Sponsor

Novartis

Generic Drug Name

LGT209

Therapeutic Area of Trial

Hypercholesterolemia

Approved Indication

Investigational

Protocol Number

CLGT209X2105

Title

A randomized, double-blind, placebo-controlled, single dose, parallel group study to assess the safety, tolerability, bioavailability, pharmacokinetics, and pharmacodynamics of subcutaneous LGT209 in hypercholesterolemic patients on stable doses of atorvastatin or simvastatin and in healthy volunteers

Study Phase

Phase I

Study Start/End Dates

First patient first visit: 08-Jul-2011

Last patient last visit: 26-Jul-2013

Study Design/Methodology

This was a randomized, double-blind, placebo-controlled, parallel group study of subcutaneous (sc) LGT209 in healthy volunteers and in hypercholesterolemic patients on stable doses of atorvastatin or simvastatin. .

Two dose levels of LGT209 were tested in patients treated with statins (Cohort 1 and Cohort 2), and one dose level of LGT209 was tested in healthy volunteers (HVs) (Cohort 3). Subjects within each cohort were randomized in a ratio of 3:1 (LGT209 (n=6): Placebo (n=2)).

Centers

3 centers in USA

Publication

None

Test Product (s), Dose(s), and Mode(s) of Administration

LGT209 (150 mg lyophilized powder in glass vial), and matching placebo, were prepared by Novartis. Study drug was administered subcutaneously (sc) as a single dose at one site (Cohort 1: 50 mg LGT209/placebo), or at two separate sites (Cohorts 2 and 3: 300 mg LGT209/placebo).

Subjects were assigned to one of the following three cohorts in a 3: 1 ratio (active: placebo):
1. Cohort 1: 50 mg LGT209 or placebo sc (1 mL injection × 1 site) in patients treated with statins
2. Cohort 2: 300 mg LGT209 or placebo sc (1 mL injections × 2 sites) in patients treated with statins
3. Cohort 3: 300 mg LGT209 or placebo sc (1 mL injections × 2 sites) in healthy volunteers.

Statistical Methods

Safety data analysis: Safety data were listed by population, treatment, subject and visit/time, and any abnormalities were flagged. Summary statistics were provided by treatment and visit/time.

Pharmacokinetic data analysis: Free LGT209, simvastatin and atorvastatin drug concentrations were summarized using descriptive statistics for each sampling point by population and treatment group.

The AUC(0-inf)/dose was calculated for each individual subject and normalized by weight. Log-transformed values of dose- and weight-normalized LGT209 AUC(0-inf) were analyzed using an ANOVA model with population and treatment (dose) as factors. To evaluate treatment groups, subject populations, and differences between treatment groups and/or subject populations, point estimates and 90% confidence intervals on the log-scale were back-transformed and reported as a comparison of geometric means and ratios of geometric means. The treatment group and subject population comparisons included: Cohort 1 vs Cohort 2, Cohort 2 vs Cohort 3, and Cohort 1 vs Cohort 3.

Pharmacodynamic and biomarker data analysis: For all pharmacodynamic and biomarker endpoints (serum LDL-cholesterol, serum PCSK9, total cholesterol, HDL-cholesterol, triglycerides, serum bile acids; results were analyzed using descriptive statistics. Mean baseline values were calculated as the average of the concentrations measured at screening, baseline and pre-dose on Day 1. The ratio from baseline, and percentage change from baseline, were calculated for each cohort by time profile. Results were represented graphically as i) individual overlaying plots, ii) arithmetic means with error bars, and iii) percentage change from baseline.

Study Population: Inclusion/Exclusion Criteria and Demographics

Key inclusion criteria

Healthy volunteers (Cohort 3):

- Male and female subjects 18 to 70 years of age (inclusive) in general good health
- Fasting LDL-cholesterol >90 mg/dL at screening

Hypercholesterolemic patients treated with statins:

- Male or female subjects 18 to 70 years of age (inclusive) in general good health

- Diagnosis of hypercholesterolemia
- Treatment with a stable dose of atorvastatin or simvastatin therapy of ≥ 40 mg once daily for ≥3 months prior to screening. Patients receiving 80 mg simvastatin were included only if they had been on this dose for at least 1 year without signs or symptoms of myopathy or other drug side effects/intolerance.
- LDL-cholesterol >70 mg/dL (fasted-state direct measurement). Screening fasted-state serum triglyceride level of <400 mg/dL

Key exclusion criteria

Healthy volunteers:

- History of hypersensitivity to any of the study drugs or to drugs of similar chemical classes
- Use of any prescription drug, herbal supplements, within four (4) weeks prior to dosing, and/or over-the-counter (OTC) medication, dietary supplements (vitamins included) within two (2) weeks prior to dosing. If needed, (i.e., incidental and time-limited) use of acetaminophen or a single antacid medication was acceptable. Aspirin use for cardiovascular risk reduction was acceptable. Oral contraceptives were allowed. Other medications were allowed if agreed upon by the Sponsor and Investigator.
- Pregnant or nursing (lactating) women
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, UNLESS they are using highly effective methods of contraception during dosing and for at least 100 days after study drug administration.

Hypercholesterolemic patients treated with statins:

- Use of concomitant medications which might impact the safety or efficacy of atorvastatin or simvastatin based on drug information in the product label.
- Use of any prescription drug, herbal supplements, within four (4) weeks prior to dosing, and/or over-the-counter (OTC) medication, dietary supplements (vitamins included) within two (2) weeks prior to dosing. If needed, (i.e., incidental and time-limited) use of acetaminophen or a single antacid medication was acceptable. Use of up to three concurrent antihypertensive medications was allowed, provided stable dosing had been achieved and documented for the prior three (3) months. Aspirin use for cardiovascular risk reduction was acceptable. Oral contraceptives were allowed. Other medications were allowed if agreed upon by the Sponsor and Investigator.
- Pregnant or nursing (lactating women)
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, UNLESS they were using highly effective methods of contraception during dosing and for at least 100 days after study drug administration

Other protocol defined inclusion/exclusion criteria applied.

Participant Flow

Subject disposition (Safety Analysis Set)

	LGT209					
	Patients treated with statins			Healthy volunteers		
	50 mg sc N=6	300 mg sc N=6	Placebo N=4	300 mg sc N=7	Placebo N=2	All subjects N=25
Subjects						
Completed	6 (100)	6 (100)	4 (100)	6 (85.7)	2 (100)	24 (96.0)
Discontinued	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)
Main cause of discontinuation						
Protocol deviation*	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)
* Protocol deviation due to non-compliance on Day 45 (healthy volunteer)						

Baseline Characteristics

Demographic summary (Safety Analysis Set)

LGT209							
		Patients on statin			Healthy volunteers		
		50 mg sc N=6	300 mg sc N=6	Placebo N=4	300 mg sc N=7	Placebo* N=2	All subjects N=25
Age (years)	Mean (SD)	45.0 (11.98)	49.7 (9.99)	56.5 (10.47)	46.9 (14.96)	55.5	49.3 (12.09)
	Median	41.0	51.5	56.0	53.0	-	48.0
	Range	36 - 68	35 - 63	47 - 67	19 - 64	46 - 65	19 - 68
Height (cm)	Mean (SD)	180.5 (3.02)	167.6 (7.74)	166.6 (7.19)	163.3 (8.08)	160.9	168.8 (9.44)
	Median	179.5	167.3	166.9	162.6	-	168.1
	Range	178.0 - 185.0	156.0 - 177.0	158.5 - 174.0	151.4 - 175.8	155.4 - 166.4	151.4 - 185.0
Weight (kg)	Mean (SD)	106.8 (11.10)	86.9 (16.73)	86.4 (8.39)	84.4 (12.97)	67.4	89.3 (16.32)
	Median	110.5	84.0	87.8	84.1	-	86.4
	Range	85.5 - 115.9	71.8 - 111.6	75.0 - 95.0	71.0 - 108.3	59.7 - 75.0	59.7 - 115.9
BMI (kg/m^2)	Mean (SD)	32.76 (2.96)	30.72 (3.69)	31.39 (5.15)	31.61 (3.45)	25.91	31.18 (3.76)
	Median	33.56	30.76	31.04	31.06	-	32.01
	Range	26.99 - 35.58	26.38 - 35.63	25.65 - 37.82	25.45 - 35.07	24.73 - 27.09	24.73 - 37.82
Sex – n (%)	Male	6 (100 %)	3 (50 %)	2 (50 %)	5 (71.4 %)	1 (50 %)	17 (68 %)
	Female	0(0.0%)	3 (50 %)	2 (50 %)	2 (28.6 %)	1 (50 %)	8 (32 %)
Race - n (%)	Caucasian	6 (100 %)	2 (33.3 %)	3 (75 %)	6 (85.7 %)	2 (100 %)	19 (76 %)
	Black	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3 %)	0 (0.0%)	1 (4 %)
	Other	0 (0.0%)	4 (66.7 %)	1 (25 %)	0 (0.0%)	0 (0.0%)	5 (20 %)
Ethnicity - n (%)	Hispanic/Latino	5 (83.3 %)	5 (83.3 %)	4 (100 %)	7 (100 %)	2 (100 %)	23 (92 %)
	Other	1 (16.7 %)	1 (16.7 %)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8 %)
BMI = body mass index *A full statistical summary was not presented for the placebo group in view of the small sample size (n=2)							

Outcome Measures

Primary Outcome Result(s)

Pharmacokinetics

Summary statistics of serum LGT209 concentrations (ng/mL) per treatment (PK analysis set)

Timepoint (hours)	Statistic	Statin Treated Patients: 50 mg LGT209 (n=6)	Statin Treated Patients: 300 mg LGT209 (n=6)	Healthy volunteers: 300 mg LGT209 (n=7)
0 h	Mean (SD)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
	Median	-	-	-
	Min; Max	-	-	-
6	Mean (SD)	224 (248)	1030 (899)	3780 (2930)
	CV% (mean)	111	87.6	77.7
	Median	190	612	3380
	Min; Max	0.00; 509	340; 2530	659; 9090
12	Mean (SD)	617 (371)	2760 (2440)	8970 (5220)
	CV% (mean)	60.2	88.4	58.1
	Median	666	1920	8910
	Min; Max	0.00; 1070	792; 7300	2940; 17800
24	Mean (SD)	911 (512)	5600 (5140)	15300 (8870)
	CV% (mean)	56.2	91.8	58.1
	Median	1040	3840	13400
	Min; Max	0.00; 1470	1830; 15500	5230; 29900
48	Mean (SD)	1240 (500)	8740 (5080)	23900 (11000)
	CV% (mean)	40.3	58.1	46.2
	Median	1260	7940	19900
	Min; Max	508; 2040	4160; 18100	11200; 38700
72	Mean (SD)	1550 (603)	10400 (4640)	27000 (11100)
	CV% (mean)	39.0	44.8	41.3
	Median	1580	9170	22200
	Min; Max	590; 2340	6180; 19200	13300; 42700
96	Mean (SD)	1630 (717)	11900 (5480)	28400 (10500)
	CV% (mean)	44.1	46.2	36.9
	Median	1590	10300	27900
	Min; Max	602; 2660	7000; 22500	16700; 39200
120	Mean (SD)	1810 (766)	13800 (7310)	27700 (7670)
	CV% (mean)	42.3	53.0	27.7
	Median	1800	12500	24300
	Min; Max	793; 2900	7080; 27900	19100; 38600
168	Mean (SD)	1980 (714)	14500 (6200)	28400 (6410)
	CV% (mean)	36.0	42.8	22.6
	Median	1940	13200	26400
	Min; Max	1070; 3040	8800; 25800	21400; 37900
240	Mean (SD)	2060 (614)	15000 (5590)	26600 (5730)
	CV% (mean)	29.9	37.4	21.5
	Median	2040	13500	23100

	Min; Max	1210; 2940	9370; 24200	20800; 34500
336	Mean (SD)	1880 (493)	13400 (4660)	23800 (4750)
	CV% (mean)	26.2	34.9	20.0
	Median	1860	12000	23900
	Min; Max	1070; 2430	9220; 20700	18800; 31900
504	Mean (SD)	1700 (429)	12200 (2870)	20500 (3730)
	CV% (mean)	25.3	23.6	18.2
	Median	1780	11800 (9080;	20700
	Min; Max	924; 2170	15700)	15000; 25200
672	Mean (SD)	1380 (360)	11800 (3010)	16900 (4770)
	CV% (mean)	26.1	25.6	28.3
	Median	1360	11500	14900
	Min; Max	796; 1880	8220; 16500	12400; 25400
1008	Mean (SD)	874 (269)	7530 (1710)	10000 (2350)
	CV% (mean)	30.8	22.7	23.4
	Median	890	7210	10400
	Min; Max	435; 1280	6040; 10700	6330; 13800
1344	Mean (SD)	523 (317)	5610 (1220)	6470 (1720)
	CV% (mean)	60.6	21.8	26.6
	Median	519	5750	6320
	Min; Max	0.00; 949	4020; 6960	3720; 9020
1680	Mean (SD)	219 (249)	4470 (1680)	3780 (1330)
	CV% (mean)	113.3	37.6	35.3
	Median	163	4220	3740
	Min; Max	0.00; 518	2770; 6930	1870; 5990
2016	Mean (SD)	0.00 (0.00)	2610 (1090)	2280 (905)
	CV% (mean)	-	41.8	39.6
	Median	-	2340	2230
	Min; Max	-	1510; 4260	1050; 3780

Summary Statistics for free LGT209 pharmacokinetic parameters (PK Analysis Set)

Parameter (unit)	Statistics	Statin Treated Patients: 50 mg LGT209 (n=6)	Statin Treated Patients: 300 mg LGT209 (n=6)	Healthy volunteers: 300 mg LGT209 (n=7)
AUC(0-inf) (day*ug/mL)	N	6	6	6
	Mean (SD)	92.8 (25.5)	834 (139)	1140 (259)
	CV%	27.4	16.7	22.7
AUClast (day*ug/mL)	N	6	6	6
	Mean (SD)	76.6 (24.2)	693 (127)	1070 (233)
	CV%	31.6	18.3	21.8
Cmax (ug/mL)	N	6	6	6
	Mean (SD)	2.08 (0.645)	16.5 (6.22)	31.7 (8.58)
	CV%	31.0	37.6	27.1
Tmax (day)	N	6	6	6
	Mean (SD)	9.62 (2.58)	13.1 (9.33)	5.36 (1.88)
	CV%	26.8	71.0	35.1

Geometric mean, treatment ratio, and 90% CI for AUC(0-inf)*body weight /dose (day*µg/mL/mg/kg) for free LGT209

Comparison	Adjusted Geometric Means			
	Test (T)	Reference (R)	Geometric mean ratio	90% CI for ratio
Statin treated patients: 50 mg LGT209 (T) vs. 300 mg LGT209 (R)	187.57	233.42	0.80	(0.67,0.97)
Statin treated patients 50 mg LGT209 (T) vs. Healthy volunteers 300 mg LGT209 (R)	187.57	315.04	0.60	(0.49,0.72)
Statin treated patients 300 mg LGT209 (T) vs. Healthy volunteers 300 mg LGT209(R)	233.42	315.04	0.74	(0.61,0.89)

Pharmacodynamics

Maximum percent lowering from mean baseline of LDL-C (mg/dL) over a complete profile (PD analysis set)

Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers: 300 mg LGT209	Statin Treated Patients: Placebo	Healthy volunteers: Placebo
N Mean	6	6	7	4	2
(SD)	-31.1 (18.3)	-45.2 (10.4)	-34.0 (7.36)	-27.4 (9.23)	-16.5 (16.1)
Minimum	-62.8	-56.8	-41.4	-35.8	-27.9
Median	-28.3	-45.5	-36.7	-29.8	-16.5
Maximum	-11.0	-32.7	-22.2	-14.3	-5.1

Summary statistics of the concentration, ratio from baseline (%), and percent change from baseline in LDL-C concentrations over time (PD Analysis Set)

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
LDL-Cholesterol Concentration	Screening	Mean (SD)	117 (25.6)	143 (41.4)	150 (28.9)	149 (33.8)	138 (3.54)
		Geo-mean (CV%)	115 (22.4)	138 (30.2)	147 (19.4)	146 (22.0)	137 (2.6)
		Median	118	138	147	141	138
		Min; Max	82.0; 157	91.0; 201	109; 200	116; 196	135; 140
LDL-Cholesterol Concentration	Baseline	Mean (SD)	112 (33.9)	91.5 (25.0)	135 (37.6)	123 (24.2)	139 (21.9)
		Geo-mean (CV%)	107 (32.9)	88.9 (25.0)	135 (37.6)	121 (20.5)	138 (16.0)
		Median	115	82.5	130	126	139
		Min; Max	66.0; 161	67.0; 134	90.0; 213	95.0; 144	123; 154
LDL-Cholesterol Concentration	Day 1 (0 h)	Mean (SD)	115 (23.3)	92.8 (27.7)	142 (23.8)	120 (24.3)	135 (9.19)
		Geo-mean (CV%)	113 (20.6)	89.7 (28.8)	141 (15.5)	118 (21.1)	134 (6.8)
		Median	115	84.5	133	124	135
		Min; Max	86.0; 148	66.0; 139	123; 191	92.0; 142	128; 141
Mean Baseline LDL-Cholesterol Concentration [c]	-	Mean (SD)	115 (26.6)	109 (25.8)	144 (29.2)	131 (24.3)	137 (9.19)
		Geo-mean (CV%)	112 (23.6)	107 (22.0)	142 (18.4)	129 (18.6)	137 (6.70)
		Median	117	103	136	127	137
		Min; Max	84.3; 155	81.0; 158	117; 201	109; 159	130; 143
LDL-Cholesterol Concentration	Day 1 (6 h)	Mean (SD)	106 (19.8)	84.2 (28.4)	130 (22.3)	109 (25.6)	129 (12.0)
		Geo-mean (CV%)	104 (19.0)	80.2 (35.7)	128 (16.3)	106 (24.3)	128 (9.40)
		Median	104	78.0	125	109	129
		Min; Max	84.0; 131	47.0; 128	105; 173	84.0; 133	120; 137
Ratio from baseline (%)		Mean (SD)	0.932 (0.0730)	0.763 (0.152)	0.916 (0.0687)	0.826 (0.0563)	0.938 (0.0248)
		Geo-mean (CV%)	0.929 (7.90)	0.750 (19.8)	0.913 (7.40)	0.824	0.938
		Median	0.935	0.769	0.897	0.818	0.938
		Min; Max	0.843; 1.03	0.580; 1.01	0.846; 1.02	0.768; 0.899	0.921; 0.956
% change from baseline		Mean (SD)	-6.84 (7.30)	-23.7 (15.2)	-8.44 (6.87)	-17.4 (5.63)	-6.17 (2.48)

		Median	-6.53	-23.1	-10.3	-18.2	-16.7
		Min; Max	-15.7; 3.16	-42.0; 1.29	-15.4; 1.96	-23.2;-10.1	-7.93;-4.42
LDL-Cholesterol Concentration	Day 2	Mean (SD)	117 (24.8)	87.8 (27.2)	153 (35.1)	115 (29.4)	136 (9.19)
		Geo-mean (CV%)	115 (21.2)	84.4 (31.9)	150 (21.0)	112 (27.5)	135 (6.80)
		Median	114	82.5	132	120	136
		Min; Max	91.0; 153	55.0; 128	128; 222	80.0; 141	129; 142
Ratio from baseline (%)		Mean (SD)	1.03 (0.103)	0.802 (0.156)	1.07 (0.127)	0.876 (0.102)	0.990 (0.000656)
		Geo-mean (CV%)	1.03 (10.1)	0.790 (18.9)	1.07 (11.7)	0.871 (12.3)	0.990 (0.100)
		Median	1.02	0.792	1.10	0.901	0.990
		Min; Max	0.879; 1.19	0.626; 1.07	0.924; 1.30	0.732; 0.970	0.990; 0.991
% change from baseline		Mean (SD)	3.08 (10.3)	-19.8 (15.6)	7.28 (12.7)	-12.4 (10.2)	-0.977 (0.0656)
		Median	2.30	-20.8	10.3	-9.85	-0.977
		Min; Max	-12.1; 18.6	-37.4; 7.07	-7.58; 29.8	-26.8;-3.04	-1.02;-0.930
LDL-Cholesterol Concentration	Day 3	Mean (SD)	116 (24.9)	83.7 (25.5)	143 (38.0)	116 (35.3)	136 (26.9)
		Geo-mean (CV%)	113 (22.0)	80.4 (32.0)	140 (23.8)	112 (32.9)	135 (20.1)
		Median	115	79.0	126	119	136
		Min; Max	90.0; 145	51.0; 119	117; 222	76.0; 152	117; 155
Ratio from baseline (%)		Mean (SD)	1.02 (0.129)	0.765 (0.155)	0.999 (0.113)	0.879 (0.152)	0.990 (0.130)
		Geo-mean (CV%)	1.01 (13.0)	0.753 (19.5)	0.993 (11.4)	0.869 (17.7)	0.985 (13.2)
		Median	1.03	0.734	1.00	0.877	0.990
		Min; Max	0.825; 1.19	0.617; 1.03	0.869; 1.13	0.695; 1.07	0.898; 1.08
% change from baseline		Mean (SD)	1.92 (12.9)	-23.5 (15.5)	-0.147 (11.3)	-12.1 (15.2)	-1.05 (13.0)
		Median	2.52	-26.6	0.00	-12.3	-1.05
		Min; Max	-17.5; 18.6	-38.3; 3.22	-13.1; 13.0	-30.5; 6.79	-10.2; 8.14
LDL-Cholesterol Concentration	Day 4	Mean (SD)	102 (22.6)	77.0 (25.3)	133 (42.1)	107 (26.6)	123 (18.4)
		Geo-mean (CV%)	99.8 (22.4)	73.2 (37.7)	128 (28.1)	104 (25.6)	122 (15.1)
		Median	101	76.5	116	106	123
		Min; Max	78.0; 135	39.0; 114	97.0; 219	84.0; 132	110; 136

Ratio from baseline (%)		Mean (SD)	0.896 (0.105)	0.698 (0.142)	0.922 (0.138)	0.813 (0.0662)	0.896 (0.0741)
		Geo-mean (CV%)	0.890 (12.5)	0.685 (21.8)	0.913 (14.3)	0.811 (8.00)	0.895 (8.30)
		Median	0.912	0.714	0.879	0.799	0.896
		Min; Max	0.707; 1.02	0.487; 0.878	0.809; 1.14	0.754; 0.899	0.844; 0.949
% change from baseline		Mean (SD)	-10.4 (10.5)	-30.2 (14.2)	-7.85 (13.8)	-18.7 (6.62)	-10.4 (7.41)
		Median	-8.8	-28.6	-12.1	-20.1	-10.4
		Min; Max	-29.3; 1.52	-51.9;-12.2	-19.4;14.4	-24.6;-10.1	-15.6;-5.12
LDL-Cholesterol Concentration	Day 5	Mean (SD)	93.3 (25.2)	69.7 (23.3)	124 (33.1)	105 (28.4)	118 (25.5)
		Geo-mean (CV%)	27.6	38.5	26.1	27.8	22.0
		Median	93.0	67.0	111	103	118
		Min; Max	63.0; 133	35.0; 101	92.0; 173	80.0; 135	100; 136
Ratio from baseline (%)		Mean (SD)	0.815 (0.115)	0.632 (0.141)	0.858 (0.153)	0.799 (0.103)	0.858 (0.128)
		Geo-mean (CV%)	14.3	23.0	16.6	12.3	15.1
		Median	0.820	0.614	0.823	0.765	0.858
		Min; Max	0.653; 0.992	0.432; 0.859	0.732; 1.14	0.719; 0.948	0.767; 0.949
% change from baseline		Mean (SD)	-18.5 (11.5)	-36.8 (14.1)	-14.2 (15.3)	-20.1 (10.3)	-14.2 (12.8)
		Median	-18	-38.6	-17.7	-23.5	-14.2
		Min; Max	-34.7; -0.760	-56.8; -14.1	-26.8; 14.4	-28.1; -5.15	-23.3; -5.12
LDL-Cholesterol Concentration	Day 6	Mean (SD)	86.5 (22.0)	67.3 (21.2)	107 (25.3)	105 (25.7)	118 (33.2)
		Geo-mean (CV%)	84.4 (23.9)	64.2 (36.1)	105 (24.1)	103 (25.4)	115 (29.3)
		Median	80.5	68.0	97.0	106	118
		Min; Max	67.0; 126	36.0; 93.0	75.0; 141	79.0; 130	94.0; 141
Ratio from baseline (%)		Mean (SD)	0.759 (0.0992)	0.614 (0.140)	0.761 (0.173)	0.800 (0.0846)	0.852 (0.186)
		Geo-mean (CV%)	0.753 (13.4)	0.601 (22.7)	0.745 (21.5)	0.796 (10.4)	0.842 (22.2)
		Median	0.784	0.584	0.676	0.788	0.852
		Min; Max	0.625; 0.890	0.444; 0.830	0.626; 1.03	0.710; 0.913	0.721; 0.984

% change from baseline		Mean (SD)	-24.1 (9.92)	-38.6 (14.0)	-23.9 (17.3)	-20 (8.46)	-14.8 (18.6)
		Median	-21.6	-41.6	-32.4	-21.2	-14.8
		Min; Max	-37.5; -11	-55.6; -17	-37.4; 3.42	-29; -8.67	-27.9; -1.63
LDL-Cholesterol Concentration	Day 8	Mean (SD)	91.2 (32.1)	62.2 (13.8)	107 (29.2)	104 (25.6)	133 (26.2)
		Geo-mean (CV%)	86.9 (36.2)	60.7 (25.8)	104 (25.0)	102 (25.3)	131 (20.1)
		Median	90.5	65.5	103	102	133
		Min; Max	55.0; 144	38.0; 76.0	80.0; 166	82.0; 130	114; 151
Ratio from baseline (%)		Mean (SD)	0.794 (0.172)	0.579 (0.122)	0.748 (0.101)	0.790 (0.0569)	0.964 (0.126)
		Geo-mean (CV%)	0.776 (24.6)	0.568 (21.4)	0.742 (14.1)	0.789 (7.2)	0.960 (13.2)
		Median	0.804	0.560	0.778	0.784	0.964
		Min; Max	0.498; 0.981	0.437; 0.733	0.594; 0.884	0.737; 0.857	0.875; 1.05
% change from baseline		Mean (SD)	-20.6 (17.2)	-42.1 (12.2)	-25.2 (10.1)	-21 (5.69)	-3.59 (12.6)
		Median	-19.6	-44	-22.2	-21.6	-3.59
		Min; Max	-50.2; -1.9	-56.3; -26.7	-40.6; -11.6	-26.3; -14.3	-12.5; 5.35
LDL-Cholesterol Concentration	Day 11	Mean (SD)	99.5 (34.5)	76.8 (14.5)	107 (18.7)	114 (25.6)	138 (14.8)
		Geo-mean (CV%)	94.2 (38.5)	75.6 (20.4)	105 (19.2)	112 (23.0)	137 (10.9)
		Median	106	81.0	106	113	138
		Min; Max	58.0; 149	55.0; 94.0	72.0 (134)	87.0; 143	127;148
Ratio from baseline (%)		Mean (SD)	0.866 (0.222)	0.677 (0.105)	0.753 (0.0885)	0.873 (0.014)	1.00 (0.0411)
		Geo-mean (CV%)	0.841 (28.3)	0.670 (16.1)	0.748 (12.1)	0.868 (11.7)	1.00 (4.1)
		Median	0.896	0.713	0.772	0.852	1.00
		Min; Max	0.526; 1.19	0.539; 0.781	0.615; 0.876	0.781; 1.00	0.974; 1.03
% change from baseline		Mean (SD)	-13.4 (22.2)	-32.2 (10.5)	-24.7 (8.85)	-12.7 (10.4)	0.349 (4.11)
		Median	-10.4	-28.7	-22.8	-14.8	0.349
		Min; Max	-47.4; 18.6	-46.1; -21.9	-38.5; -12.4	-21.9; 0.468	-2.56; 3.26
LDL-Cholesterol	Day 15	Mean (SD)	102 (40.7)	71.2 (15.4)	108 (26.4)	120 (11.9)	138 (26.9)

Concentration		Geo-mean (CV%)	93.8 (48.5)	69.6 (24.2)	106 (21.7)	119 (10.0)	137 (19.8)
		Median	114	73.0	99.0	120	138
		Min; Max	50.0; 155	45.0; 93.0	89.0; 164	109; 131	119; 157
Ratio from baseline (%)		Mean (SD)	0.882 (0.289)	0.664 (0.138)	0.756 (0.0669)	0.929 (0.0864)	1.00 (0.129)
		Geo-mean (CV%)	0.837 (38.1)	0.652 (22.1)	0.753 (8.8)	0.926 (9.6)	1.00 (12.9)
		Median	0.944	0.694	0.750	0.950	1.00
		Min; Max	0.453; 1.29	0.462; 0.856	0.682; 0.866	0.811; 1.01	0.913; 1.10
% change from baseline		Mean (SD)	-11.8 (28.9)	-33.6 (13.8)	-24.4 (6.69)	-7.08 (8.64)	0.420 (12.9)
		Median	-5.61	-30.6	-25	-5.03	0.420
		Min; Max	-54.7; 28.9	-53.8; 14.4	-31.8; -13.4	-18.9; 0.610	-8.7; 9.53
LDL-Cholesterol Concentration	Day 22	Mean (SD)	109 (53.4)	88.5 (17.6)	113 (10.5)	123 (17.6)	139 (10.6)
		Geo-mean (CV%)	97.8 (56.5)	87.2 (18.1)	113 (9.5)	112 (14.3)	138 (7.7)
		Median	107	84.0	116	121	139
		Min; Max	53.0; 188	72.0; 123	96.0; 127	105; 145	131; 146
Ratio from baseline (%)		Mean (SD)	0.922 (0.301)	0.841 (0.219)	0.806 (0.0887)	0.947 (0.0526)	1.01 (0.00954)
		Geo-mean (CV%)	0.873 (39.1)	0.817 (27.8)	0.801 (12.1)	0.946 (5.5)	1.01 (0.9)
		Median	1.02	0.821	0.832	0.936	1.01
		Min; Max	0.480; 1.21	0.532; 1.13	0.631; 0.869	0.899; 1.01	1.01; 1.02
% change from baseline		Mean (SD)	-7.85 (30.1)	-15.9 (21.9)	19.4 (8.87)	-5.34 (5.26)	1.19 (0.954)
		Median	2.17	-17.9	-16.8	-6.38	1.19
		Min; Max	-52; 21.0	-46; 13.2	-36.9; -13.1	-10.1; 1.50	0.512; 1.86
LDL-Cholesterol Concentration	Day 29	Mean (SD)	120 (44.5)	90.2 (13.8)	115 (16.9)	120 (15.9)	132 (21.2)
		Geo-mean (CV%)	112 (44.0)	89.3 (15.3)	114 (15.3)	120 (13.9)	131 (16.2)
		Median	130	87.5	115	129	132
		Min; Max	62.0; 172	76.0; 109	88.0; 139	102; 130	117; 147
Ratio from baseline (%)		Mean (SD)	1.04 (0.300)	0.858 (0.201)	0.816 (0.0811)	0.971 (0.181)	0.962 (0.0904)

		Geo-mean (CV%)	1.00 (33.8)	0.836 (26.4)	0.812 (10.3)	0.960 (18.5)	0.960 (9.4)
		Median	1.10	0.888	0.833	0.933	0.962
		Min; Max	0.562; 1.41	0.532; 1.08	0.690; 0.910	0.811; 1.17	0.898; 1.03
% change from baseline		Mean (SD)	4.40 (30.0)	-14.2 (20.1)	-18.4 (8.11)	-2.94 (18.1)	-3.84 (9.04)
		Median	9.80	-11.2	-16.7	-6.71	-3.84
		Min; Max	-43.8; 41.4	-46.8; 7.92	-31; -9.05	-18.9; 16.8	-10.2; 2.56
LDL-Cholesterol Concentration	Day 43	Mean (SD)	127 (59.4)	95.7 (26.8)	117 (29.4)	118 (14.4)	134 (36.1)
		Geo-mean (CV%)	114 (56.9)	92.3 (30.6)	114 (25.7)	117 (12.3)	131 (27.9)
		Median	130	97.0	122	117	134
		Min; Max	53.0; 209	59.0; 126	84.0; 165	104; 133	108; 159
Ratio from baseline (%)		Mean (SD)	1.09 (0.396)	0.893 (0.248)	0.822 (0.128)	0.930 (0.224)	0.969 (0.198)
		Geo-mean (CV%)	1.02 (45.4)	0.864 (28.3)	0.813 (16.3)	0.909 (25.5)	0.959 (20.8)
		Median	1.18	0.834	0.820	25.5	20.8
		Min; Max	0.480; 1.53	0.627; 1.21	0.624; 0.967	0.935	0.969
% change from baseline		Mean (SD)	9.42 (39.6)	-10.7 (24.8)	-17.8 (12.8)	-7.01 (22.4)	-3.1 (19.8)
		Median	17.7	-16.6	-18	-6.45	-3.1
		Min; Max	-52; 52.9	-37.3; 20.6	-37.6; -3.32	-34.6; 19.5	-17.1; 10.9
LDL-Cholesterol Concentration	Day 57	Mean (SD)	127 (70.0)	106 (23.2)	120 (17.8)	132 (23.3)	145
		Geo-mean (CV%)	110 (70.1)	103 (23.0)	118 (15.7)	130 (17.5)	-
		Median	128	109	120	127	145
		Min; Max	41.0; 237	78.0; 128	90.0; 145	113; 161	145; 145
Ratio from baseline (%)		Mean (SD)	1.09 (0.483)	0.982 (0.187)	0.858 (0.165)	1.04 (0.304)	1.11
		Geo-mean (CV%)	0.977 (59.6)	0.967 (19.6)	0.843 (21.1)	1.01 (29.7)	-
		Median	1.08	0.976	0.884	1.01	1.11
		Min; Max	0.372; 1.65	0.752; 1.21	0.586; 1.06	0.711; 1.45	1.11; 1.11
% change from baseline		Mean (SD)	8.91 (48.3)	-1.78 (18.7)	-14.2 (16.5)	4.35 (30.4)	11.3
		Median	8.25	-2.35	-11.6	0.857	11.3

		Min; Max	-62.8; 65.4	-24.8; 20.6	-41.4; 6.36	-28.9; 44. 6	11.3; 11.3
LDL-Cholesterol Concentration	Day 71	Mean (SD)	131 (53.4)	95.2 (16.7)	116 (29.8)	139 (25.4)	142 (28.3)
		Geo-mean (CV%)	121 (47.4)	93.8 (19.1)	114 (24.0)	137 (18.9)	141 (20.3)
		Median	137	100	104	140	142
		Min; Max	62.0; 208	68.0; 113	88.0; 169	108; 169	122; 162
Ratio from baseline (%)		Mean (SD)	1.14 (0.384)	0.900 (0.204)	0.812 (0.0883)	1.07 (0.143)	0.03 (0.137)
		Geo-mean (CV%)	1.08 (39.2)	0.878 (25.3)	0.808 (10.4)	1.07 (13.5)	1.03 (13.4)
		Median	1.14	1.01	0.780	1.09	1.03
		Min; Max	0.562; 1.69	0.620; 1.06	0.743; 0.976	0.918; 1.20	0.936; 1.13
% change from baseline		Mean (SD)	14.0 (38.4)	-10 (20.4)	-18.8 (8.83)	7.42 (14.3)	3.31 (13.7)
		Median	13.9	1.23	-22	8.76	3.31
		Min; Max	-43.8; 68.8	-38; 5.94	-25.7; -2.44	-8.18; 20.4	-6.39; 13.0
LDL-Cholesterol Concentration	EOS	Mean (SD)	151 (61.9)	106 (28.5)	124 (17.7)	119 (19.1)	124 (19.1)
		Geo-mean (CV%)	138 (52.0)	103 (26.2)	122 (14.5)	118 (15.9)	123 (15.6)
		Median	169	92.0	122	115	124
		Min; Max	71.0; 210	77.0; 144	102; 145	102; 143	110; 137
Ratio from baseline (%)		Mean (SD)	1.31 (0.455)	1.01 (0.319)	0.878 (0.114)	0.932 (0.206)	0.900 (0.0791)
		Geo-mean (CV%)	1.23 (41.4)	0.964 (34.9)	0.872 (13.1)	0.913 (24.8)	0.898 (8.80)
		Median	1.37	1.02	0.863	0.983	0.900
		Min; Max	0.644; 1.86	0.582; 1.37	0.720; 1.04	0.642; 1.12	0.844; 0.956
% change from baseline		Mean (SD)	30.8 (45.5)	0.952 (31.9)	-12.2 (11.4)	-6.77 (20.6)	-10 (7.91)
		Median	37.0	1.72	-13.7	-1.75	-10
		Min; Max	-35.6; 85.9	-41.8; 37.3	-28; 4.16	-35.8; 12.3	-15.6; -4.42

a 300 mg HV: n=6 on Day 5, 22, 29, 57, 71, EOS

b Placebo HV: n=1 on Day 57

c Mean baseline values were calculated as the average of the concentrations measured at screening, baseline, and pre-dose on Day 1

Summary statistics of values, ratio and percent change from baseline for PCSK9 (ng/mL) by time profile (PD analysis set)

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
PCSK9 Concentration	Screening (Day -7)	Mean (SD)	183 (41.2)	221 (86.8)	116 (24.0)	211 (45.3)	107 (20.1)
		Geo-mean (CV%)	179 (23.7)	210 (34.3)	114 (20.2)	207 (22.7)	106 (19.1)
		Median	186	203	111	216	107
		Min; Max	125; 240	152; 391	83.2; 162	155; 258	92.6; 121
PCSK9 Concentration	Baseline	Mean (SD)	176 (43.5)	206 (43.5)	164 (61.7)	228 (56.8)	112 (12.7)
		Geo-mean (CV%)	172 (23.4)	202 (22.7)	154 (38.0)	222 (26.2)	112 (11.4)
		Median	169	219	145	227	112
		Min; Max	133; 254	149; 247	106; 258	159; 298	103; 121
PCSK9 Concentration	Day 1 (0 h)	Mean (SD)	175 (30.5)	229 (60.6)	114 (36.5)	224 (64.0)	99.4 (33.4)
		Geo-mean (CV%)	173 (17.3)	222 (27.9)	109 (36.2)	239 (24.7)	96.6 (35.3)
		Median	177	230	105	222	99.4
		Min; Max	140;223	151; 314	58.2; 159	198; 336	75.8; 123
Mean Baseline PCSK9 Concentration[c]	-	Mean (SD)	178 (24.6)	219 (43.8)	131 (34.3)	228 (46.8)	106 (22.1)
		Geo-mean (CV%)	177 (13.9)	215 (20.0)	128 (24.3)	224 (19.1)	105 (21.2)
		Median	177	219	117	208	106
		Min; Max	145; 215	172; 285	104; 192	197; 297	90.5; 122
PCSK9 Concentration	Day 1 (6 h)	Mean (SD)	152 (23.2)	204 (56.1)	135 (60.6)	200 (44.2)	89.0 (21.2)
		Geo-mean (CV%)	150 (15.9)	197 (30.7)	126 (37.9)	196 (22.3)	87.7 (24.4)
		Median	156	219	114	195	89.0
		Min; Max	121; 175	122; 278	88.9; 265	155; 254	74.0; 104
Ratio from baseline (%)		Mean (SD)	0.861 (0.150)	0.924 (0.143)	1.01 (0.209)	0.879 (0.110)	0.836 (0.0260)
		Geo-mean (CV%)	0.850 (18.1)	0.914 (15.8)	0.987 (20.7)	0.874 (12.1)	0.836 (3.1)
		Median	0.869	0.917	1.00	0.846	0.836
		Min; Max	0.629; 1.09	0.709; 1.14	0.718; 1.38	0.785; 1.04	0.818; 0.855
% change from baseline		Mean (SD)	-13.9 (15.0)	-7.95 (14.3)	0.550 (20.9)	-12.1 (11.0)	-16.4 (2.60)

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
		Median	-13.1	-8.27	0.286	-15.4	-16.4
		Min; Max	-37.1; 8.70	-29.1; 14.4	-28.2; 38.0	-21.5; 3.85	-18.2; -14.5
PCSK9 Concentration	Day 1 (12 h)	Mean (SD)	221 (24.9)	282 (77.9)	187 (64.0)	237 (44.5)	86.2 (6.79)
		Geo-mean (CV%)	219 (11.6)	273 (26.6)	179 (33.3)	234 (18.3)	86.1 (7.9)
		Median	225	255	182	227	86.2
		Min; Max	188; 248	213; 409	110; 313	196; 297	81.4; 91.0
Ratio from baseline (%)		Mean (SD)	1.26 (0.199)	1.30 (0.308)	1.43 (0.333)	1.05 (0.124)	0.824 (0.107)
		Geo-mean (CV%)	1.24 (16.5)	1.27 (24.9)	1.40 (25.6)	1.04 (11.4)	0.820 (13.1)
		Median	1.32	1.34	1.41	1.01	0.824
		Min; Max	1.01; 1.51	0.906; 1.71	0.889; 1.83	0.944; 1.23	0.748; 0.900
% change from baseline		Mean (SD)	25.6 (19.9)	30.3 (30.8)	43.4 (33.3)	4.71 (12.4)	-17.6 (10.7)
		Median	32.1	33.7	40.6	0.905	-17.6
		Min; Max	0.867; 50.9	-9.42; 71.1	-11.1; 83.0	-5.62; 22.6	-25.2; -10
PCSK9 Concentration	Day 2	Mean (SD)	181; 50.5	296 (83.4)	177 (69.7)	218 (47.9)	89.6 (24.6)
		Geo-mean (CV%)	176 (24.9)	285 (32.7)	167 (36.8)	87.9 (21.1)	87.9 (28.4)
		Median	167	329	162	202	89.6
		Min; Max	143; 279	174; 370	105; 317	183; 285	72.2; 107
Ratio from baseline (%)		Mean (SD)	1.01 (0.216)	1.35 (0.306)	1.33 (0.271)	0.957 (0.0744)	0.839 (0.0575)
		Geo-mean (CV%)	0.996 (21.2)	1.32 (22.5)	1.31 (22.8)	0.955 (7.6)	0.838 (6.9)
		Median	0.940	1.30	1.46	0.943	0.839
		Min; Max	0.759; 1.30	1.01; 1.83	0.849; 1.65	0.885; 1.06	0.798; 0.879
% change from baseline		Mean (SD)	1.45 (21.6)	35.1 (30.6)	33.4 (27.1)	-4.25 (7.44)	-16.1 (5.75)
		Median	-6.01	30.1	45.7	-5.71	-16.1
		Min; Max	-24.1; 29.8	1.16; 82.6	-15.1; 65.1	-11.5; 5.94	-20.2; -12.1
PCSK9	Day 3	Mean (SD)	195 (55.0)	332 (66.5)	203 (54.2)	231 (71.1)	101 (24.0)

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
Concentration		Geo-mean (CV%)	190 (24.7)	327 (21.0)	197 (26.6)	223 (28.2)	99.6 (24.4)
		Median	176	340	206	201	101
		Min; Max	159; 304	243; 402	147; 296	185; 336	84.0; 118
Ratio from baseline (%)		Mean (SD)	1.09 (0.185)	1.53 (0.242)	1.57 (0.286)	0.999 (0.0945)	0.949 (0.0292)
		Geo-mean (CV%)	1.08 (16.8)	1.52 (15.2)	1.54 (18.2)	0.996 (9.2)	0.949 (3.1)
		Median	1.06	1.49	1.51	0.972	0.949
		Min; Max	0.837; 1.41	1.26; 1.96	1.19; 2.00	0.923; 1.13	0.929; 0.970
% change from baseline		Mean (SD)	8.86 (18.5)	53.4 (24.2)	56.6 (28.6)	-0.0739 (9.45)	-5.08 (2.92)
		Median	6.4	49.3	51.2	-2.8	-5.08
		Min; Max	-16.3; 41.4	25.9; 96.2	18.8; 99.7	-7.69; 13.0	-7.15; -3.01
PCSK9 Concentration	Day 4	Mean (SD)	229 (55.4)	359 (113)	344 (127)	239 (89.2)	137 (37.5)
		Geo-mean (CV%)	224 (22.9)	345 (30.8)	326 (35.7)	228 (36.3)	134 (28.4)
		Median	211	344	295	215	137
		Min; Max	180; 326	230; 559	204; 575	163; 363	110; 163
Ratio from baseline (%)		Mean (SD)	1.28 (0.201)	1.68 (0.591)	2.60 (0.538)	1.03 (0.196)	1.28 (0.0875)
		Geo-mean (CV%)	1.27 (16.6)	1.61 (31.5)	2.55 (20.9)	1.01 (19.5)	1.28 (6.9)
		Median	1.34	1.46	2.38	1.03	1.28
		Min; Max	0.972; 1.52	1.20; 2.80	1.88; 3.45	0.826; 1.22	1.22; 1.34
% change from baseline		Mean (SD)	28.1 (20.1)	67.6 (59.1)	160 (53.8)	2.9 (19.6)	27.8 (8.75)
		Median	33.5	45.6	138	3.46	27.8
		Min; Max	-2.77; 51.6	19.7; 180	87.6; 245	-17.4; 22.1	21.6; 34.0
PCSK9 Concentration	Day 5	Mean (SD)	240 (84.4)	392 (105)	352 (172)	231 (41.7)	125 (13.4)
		Geo-mean (CV%)	228 (33.9)	381 (26.5)	317 (53.8)	228 (18.3)	124 (10.8)
		Median	198	383	334	227	125
		Min; Max	165; 366	266; 570	176; 625	194; 275	115; 134
Ratio from baseline (%)		Mean (SD)	1.38 (0.600)	1.81 (0.406)	2.64 (1.06)	228 (46.8)	106 (22.1)

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
		Geo-mean (CV%)	1.29 (38.9)	1.81 (22.7)	2.47 (42.3)	1.01 (18.7)	1.18 (32.6)
		Median	1.16	1.77	2.57	208	1.06
		Min; Max	0.858; 2.52	1.37; 2.38	1.56; 4.28	197; 297	90.5; 122
% change from baseline		Mean (SD)	38.0 (60.0)	80.8 (40.6)	164 (106)	2.85 (20.3)	21.3 (37.9)
		Median	15.9	77.3	157	-3.63	21.3
		Min; Max	-14.2; 152	36.7; 138	56.0; 328	-13.6; 32.2	-5.48; 48.1
PCSK9 Concentration	Day 6	Mean (SD)	240 (96.5)	383 (142)	300 (108)	215 (62.9)	159 (7.07)
		Geo-mean (CV%)	225 (41.5)	360 (40.0)	283 (39.5)	208 (31.2)	159 (4.5)
		Median	212	387	249	214	159
		Min; Max	147; 377	210; 609	155; 440	140; 294	154; 164
Ratio from baseline (%)		Mean (SD)	1.38 (0.669)	1.75 (0.562)	2.27 (0.532)	0.938 (0.154)	1.53 (0.251)
		Geo-mean (CV%)	1.27 (45.7)	1.68 (34.5)	2.21 (26.3)	0.928 (18.1)	1.51 (16.6)
		Median	1.21	1.79	2.31	1.00	1.53
		Min; Max	0.853; 2.60	1.06; 2.53	1.33; 3.12	0.709; 1.04	1.35; 1.70
% change from baseline		Mean (SD)	38.5 (66.9)	75.4 (56.2)	127 (53.2)	-618 (15.4)	52.5 (25.1)
		Median	20.7	78.6	131	0.242	52.5
		Min; Max	-14.7; 160	6.37; 153	32.9; 212	-29.1; 3.85	34.8; 70.2
PCSK9 Concentration	Day 8	Mean (SD)	224 (63.1)	427 9124)	275 (85.2)	235 (58.2)	140 (9.19)
		Geo-mean (CV%)	217 (29.7)	424 (26.2)	263 (34.5)	230 (23.9)	139 (6.6)
		Median	214	386	295	221	140
		Min; Max	136; 322	343; 662	161; 371	180; 317	133; 146
Ratio from baseline (%)		Mean (SD)	1.28 (0.367)	2.02 (0.493)	2.13 (0.635)	1.03 (0.114)	1.34 (0.191)
		Geo-mean (CV%)	1.23 (32.3)	1.97 (24.4)	2.06 (29.2)	1.02 (11.7)	1.33 (14.4)
		Median	1.24	1.94	2.19	1.06	1.34
		Min; Max	0.707; 1.81	1.43; 2.81	1.38; 3.32	0.867; 1.14	1.20; 1.47
% change from baseline		Mean (SD)	27.5 (36.7)	102 (49.3)	113 (63.5)	2.90 (11.4)	33.5 (19.1)
		Median	24.1	93.9	119	5.71	33.5
		Min; Max	-29.3; 80.7	42.5; 181	38.0; 232	-13.3; 13.5	20.0; 47.0

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
PCSK9 Concentration	Day 11	Mean (SD)	239 (58.7)	442 (140)	307 (147)	252 (62.6)	136 (59.5)
		Geo-mean (CV%)	231 (30.9)	425 (29.4)	279 (49.2)	246 (25.1)	129 (47.7)
		Median	254	376	266	245	136
		Min; Max	128; 293	332; 689	164; 523	184; 334	93.8; 178
Ratio from baseline (%)		Mean (SD)	1.37 (0.397)	2.04 (0.581)	2.28 (0.693)	1.10 (0.126)	1.25 (0.301)
		Geo-mean (CV%)	1.31 (36.9)	1.98 (28.1)	2.18 (33.5)	1.10 (11.8)	1.23 (24.7)
		Median	1.47	1.92	2.57	1.12	1.25
		Min; Max	0.666; 1.72	1.39; 2.99	1.33; 3.14	0.932; 1.24	1.04; 1.46
% change from baseline		Mean (SD)	37.2 (39.7)	104 (58.1)	128 (69.3)	10.2 (12.6)	25.0 (30.1)
		Median	46.7	92.0	157	12.0	25.0
		Min; Max	-33.4; 71.7	39.5; 199	32.5; 214	-6.76; 23.6	3.86; 46.3
PCSK9 Concentration	Day 15	Mean (SD)	217 (51.5)	382 (142)	272 (43.9)	252 (31.8)	141 (2.83)
		Geo-mean (CV%)	213 (21.2)	362 (36.8)	269 (15.5)	250 (12.3)	141 (2.0)
		Median	193	339	257	244	141
		Min; Max	185; 317	226; 625	235; 352	223; 296	139; 143
Ratio from baseline (%)		Mean (SD)	1.22 (0.209)	1.75 (0.501)	2.13 (0.386)	1.12 (0.101)	1.36 (0.255)
		Geo-mean (CV%)	1.20 (17.3)	1.68 (29.9)	2.10 (18.7)	1.11 (9.2)	1.34 (19.1)
		Median	1.21	1.70	2.11	1.13	1.36
		Min; Max	1.01; 1.47	1.28; 2.31	1.53; 2.72	0.996; 1.21	1.19; 1.54
% change from baseline		Mean (SD)	22.0 (20.9)	74.5 (50.1)	113 (38.6)	11.8 (10.1)	35.6 (25.5)
		Median	20.5	70.4	111	13.5	35.6
		Min; Max	0.867; 47.4	28.0; 131	53.1; 172	-0.448; 20.7	17.5; 53.6
PCSK9 Concentration	Day 22	Mean (SD)	233 (51.6)	404 (157)	250 (76.7)	205 (31.8)	127 (49.5)
		Geo-mean (CV%)	229 (21.8)	380 (40.1)	241 (31.3)	203 (15.1)	122 (41.7)
		Median	229	370	237	199	127
		Min; Max	171; 321	241; 634	163; 364	174; 249	92.0; 162
Ratio from baseline (%)		Mean (SD)	1.32 (0.290)	1.87 (0.713)	1.89 (0.595)	0.909 (0.0937)	1.17 (0.222)

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
		Geo-mean (CV%)	1.30 (22.4)	1.77 (39.0)	1.82 (30.9)	0.906 (10.1)	1.16 (19.2)
		Median	1.33	1.81	1.79	0.883	1.17
		Min; Max	1.00; 1.74	1.12; 3.06	1.32; 2.88	0.837; 1.03	1.02; 1.33
% change from baseline		Mean (SD)	32.2 (29.0)	87.3 (71.3)	88.8 (59.5)	-9.07 (9.37)	17.4 (22.2)
		Median	33.4	81.4	79.4	-11.7	17.4
		Min; Max	0.00; 74.5	12.1; 206	31.7; 188	-16..3; 3.38	1.69; 33.2
PCSK9 Concentration	Day 29	Mean (SD)	203 (29.9)	350 (107)	260 (102)	176 (39.5)	136 (66.8)
		Geo-mean (CV%)	201 (15.3)	336 (32.8)	245 (39.5)	173 (22.4)	127 (54.9)
		Median	209	333	232	169	136
		Min; Max	159; 233	203; 505	139; 443	141; 219	88.6; 183
Ratio from baseline (%)		Mean (SD)	1.15 (0.171)	1.62 (0.486)	1.96 (0.663)	0.867 (0.221)	1.24 (0.371)
		Geo-mean (CV%)	1.14 (15.1)	1.56 (29.0)	1.85 (39.6)	0.849 (25.3)	1.21 (31.1)
		Median	1.17	1.54	2.12	0.831	1.24
		Min; Max	0.930; 1.39	1.18; 2.45	1.12; 2.66	0.679; 1.11	0.979; 1.50
% change from baseline		Mean (SD)	15.2 (17.1)	61.7 (48.6)	95.5 (66.3)	-13.3 (22.1)	24.2 (37.1)
		Median	16.6	53.5	112	-18.8	24.2
		Min; Max	-7.02; 38.5	18.0; 145	12.3; 166	-32.1; 11.0	-2.06; 50.4
PCSK9 Concentration	Day 43	Mean (SD)	210 (31.9)	351 (107)	215 (23.9)	190 (48.3)	79.7 (4.45)
		Geo-mean (CV%)	208 (15.3)	340 (28.1)	214 (11.2)	185 (27.2)	79.6 (5.6)
		Median	215	331	218	192	79.7
		Min; Max	172; 259	264; 551	183; 244	130; 246	76.5; 82.8
Ratio from baseline (%)		Mean (SD)	1.21 (0.314)	1.68 (0.726)	1.71 (0.370)	0.837 (0.153)	0.772 (0.203)
		Geo-mean (CV%)	1.18 (24.2)	1.58 (36.9)	1.67 (22.9)	0.825 (19.8)	0.759 (27.0)
		Median	1.13	1.51	1.70	0.872	0.772
		Min; Max	0.925; 1.79	1.11; 3.12	1.14; 2.24	0.626; 0.976	0.629; 0.915
% change from baseline		Mean (SD)	20.8 (31.4)	67.8 (72.6)	70.9 (37.0)	-16.3 (15.3)	-22.8 (20.3)

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
		Median	13.4	51.3	69.7	-12.8	-22.8
		Min; Max	-7.45; 78.6	10.9; 212	13.5; 124	-37.4; -2.4	-37.1; -8.47
PCSK9 Concentration	Day 57	Mean (SD)	183 (40.5)	290 (65.7)	261 (135)	205 (24.0)	70.8
		Geo-mean (CV%)	179 (23.1)	285 (21.8)	237 (49.3)	204 (12.4)	-
		Median	187	262	185	214	70.8
		Min; Max	137; 233	228; 389	167; 477	170; 223	70.8; 70.8
Ratio from baseline (%)		Mean (SD)	1.04 (0.248)	1.39 (0.474)	1.84 (0.537)	0.940 (0.250)	0.783
		Geo-mean (CV%)	1.02 (25.4)	1.32 (33.8)	1.79 (26.1)	0.910 (32.1)	-
		Median	1.07	1.36	1.61	1.03	0.783
		Min; Max	0.712; 1.36	0.912; 2.20	1.43; 2.86	0.572; 1.13	0.783; 0.783
% change from baseline		Mean (SD)	4.26 (24.8)	38.6 (47.4)	84.0 (53.7)	-5.97 (25.0)	-21.7
		Median	7.37	35.7	60.7	2.97	-21.7
		Min; Max	-28.8; 36.0	-8.77; 120	43.1; 186	-42.8; 13.0	-21.7; -21.7
PCSK9 Concentration	Day 71	Mean (SD)	204 (73.4)	302 (135)	200 (48.6)	179 (31.1)	106 (48.9)
		Geo-mean (CV%)	193 (36.3)	280 (43.6)	195 (24.2)	177 (18.4)	101 (50.5)
		Median	175	270	187	186	106
		Min; Max	123; 307	170; 541	143; 274	139; 204	71.9; 141
Ratio from baseline (%)		Mean (SD)	1.14 (0.344)	1.44 (0.821)	1.54 (0.472)	0.821 (0.242)	0.977 (0.257)
		Geo-mean (CV%)	1.09 (31.1)	1.30 (48.4)	1.47 (33.9)	0.787 (36.4)	0.960 (27.2)
		Median	1.12	1.24	1.59	0.917	0.977
		Min; Max	0.719; 1.67	0.853; 3.07	0.880; 2.22	0.467; 0.981	0.795; 1.16
% change from baseline		Mean (SD)	13.8 (34.4)	44.2 (82.1)	53.8 (47.2)	-17.9 (24.2)	-2.32 (25.7)
		Median	12.1	24.0	59.3	-8.3	-2.32
		Min; Max	-28.1; 67.5	-14.7; 207	-12; 122	-53.3; -1.92	-20.5; 15.9
PCSK9	EOS	Mean (SD)	202 (44.1)	296 (112)	166 (36.5)	216 (24.7)	144 (45.3)

	Day	Statistic	Statin Treated Patients: 50 mg LGT209	Statin Treated Patients: 300 mg LGT209	Healthy volunteers 300 mg LGT209	Statin Treated Patients Placebo	Healthy volunteers Placebo
Concentration		Geo-mean (CV%)	197 (24.8)	279 (37.4)	162 (23.4)	215 (11.1)	140 (32.8)
		Median	210	298	170	208	144
		Min; Max	127; 246	186; 493	116; 207	196; 251	112; 176
Ratio from baseline (%)		Mean (SD)	1.13 (0.191)	1.40 (0.691)	1.26 (0.335)	0.973 (0.200)	1.43 (0.725)
		Geo-mean (CV%)	1.12 (18.8)	1.30 (40.5)	1.22 (25.2)	0.957 (21.6)	1.34 (56.8)
		Median	1.15	1.17	1.11	0.982	1.43
		Min; Max	0.789; 1.34	0.933; 2.79	0.938; 1.83	0.720; 1.21	0.921; 1.95
% change from baseline		Mean (SD)	13.2 (19.1)	40.0 (69.1)	25.7 (33.5)	-2.68 (20.0)	43.3 (72.5)
		Median	15.4	16.7	10.6	-1.78	43.3
		Min; Max	-21.1; 34.2	-6.69; 179	-6.25; 83.0	-28; 20.9	-7.95; 94.5

a 300 mg HV: n=6 on Day 5, 22, 29, 57, 71, EOS

b Placebo HV: n=1 on Day 57

c Mean baseline values were calculated as the average of the concentrations measured at screening, baseline, and pre-dose on Day 1

Secondary Outcome Result(s)

Summary statistics of plasma atorvastatin concentrations (ng/mL) (PK Analysis Set)

Day / Timepoint (hours)	Statistic	Statin Treated Patients: 300 mg LGT209 (n=2)
Day -7 (0 h)	Mean (SD)	0.00
	Median	-
	Min; Max	-
Day -5 (0 h)	Mean (SD)	1.30 (0.028)
	CV% (mean)	2.2
	Median	1.30
	Min; Max	1.28; 1.32
Day -3 (0 h)	Mean (SD)	1.00 (0.066)
	CV% (mean)	6.60
	Median	1.00
	Min; Max	0.957; 1.05
Day -1 (0 h)	Mean (SD)	1.23 (0.477)
	CV% (mean)	38.7
	Median	1.23

	Min; Max	0.896; 1.57
Day -1 (1 h)	Mean (SD)	27.7 (17.9)
	CV% (mean)	34.7
	Median	27.7
	Min; Max	15.0; 40.3
Day 1 (0 h)	Mean (SD)	1.15 (0.305)
	CV% (mean)	26.4
	Median	1.15
	Min; Max	0.939; 1.37
Day 3 (0 h)	Mean (SD)	1.20 (0.219)
	CV% (mean)	18.3
	Median	1.20
	Min; Max	1.04; 1.35
Day 5 (0 h)	Mean (SD)	0.940 (0.0742)
	CV% (mean)	7.90
	Median	0.940
	Min; Max	0.887; 0.992
Day 8 (0 h)	Mean (SD)	0.545 (0.771)
	CV% (mean)	141
	Median	0.545
	Min; Max	0.00; 1.09
Day 8 (1 h)	Mean (SD)	20.4 (4.45)
	CV% (mean)	21.9
	Median	20.4
	Min; Max	17.2; 23.5
Day 11 (0 h)	Mean (SD)	0.660 (0.933)
	CV% (mean)	141
	Median	0.660
	Min; Max	0.00; 1.32
Day 15 (0 h)	Mean (SD)	0.785 (1.11)
	CV% (mean)	141
	Median	0.785
	Min; Max	0.00; 1.57

Summary statistics of plasma simvastatin concentrations (ng/mL) (PK Analysis set)

Day / Timepoint (hours)	**Statistic**	**Statin Treated Patients: 50 mg LGT209 (n=8)**	**Statin Treated Patients: 300 mg LGT209 (n=6)**
Day -7 (0 h)	Mean (SD)	0.478 (0.708)	0.391 (0.305)
	Median	0.266	0.294
	Min; Max	0.00; 2.12	0.124; 0.931
Day -5 (0 h)	Mean (SD)	0.520 (0.425)	0.956 (1.17)
	CV% (mean)	81.7	123
	Median	0.502	0.261
	Min; Max	0.00; 1.22	0.140; 2.71
Day -3 (0 h)	Mean (SD)	0.585 (0.552)	0.637 (0.765)
	CV% (mean)	94.3	120

	Median	0.480	0.178
	Min; Max	0.00; 1.82	0.105; 1.78
Day -1 (0 h)	Mean (SD)	0.434 (0.379)	1.11 (0.978)
	CV% (mean)	87.2	88.0
	Median	0.399	1.08
	Min; Max	0.00; 1.10	0.149; 2.82
Day -1 (1 h)	Mean (SD)	14.3 (10.0)	12.0 (6.56)
	CV% (mean)	70.3	54.8
	Median	11.8	12.9
	Min; Max	0.00; 28.1	1.57; 19.2
Day 1 (0 h)	Mean (SD)	0.603 (0.523)	1.34 (1.36)
	CV% (mean)	86.8	102
	Median	0.429	0.736
	Min; Max	0.00; 1.68	0.293; 3.83
Day 3 (0 h)	Mean (SD)	0.679 (0.435)	1.14 (0.957)
	CV% (mean)	64.1	83.7
	Median	0.691	0.955
	Min; Max	0.00; 1.37	0.211; 2.74
Day 5 (0 h)	Mean (SD)	0.308 (0.186)	1.01 (1.09)
	CV% (mean)	60.4	107
	Median	0.273	0.648
	Min; Max	0.00; 0.644	0.0955; 2.74
Day 8 (0 h)	Mean (SD)	0.158 (0.186)	0.623 (0.723)
	CV% (mean)	117.7	116
	Median	0.0695	0.291
	Min; Max	0.00; 0.455	0.109; 1.99
Day 8 (1 h)	Mean (SD)	12.9 (9.09)	15.1 (13.2)
	CV% (mean)	70.5	87.4
	Median	11.0	10.2
	Min; Max	0.00; 27.4	1.66; 39.1
Day 11 (0 h)	Mean (SD)	1.01 (1.65)	0.691 (0.882)
	CV% (mean)	164	128
	Median	0.224	0.144
	Min; Max	0.00; 4.76	0.00; 2.04
Day 15 (0 h)	Mean (SD)	1.52 (2.43)	1.27 (1.80)
	CV% (mean)	159.6	142
	Median	0.628	0.250
	Min; Max	0.00; 6.91	0.124; 4.50

Safety Results

Incidence of AEs by primary system organ class- n (percent) of subjects (Safety Analysis Set)

	LGT209		
	Patients treated with statins	**Healthy volunteers**	

	50 mg LGT209 N=6 n (%)	300 mg LGT209 N=6 n (%)	Placebo N=4 n (%)	300 mg LGT209 N=7 n (%)	Placebo N=2 n (%)	All subjects N=25 n (%)
Subjects with AE(s)	2 (33.3)	4 (66.7)	3 (75.0)	4 (57.1)	1 (50.0)	14 (56.0)
System organ class						
General disorders and administration site conditions	0 (0.0)	2 (33.3)	3 (75.0)	1 (14.3)	0 (0.0)	6 (24.0)
Infections and infestations	0 (0.0)	2 (33.3)	1 (25.0)	2 (28.6)	0 (0.0)	5 (20.0)
Musculoskeletal and connective tissue disorders	1 (16.7)	3 (50.0)	0 (0.0)	0 (0.0)	1 (50.0)	5 (20.0)
Skin and subcutaneous tissue disorders	2 (33.3)	2 (33.3)	1 (25.0)	0 (0.0)	0 (0.0)	5 (20.0)
Injury, poisoning and procedural complications	2 (33.3)	0 (0.0)	1 (25.0)	0 (0.0)	1 (50.0)	4 (16.0)
Nervous system disorders	0 (0.0)	0 (0.0)	1 (25.0)	2 (28.6)	0 (0.0)	3 (12.0)
Eye disorders	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)
Gastrointestinal disorders	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)
Investigations	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)

Incidence of AEs by preferred term- n (percent) of subjects (Safety Analysis Set)

	LGT209					
	Patients treated with statins			Healthy volunteers		
	50 mg LGT209 N=6 n (%)	300 mg LGT209 N=6 n (%)	Placebo N=4 n (%)	50 mg LGT209 N=6 n (%)	300 mg LGT209 N=6 n (%)	All subjects N=25 n (%)
Subjects with AE(s)	2 (33.3)	4 (66.7)	3 (75.0)	4 (57.1)	1 (50.0)	14 (56.0)
Preferred term						
Back pain	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.0)
Contusion	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	2 (8.0)
Headache	0 (0.0)	0 (0.0)	1 (25.0)	1 (14.3)	0 (0.0)	2 (8.0)
Injection site erythema	0 (0.0)	0 (0.0)	2 (50.0)	0 (0.0)	0 (0.0)	2 (8.0)
Non-cardiac chest pain	0 (0.0)	1 (16.7)	1 (25.0)	0 (0.0)	0 (0.0)	2 (8.0)
Pain in extremity	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (50.0)	2 (8.0)
Urinary tract infection	0 (0.0)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)	2 (8.0)
Abdominal discomfort	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)
Arthropod bite	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)
Blood creatine phosphokinase increased	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)
Bronchitis	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Cervicobrachial syndrome	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)
Conjunctivitis	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)
Dermatitis	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Injection site hemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)
Injection site swelling	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Injection site warmth	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)
Intervertebral disc degeneration	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (4.0)
Ligament sprain	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (4.0)
Muscle spasms	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Nasal congestion	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)
Neck pain	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Otitis externa	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)
Pharyngitis	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Presyncope	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)
Pruritus	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)

	LGT209					
	Patients treated with statins			Healthy volunteers		
	50 mg LGT209 N=6 n (%)	300 mg LGT209 N=6 n (%)	Placebo N=4 n (%)	50 mg LGT209 N=6 n (%)	300 mg LGT209 N=6 n (%)	All subjects N=25 n (%)
Pruritus generalized	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Rash	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Skin mass	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Upper respiratory tract infection	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Urticaria	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Venomous sting	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
Viral pharyngitis	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	1 (4.0)
Viral upper respiratory tract infection	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	0 (0.0)	1 (4.0)

Date of Clinical Trial Report

26 MAR 2013

Date Inclusion on Novartis Clinical Trial Results Database

09 MAY 2013

Date of Latest Update