

Supplemental Table 1. Individual and mean VLDL apoB pool size (PS), fractional clearance (FCR) and production rates (PR) during treatments.

	VLDL					
	PS (mg)	PS (mg)	FCR ^a (pools/day)	FCR ^b (pools/day)	PR (mg/kg/day)	PR (mg/kg/day)
Panel A Subject	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
1	38	53	27.44	14.73	14.51	10.80
2	245	214	5.90	6.94	16.34	16.84
3	295	202	4.72	11.21	15.71	25.02
4	148	163	6.53	5.71	12.34	12.12
5	178	127	8.73	10.98	17.59	15.81
6	167	115	4.53	5.98	10.37	9.71
7	55	44	11.94	9.21	11.71	7.05
8	283	109	4.55	8.01	13.32	9.23
9	165	178	5.67	7.23	10.21	14.08
10	122	107	5.83	8.85	8.13	10.84
11	354	336	4.07	4.10	15.94	15.84
12	255	142	5.10	10.42	14.96	17.02
13	209	124	5.53	6.23	10.97	7.31
14	196	91	4.72	5.31	16.02	8.39
15	309	191	3.78	20.81	11.39	37.55
16	119	90	10.09	19.89	12.03	18.52
17	105	87	7.80	15.86	10.21	17.06
18	174	121	6.30	7.56	12.96	9.83
19	213	241	12.18	7.41	45.11	32.33
20	192	100	7.03	11.17	13.25	10.85
21	199	140	6.24	8.66	12.78	12.48
22	531	438	6.66	4.73	29.96	18.07
23	212	285	20.07	15.37	44.63	44.96
24	384	139	9.02	8.05	34.43	11.85
25	131	61	8.40	28.23	13.30	20.20
26	487	269	6.26	9.67	23.52	20.20
27	210	291	6.20	7.16	18.29	28.94
28	111	115	8.77	13.69	9.55	15.59
29	371	99	5.47	11.15	18.73	10.44

Panel B Subject	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
1	135	155	4.19	5.51	7.54	11.38
2	146	104	12.92	14.17	21.74	17.02
3	164	269	6.36	5.44	9.45	13.68
4	97	154	6.91	7.68	10.29	17.88
5	243	143	4.67	8.76	12.44	13.80
6	160	171	4.98	5.52	11.21	13.33
7	365	218	4.62	12.21	19.50	31.42
8	279	280	6.76	6.96	19.39	20.52
9	117	156	11.10	31.15	24.93	92.67
10	204	189	4.51	6.86	12.43	17.52

Supplemental Table 2. Individual and mean IDL apoB pool size (PS), fractional clearance (FCR) and production rates (PR) during treatments.

	IDL					
	PS (mg)	PS (mg)	FCR ^a (pools/day)	FCR ^b (pools/day)	PR (mg/kg/day)	PR (mg/kg/day)
Panel A Subject	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
1	73	38	2.02	4.50	2.07	2.35
2	108	81	5.76	6.91	7.02	6.34
3	140	92	3.43	6.08	5.41	6.18
4	87	81	5.87	7.25	6.49	7.67
5	130	124	3.17	2.36	4.67	3.30
6	140	79	2.71	3.60	5.18	4.02
7	18	22	10.90	6.75	3.48	2.64
8	150	45	5.34	5.09	8.28	2.43
9	79	55	5.11	7.19	4.41	4.34
10	122	58	5.26	7.12	7.33	4.71
11	184	87	6.25	10.51	12.74	10.54
12	138	78	3.87	5.81	5.72	5.20
13	188	96	4.53	4.30	8.10	3.91
14	119	48	3.74	7.51	7.72	6.32
15	203	134	3.13	4.40	6.22	5.58
16	85	20	4.44	7.53	3.78	1.59
17	68	32	5.47	9.89	4.60	3.87
18	27	3	6.03	5.13	1.93	0.18
19	43	35	3.57	4.45	2.69	2.84
20	7	12	6.85	7.44	0.49	0.87
21	38	28	5.12	13.89	2.01	4.06
22	151	83	2.94	4.33	3.78	3.14
23	134	93	13.74	9.06	19.23	8.64
24	130	23	3.62	8.54	4.67	2.11
25	113	26	4.07	4.81	5.56	1.49
26	100	56	5.12	1.02	3.97	0.44
27	23	46	8.21	6.24	2.70	3.96
28	13	11	7.27	8.38	0.95	0.90
29	23	5	6.63	5.61	1.40	0.28

Panel B Subject	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
1	169	70	2.43	3.91	5.46	3.64
2	106	79	8.79	7.94	10.75	7.21
3	60	126	6.25	5.46	3.40	6.46
4	96	79	3.65	7.13	5.34	8.57
5	171	181	4.28	6.36	8.01	12.65
6	80	80	3.74	3.84	4.20	4.32
7	153	66	2.47	4.06	4.35	3.18
8	123	75	4.86	3.77	6.16	2.98
9	78	72	2.85	6.79	4.31	9.35
10	99	44	2.35	4.51	3.14	2.68

Supplemental Table 3. Individual and mean LDL apoB pool size (PS), fractional clearance (FCR) and production rates (PR) during treatments.

	LDL					
	PS (mg)	PS (mg)	FCR ^a (pools/day)	FCR ^b (pools/day)	PR (mg/kg/day)	PR (mg/kg/day)
Panel A Subject	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
1	2126	1512	0.46	0.53	13.63	10.96
2	2592	2089	0.65	0.65	19.04	15.44
3	2133	1747	0.49	0.78	11.84	15.17
4	2123	1813	0.43	0.51	11.61	12.12
5	2134	1539	0.45	0.56	10.94	9.74
6	1711	1450	0.35	0.46	8.23	9.44
7	816	842	0.62	0.67	8.90	9.93
8	2174	2126	0.59	0.49	13.29	11.04
9	1850	1500	0.45	0.62	9.04	10.18
10	2431	1701	0.36	0.53	9.84	10.25
11	2298	1920	0.40	0.55	10.23	12.13
12	1875	1655	0.69	0.51	14.94	9.78
13	2363	2493	0.56	0.40	12.62	9.56
14	1326	1027	0.48	0.58	10.96	10.38
15	3242	3937	0.34	0.36	10.86	13.49
16	3296	1449	0.43	1.13	14.26	16.98
17	2341	1602	0.36	0.88	10.51	17.38
18	3252	3763	0.35	0.25	13.41	10.17
19	1459	1217	0.38	0.50	9.62	11.12
20	3461	2180	0.36	0.52	12.23	11.02
21	2694	1905	0.36	0.64	9.88	12.48
22	3813	2439	0.35	0.65	11.21	13.73
23	3183	2763	0.23	0.92	7.70	26.17
24	2372	1936	0.54	0.70	12.79	14.38
25	3578	3432	0.29	0.23	12.46	9.43
26	3679	3139	0.45	0.42	12.87	10.24
27	2608	2083	0.46	0.56	16.70	16.04
28	2991	2613	0.33	0.60	9.67	15.52
29	4037	3255	0.45	0.34	16.88	10.48

Panel B Subject	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
1	2545	1940	0.26	0.40	8.65	10.24
2	3080	2631	0.53	0.44	18.84	13.46
3	2494	3017	0.41	0.49	9.27	13.96
4	1526	1462	0.42	0.79	9.72	17.42
5	4265	2962	0.32	0.56	15.07	16.44
6	3724	2430	0.28	0.39	14.60	13.35
7	3492	3158	0.36	0.38	14.40	14.04
8	2960	2626	0.44	0.41	13.38	11.28
9	2435	1550	0.63	0.64	29.56	18.87
10	3050	2534	0.20	0.28	8.08	9.65

Supplemental Table 4: Concentrations of apoB-containing lipoprotein particle subspecies determined by NMR.

	Panel A (N=29)				Panel B (N=10)				All Subjects (N=39)			
	Period 1 (ATV)	Period 2 (MK+ATV)	% change from Period 1 (95% CI)	p-value	Period 1 (PBO)	Period 2 (MK)	% change from Period 1 (95% CI)	p-value	Period 1	Period 2	% change from Period 1 (95% CI)	p-value
VLDL & Chylomicron Particles (total), (nmol/L)	41.66 (53.10)	40.17 (45.13)	-3.59 (-19.24, 15.09)	0.678	52.28 (70.61)	46.10 (45.16)	-11.81 (-34.78, 19.24)	0.404	46.67 (57.88)	43.03 (44.98)	-7.79 (-22.59, 9.83)	0.353
Large VLDL & Chylomicrons Particles*, (nmol/L)	0.80 (1.70)	0.50 (1.80)	-25.46 (-57.25, 41.42)	0.349	2.05 (3.00)	0.75 (1.20)	-61.53 (-85.71, -23.29)	0.014	0.90 (1.90)	0.60 (1.80)	-39.00 (-62.20, -0.00)	0.049
Medium VLDL Particles*, (nmol/L)	11.20 (14.70)	26.10 (17.90)	84.88 (40.66, 157.35)	<.001	15.80 (19.90)	24.15 (28.60)	64.93 (13.48, 336.49)	0.014	13.10 (17.20)	26.10 (20.50)	78.68 (42.73, 138.85)	<.001
Small VLDL Particles*, (nmol/L)	30.40 (22.60)	15.60 (11.80)	-50.04 (-65.43, -33.43)	<.001	39.10 (13.40)	20.85 (15.60)	-48.18 (-75.04, -14.57)	0.027	32.10 (25.10)	17.90 (13.60)	-51.47 (-63.91, -35.08)	<.001
IDL Particles*, (nmol/L)	28.00 (47.00)	3.50 (0.00)	-77.95 (-86.25, -58.89)	<.001	65.00 (48.00)	3.50 (34.50)	-78.82 (-93.51, -20.80)	0.020	32.00 (63.00)	3.50 (0.00)	-78.13 (-85.99, -65.84)	<.001
LDL Particles (total)*, (nmol/L)	980.00 (237.00)	570.00 (229.00)	-44.71 (-52.76, -34.08)	<.001	1417.00 (72.00)	702.50 (635.00)	-43.51 (-60.49, -16.75)	0.010	1109.00 (456.00)	599.00 (393.00)	-44.70 (-52.31, -35.35)	<.001
Large LDL Particles, (nmol/L)	318.00 (53.71)	331.85 (46.43)	4.36 (-13.43, 25.80)	0.647	323.10 (57.38)	366.44 (33.54)	13.41 (-17.49, 55.90)	0.428	320.54 (53.80)	348.71 (43.18)	8.79 (-9.54, 30.83)	0.361
Medium Small LDL Particles*, (nmol/L)	127.00 (77.00)	50.00 (80.00)	-68.70 (-87.66, -47.24)	<.001	215.50 (42.00)	51.50 (129.00)	-70.33 (-95.79, -36.31)	0.010	160.00 (95.00)	50.00 (94.00)	-69.35 (-87.07, -52.29)	<.001
Small LDL Particles (total)*, (nmol/L)	649.00 (317.00)	175.00 (329.00)	-75.02 (-86.89, -60.29)	<.001	986.00 (213.00)	276.50 (692.00)	-75.21 (-94.25, -29.07)	0.010	730.00 (424.00)	175.00 (411.00)	-75.13 (-85.39, -62.74)	<.001
Very Small LDL Particles*, (nmol/L)	522.00 (249.00)	152.00 (266.00)	-81.20 (-94.37, -60.58)	<.001	789.00 (151.00)	225.00 (552.00)	-77.08 (-94.75, -27.27)	0.010	570.00 (338.00)	152.00 (329.00)	-80.00 (-92.70, -63.14)	<.001

Abbreviations: atorvastatin (ATV), anacetrapib (MK), placebo (PBO)

Mixed model analysis performed on log scale for the endpoints that satisfy normality. Geometric Mean (% CV) displayed under Period 1 and Period 2. Geometric Mean Ratio (95% CI) displayed under % Change from baseline.

*Non-parametric method used. Median (IQR) on raw scale displayed under Period 1 and Period 2. Hodges-Lehmann estimate (95% CI) back transformed from log scale displayed under % Change from baseline. p-value from Wilcoxon signed rank test.

Treatment corresponding to Panel A Period 1: 20 mg ATV + PBO to anacetrapib.

Treatment corresponding to Panel A Period 2: 20 mg ATV + 100 mg anacetrapib.

Treatment corresponding to Panel B Period 1: PBO to ATV + PBO to anacetrapib.

Treatment corresponding to Panel B Period 2: PBO to ATV + 100 mg anacetrapib.

Supplemental Table 5. Individual and mean PCSK9 pool size (PS), fractional clearance (FCR) and production rates (PR) during treatments.

	PCSK9					
	PS (mg)	PS (mg)	FCR ^a (pools/day)	FCR ^b (pools/day)	PR (mg/kg/day)	PR (mg/kg/day)
Panel A Subject	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
1	928	1095	3.78	2.55	49.14	39.05
2	986	969	2.09	1.88	23.20	20.84
3	908	833	2.56	2.18	26.87	20.60
4	925	862	1.65	2.09	19.80	23.33
5	1230	1809	2.06	1.84	28.49	37.15
6	785	846	1.58	1.32	17.51	15.44
7	555	581	1.32	2.07	13.05	21.28
8	921	1060	1.30	1.35	12.68	14.97
9	815	904	1.92	1.84	16.78	17.96
10	648	824	1.02	0.83	7.49	7.84
11	656	666	1.69	1.76	12.33	13.53
12	1270	1343	2.27	1.84	33.27	28.27
13	2092	1601	1.77	1.35	34.95	20.51
14	872	972	1.97	1.98	31.15	34.43
15	2236	2356	2.07	1.63	45.53	37.46
16	1068	1445	2.41	3.85	27.32	55.80
17	800	603	2.03	1.74	19.58	13.03
18	1033	1398	2.22	1.40	25.43	23.10
19	610	717	2.16	2.68	22.33	33.40
20	841	946	1.32	1.49	11.14	13.82
21	1297	1249	1.83	1.77	23.90	22.70
22	1228	1186	2.13	1.75	23.16	17.60
23	932	944	2.03	1.83	19.41	18.08
24	684	1000	1.72	1.44	11.74	14.36
25	634	865	1.84	1.62	14.38	16.92
26	839	841	1.70	2.02	11.12	13.17
27	622	635	1.98	2.24	17.26	20.03
28	963	1061	1.85	2.09	17.34	21.84
29	940	791	1.49	1.59	12.81	11.61

Panel B Subject	Period 1	Period 2	Period 1	Period 2	Period 1	Period 2
1	749	909	3.90	2.28	38.82	27.77
2	1202	1426	2.76	2.39	38.33	39.77
3	1113	1053	1.23	2.42	12.69	23.98
4	450	679	1.89	2.67	13.19	27.86
5	1035	1182	1.27	1.95	14.38	25.74
6	864	565	1.56	1.50	19.18	11.97
7	605	504	2.32	2.46	16.34	14.37
8	635	588	1.84	1.92	12.41	11.60
9	669	443	1.17	1.77	14.29	15.13
10	463	313	1.28	1.72	8.33	7.29