	1/19 (5.26%)	0/39 (0%)
Pyrexia [A] †	0/19 (0%)	3/39 (7.69%)
Hepatobiliary disorders		
Hepatic function abnormal [A] †	0/19 (0%)	1/39 (2.56%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Hepatic steatosis [A] †	0/19 (0%)	4/39 (10.26%)
Liver tenderness [A] †	0/19 (0%)	1/39 (2.56%)
Immune system disorders		
Allergy to plants [A] †	0/19 (0%)	1/39 (2.56%)
Infections and infestations		
Cellulitis [A] †	0/19 (0%)	1/39 (2.56%)
Gastroenteritis [A] †	1/19 (5.26%)	2/39 (5.13%)
Gastroenteritis viral [A] †	0/19 (0%)	1/39 (2.56%)
Hordeolum [A] †	0/19 (0%)	1/39 (2.56%)
Impetigo [A] †	0/19 (0%)	1/39 (2.56%)
Influenza [A] †	0/19 (0%)	1/39 (2.56%)
Lower respiratory tract infection [A] †	1/19 (5.26%)	0/39 (0%)
Nasopharyngitis [A] †	1/19 (5.26%)	4/39 (10.26%)
Onychomycosis [A] †	0/19 (0%)	1/39 (2.56%)
Pharyngitis [A] †	0/19 (0%)	1/39 (2.56%)
Pleurisy viral [A] †	0/19 (0%)	1/39 (2.56%)
Pyelonephritis [A] †	0/19 (0%)	1/39 (2.56%)
Sinusitis [A] †	0/19 (0%)	1/39 (2.56%)
Skin infection [A] †	0/19 (0%)	1/39 (2.56%)
Upper respiratory tract infection [A] †	0/19 (0%)	1/39 (2.56%)
Urinary tract infection [A] †	1/19 (5.26%)	3/39 (7.69%)
Viral upper respiratory tract infection [A] †	0/19 (0%)	1/39 (2.56%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Injury, poisoning and procedural complications		
Animal bite [A] †	0/19 (0%)	1/39 (2.56%)
Animal scratch [A] †	0/19 (0%)	1/39 (2.56%)
Arthropod bite [A] †	0/19 (0%)	1/39 (2.56%)
Contusion [A] †	1/19 (5.26%)	1/39 (2.56%)
Epicondylitis [A] †	0/19 (0%)	1/39 (2.56%)
Post procedural complication [A] †	0/19 (0%)	1/39 (2.56%)
Post procedural haematoma [A] †	0/19 (0%)	1/39 (2.56%)
Investigations		
Alanine aminotransferase increased [A] †	0/19 (0%)	7/39 (17.95%)
Aspartate aminotransferase increased [A] †	0/19 (0%)	4/39 (10.26%)
Blood alkaline phosphatase increased [A] †	0/19 (0%)	1/39 (2.56%)
Blood creatine phosphokinase increased [A] †	1/19 (5.26%)	1/39 (2.56%)
Blood creatinine increased [A] †	0/19 (0%)	3/39 (7.69%)
Blood lactate dehydrogenase increased [A] †	0/19 (0%)	2/39 (5.13%)
Cardiac murmur [A] †	0/19 (0%)	1/39 (2.56%)
Electrocardiogram PR prolongation [A] †	0/19 (0%)	1/39 (2.56%)
Epstein-Barr virus antibody positive [A] †	0/19 (0%)	1/39 (2.56%)
Hepatic enzyme increased [A] †	0/19 (0%)	1/39 (2.56%)
Liver function test abnormal [A] †	0/19 (0%)	1/39 (2.56%)
Platelet count decreased [A] †	1/19 (5.26%)	0/39 (0%)
Prothrombin time prolonged [A] †	1/19 (5.26%)	0/39 (0%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Weight increased [A] †	0/19 (0%)	1/39 (2.56%)
Metabolism and nutrition disorders		
Glucose tolerance impaired [A] †	0/19 (0%)	1/39 (2.56%)
Hyperuricaemia [A] †	1/19 (5.26%)	0/39 (0%)
Type 2 diabetes mellitus [A] †	1/19 (5.26%)	0/39 (0%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	1/19 (5.26%)	1/39 (2.56%)
Arthritis [A] †	0/19 (0%)	1/39 (2.56%)
Back pain [A] †	0/19 (0%)	1/39 (2.56%)
Groin pain [A] †	0/19 (0%)	2/39 (5.13%)
Intervertebral disc protrusion [A] †	0/19 (0%)	1/39 (2.56%)
Muscle spasms [A] †	0/19 (0%)	1/39 (2.56%)
Musculoskeletal pain [A] †	0/19 (0%)	1/39 (2.56%)
Musculoskeletal stiffness [A] †	1/19 (5.26%)	0/39 (0%)
Myalgia [A] †	1/19 (5.26%)	3/39 (7.69%)
Osteoarthritis [A] †	0/19 (0%)	1/39 (2.56%)
Osteochondrosis [A] †	0/19 (0%)	1/39 (2.56%)
Pain in extremity [A] †	1/19 (5.26%)	3/39 (7.69%)
Pain in jaw [A] †	0/19 (0%)	1/39 (2.56%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Benign breast neoplasm [A] †	0/19 (0%)	1/39 (2.56%)
Nervous system disorders		
Cerebrovascular accident [A] †	0/19 (0%)	1/39 (2.56%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Dizziness [A] †	0/19 (0%)	2/39 (5.13%)
Headache [A] †	1/19 (5.26%)	1/39 (2.56%)
Lethargy [A] †	0/19 (0%)	1/39 (2.56%)
Migraine [A] †	1/19 (5.26%)	1/39 (2.56%)
Restless legs syndrome [A] †	1/19 (5.26%)	0/39 (0%)
Somnolence [A] †	0/19 (0%)	1/39 (2.56%)
Syncope [A] †	0/19 (0%)	2/39 (5.13%)
Tremor [A] †	0/19 (0%)	1/39 (2.56%)
Psychiatric disorders		
Anxiety [A] †	0/19 (0%)	1/39 (2.56%)
Bipolar disorder [A] †	0/19 (0%)	1/39 (2.56%)
Depression [A] †	0/19 (0%)	1/39 (2.56%)
Insomnia [A] †	0/19 (0%)	1/39 (2.56%)
Renal and urinary disorders		
Proteinuria [A] †	1/19 (5.26%)	2/39 (5.13%)
Renal cyst [A] †	0/19 (0%)	1/39 (2.56%)
Respiratory, thoracic and mediastinal disorders		
Bronchitis chronic [A] †	0/19 (0%)	1/39 (2.56%)
Cough [A] †	0/19 (0%)	2/39 (5.13%)
Dyspnoea [A] †	0/19 (0%)	1/39 (2.56%)
Dyspnoea exertional [A] †	0/19 (0%)	1/39 (2.56%)
Skin and subcutaneous tissue disorders		
Alopecia [A] †	0/19 (0%)	1/39 (2.56%)

	Placebo	Mipomersen
	Affected/At Risk (%)	Affected/At Risk (%)
Blister [A] †	1/19 (5.26%)	0/39 (0%)
Dermatitis [A] †	0/19 (0%)	1/39 (2.56%)
Dermatitis allergic [A] †	1/19 (5.26%)	1/39 (2.56%)
Ecchymosis [A] †	0/19 (0%)	1/39 (2.56%)
Hyperkeratosis [A] †	0/19 (0%)	1/39 (2.56%)
Pruritus [A] †	1/19 (5.26%)	0/39 (0%)
Xanthoma [A] †	0/19 (0%)	1/39 (2.56%)
Vascular disorders		
Flushing [A] †	0/19 (0%)	1/39 (2.56%)
Hot flush [A] †	0/19 (0%)	1/39 (2.56%)
Hypertension [A] †	0/19 (0%)	3/39 (7.69%)
Orthostatic hypotension [A] †	0/19 (0%)	1/39 (2.56%)
Peripheral arterial occlusive disease [A] †	0/19 (0%)	1/39 (2.56%)

† 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.

In multi-site studies, PI can publish site data after a multi-centered publication or 12 months after study completion. PI gives Genzyme a draft 60 days before publication. Genzyme can ask that confidential information be removed, and can defer publication another 6 months (contracts have variable timeframes) upon notifying PI that it will file a patent application on inventions contained in the draft.

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