

Supplementary Information

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A Drug–Drug Interaction Study Evaluating the Pharmacokinetic Consequences of Obicetrapib Therapy on Atorvastatin or Rosuvastatin Levels in Healthy Volunteers

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Supplemental Table 1. Descriptive statistics for plasma atorvastatin concentrations (ng/mL) – Cohort 1^a

Treatment	Day	Time (h)	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
Atorvastatin (N=42)	-4	0	-	0.000	0.000	-
		0.25	-	0.126	0.303	240.08
		0.5	-	2.951	5.435	184.14
		0.75	-	9.672	15.886	164.24
		1	-	12.414	15.760	126.95
		1.33	9.809	17.665	18.861	106.77
		1.67	12.783	20.319	20.296	99.89
		2	13.634	20.060	18.868	94.06
		2.5	14.647	17.853	12.209	68.39
		3	14.577	17.182	10.880	63.32
		3.5	13.805	16.141	9.810	60.77
		4	12.450	14.456	8.516	58.91
		5	11.807	14.089	9.013	63.97
		6	8.253	9.423	5.046	53.55
		7	5.989	6.766	3.568	52.73
		9	4.196	4.761	2.411	50.63
		12	2.977	3.542	2.308	65.18
		16	1.517	1.789	1.180	65.94
		24	0.677	0.829	0.607	73.24
		36	0.444	0.592	0.560	94.57
		48	-	0.220	0.222	100.95
		72	-	0.035	0.068	194.65
		96	-	0.004	0.025	648.07
		120	-	0.000	0.000	-
Atorvastatin + Obicetrapib (N=40)	12	0	-	0.000	0.000	-
		0.25	-	0.085	0.175	206.54
		0.5	-	1.356	4.650	343.03
		0.75	-	5.544	10.375	187.14

Treatment	Day	Time (h)	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
		1	-	13.051	14.975	114.74
		1.33	11.671	18.902	18.117	95.84
		1.67	15.231	22.243	16.985	76.36
		2	16.663	22.151	14.909	67.31
		2.5	16.143	19.024	11.087	58.28
		3	15.380	17.654	9.757	55.27
		3.5	13.603	15.839	9.889	62.43
		4	12.041	14.028	8.987	64.07
		5	10.967	12.425	6.569	52.87
		6	7.711	8.806	5.842	66.35
		7	5.580	6.105	2.718	44.52
		9	3.624	3.981	1.701	42.73
		12	2.325	2.680	1.727	64.46
		16	1.227	1.382	0.730	52.83
		24	0.463	0.542	0.330	60.97
		36	-	0.382	0.307	80.43
		48	-	0.096	0.104	107.92
		72	-	0.012	0.039	309.15
		96	-	0.000	0.000	-
		120	-	0.000	0.000	-

^aLower limit of quantitation is 0.1 ng/mL. Any concentration below this limit is reported as 0. Geometric mean was not reported if any zero values were present at that timepoint.

Supplemental Table 2. Descriptive statistics for plasma ortho-hydroxy atorvastatin concentrations (ng/mL) – Cohort 1^a

Treatment	Day	Time (h)	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
Atorvastatin (N=42)	-4	0	-	0.000	0.000	-
		0.25	-	0.000	0.000	-
		0.5	-	0.423	0.963	227.84
		0.75	-	3.627	5.961	164.36
		1	-	6.347	8.675	136.68
		1.33	-	9.834	9.402	95.61
		1.67	-	12.294	9.334	75.92
		2	-	13.532	9.607	70.99
		2.5	11.438	14.417	9.252	64.18
		3	13.145	15.370	8.392	54.60
		3.5	13.777	15.671	7.837	50.01
		4	13.943	15.785	7.704	48.80
		5	13.201	14.910	7.169	48.08
		6	9.924	11.186	5.412	48.38
		7	7.968	8.916	4.293	48.15
		9	6.191	6.799	2.977	43.79
		12	4.126	4.757	2.848	59.86
		16	2.119	2.419	1.373	56.74
		24	1.075	1.274	0.871	68.34
		36	0.801	0.957	0.746	77.94
		48	0.318	0.370	0.222	60.03
		72	-	0.108	0.121	112.09
		96	-	0.020	0.060	298.07
		120	-	0.005	0.024	453.60
Atorvastatin + Obicetrapib (N=40)	12	0	-	0.000	0.000	-
		0.25	-	0.000	0.000	-
		0.5	-	0.155	0.807	519.67
		0.75	-	1.440	4.090	284.13

Treatment	Day	Time (h)	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
		1	-	4.981	6.840	137.32
		1.33	-	9.775	9.553	97.73
		1.67	-	13.091	9.688	74.00
		2	10.480	15.218	10.114	66.46
		2.5	12.341	15.224	8.477	55.68
		3	14.584	17.030	9.179	53.90
		3.5	14.816	17.032	9.434	55.39
		4	14.704	16.781	9.036	53.84
		5	14.354	16.314	8.971	54.99
		6	11.379	13.035	8.497	65.19
		7	8.782	9.689	4.520	46.65
		9	6.264	6.843	2.948	43.08
		12	3.983	4.455	2.506	56.26
		16	2.123	2.376	1.287	54.16
		24	0.933	1.085	0.722	66.55
		36	0.695	0.837	0.635	75.91
		48	-	0.247	0.144	58.38
		72	-	0.055	0.079	144.13
		96	-	0.004	0.022	632.46
		120	-	0.000	0.000	-

^aLower limit of quantitation is 0.1 ng/mL. Any concentration below this limit is reported as 0. Geometric mean was not reported if any zero values were present at that timepoint.

Supplemental Table 3. Descriptive statistics for plasma para-hydroxy atorvastatin concentrations (ng/mL) – Cohort 1^a

Treatment	Day	Time (h)	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
Atorvastatin (N=42)	-4	0	-	0.0000	0.0000	-
		0.25	-	0.0000	0.0000	-
		0.5	-	0.0097	0.0239	247.05
		0.75	-	0.0677	0.1297	191.59
		1	-	0.1013	0.1595	157.37
		1.33	-	0.1756	0.2410	137.19
		1.67	-	0.2229	0.2633	118.12
		2	-	0.2598	0.2888	111.16
		2.5	0.2186	0.3139	0.3004	95.70
		3	0.2932	0.3859	0.3151	81.66
		3.5	0.3723	0.4799	0.3805	79.29
		4	0.4357	0.5653	0.4758	84.18
		5	0.5730	0.7692	0.7479	97.24
		6	0.5238	0.6362	0.4250	66.80
		7	0.4842	0.5826	0.3742	64.23
		9	0.4902	0.5620	0.2836	50.46
		12	0.4814	0.5762	0.3534	61.34
		16	0.3267	0.3682	0.1796	48.77
		24	0.2502	0.2962	0.1774	59.90
		36	0.2323	0.2865	0.2053	71.64
		48	0.1259	0.1558	0.1098	70.50
		72	0.0606	0.0762	0.0531	69.76
		96	-	0.0413	0.0325	78.54
		120	-	0.0195	0.0222	113.72
Atorvastatin + Obicetrapib (N=40)	12	0	-	0.0000	0.0000	-
		0.25	-	0.0000	0.0000	-
		0.5	-	0.0038	0.0206	541.05
		0.75	-	0.0302	0.0862	285.03

Treatment	Day	Time (h)	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
		1	-	0.1047	0.1678	160.29
		1.33	-	0.1903	0.2378	124.97
		1.67	-	0.2601	0.2437	93.70
		2	-	0.3093	0.2762	89.32
		2.5	-	0.3480	0.2986	85.79
		3	0.3361	0.4507	0.3760	83.43
		3.5	0.4074	0.5165	0.3700	71.64
		4	0.4782	0.5920	0.3974	67.12
		5	0.6276	0.8057	0.6435	79.87
		6	0.5863	0.7847	0.9652	123.00
		7	0.5566	0.6654	0.4771	71.70
		9	0.5433	0.6177	0.3182	51.52
		12	0.5043	0.5894	0.3777	64.09
		16	0.3699	0.4158	0.2118	50.94
		24	0.2325	0.2683	0.1526	56.86
		36	0.2195	0.2766	0.2350	84.96
		48	0.0969	0.1116	0.0646	57.89
		72	0.0475	0.0556	0.0337	60.54
		96	-	0.0310	0.0268	86.20
		120	-	0.0165	0.0165	99.26

^aLower limit of quantitation is 0.1 ng/mL. Any concentration below this limit is reported as 0. Geometric mean was not reported if any zero values were present at that timepoint.

Supplemental Table 4. Descriptive statistics for plasma rosuvastatin concentrations (ng/mL) – Cohort 2^a

Treatment	Day	Time (h)	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
Rosuvastatin (N=32)	-4	0	-	0.000	0.000	-
		0.5	-	0.832	1.141	137.25
		1	1.655	2.430	2.323	95.61
		1.5	3.213	4.547	4.249	93.46
		2	4.530	6.014	4.948	82.27
		2.5	5.536	7.130	5.204	72.99
		3	6.553	8.113	5.414	66.74
		3.5	7.428	8.880	5.589	62.94
		4	7.861	9.251	5.534	59.82
		4.5	10.441	12.033	6.729	55.92
		5	8.827	9.857	4.722	47.91
		6	6.988	7.870	4.026	51.16
		7	5.611	6.388	3.525	55.17
		9	4.383	5.071	2.881	56.80
		12	2.906	3.508	2.394	68.24
		16	1.766	2.117	1.499	70.83
		24	1.285	1.536	1.051	68.46
		36	0.853	0.983	0.566	57.57
		48	0.520	0.646	0.491	76.01
		72	-	0.309	0.250	81.04
		96	-	0.092	0.120	131.26
		120	-	0.021	0.051	245.39
Rosuvastatin + Obicetrapib (N=31)	12	0	-	0.000	0.000	-
		0.5	-	0.887	1.152	129.80
		1	-	2.226	2.337	105.02
		1.5	2.868	3.932	3.137	79.78
		2	4.580	5.978	4.332	72.46
		2.5	5.667	6.931	4.302	62.06

Treatment	Day	Time (h)	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
		3	6.417	7.883	5.050	64.06
		3.5	6.914	8.294	5.096	61.45
		4	7.572	8.871	5.163	58.19
		4.5	9.846	11.368	6.209	54.62
		5	8.626	9.907	5.482	55.33
		6	6.640	7.623	4.411	57.87
		7	5.411	6.275	4.133	65.87
		9	4.025	4.592	2.647	57.64
		12	2.528	2.957	1.850	62.56
		16	1.547	1.826	1.196	65.47
		24	1.128	1.327	0.825	62.16
		36	0.818	0.976	0.646	66.13
		48	0.453	0.523	0.331	63.24
		72	-	0.253	0.279	110.27
		96	-	0.117	0.215	183.40
		120	-	0.058	0.114	195.67

^aLower limit of quantitation is 0.1 ng/mL. Any concentration below this limit is reported as 0. Geometric mean was not reported if any zero values were present at that timepoint.

Supplemental Table 5. Descriptive statistics for plasma obicetrapib concentrations (ng/mL) – Cohort 1^a

Treatment	Day	Time (h)	N	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
Obicetrapib	1	0	42	-	0	0	-
	10	0	41	232	238	54	22.66
	11	0	41	236	241	51	20.92
	12	0	40	240	244	43	17.47

^aLower limit of quantitation is 0.5 ng/mL. Any concentration below this limit is reported as 0. Geometric mean was not reported if any zero values were present at that timepoint.

Supplemental Table 6. Descriptive statistics for plasma obicetrapib concentrations (ng/mL) – Cohort 2^a

Treatment	Day	Time (h)	N	Geometric Mean	Arithmetic Mean	Standard Deviation	Coefficient of Variation (%)
Obicetrapib	1	0	32	-	0	0	-
	10	0	32	242	248	59	23.76
	11	0	32	248	255	64	25.16
	12	0	32	249	255	57	22.38

^aLower limit of quantitation is 0.5 ng/mL. Any concentration below this limit is reported as 0. Geometric mean was not reported if any zero values were present at that timepoint.