

Supplementary Material

Phase II (NAVIGATE-AD study) Results of LY3202626 Effects on Patients with Mild Alzheimer's Disease Dementia

Supplementary Table 1. LS mean (SE) change from baseline as measured by vMRI

Volume (mm ³)	Placebo	LY3202626 3 mg	LY3202626 12 mg	Pairwise p-values	
				3 mg versus PBO	12 mg versus PBO
Entorhinal cortex, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 2621.2 (768.9)	[N=38] 2668.2 (707.5)	[N=60] 2779.1 (603.5)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -90.4 (18.5)	[N=15] -140.4 (13.1)	[N=12] -134.4 (14.8)	0.038	0.078
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -78.8 (9.3)	[N=38] -115.6 (11.8)	[N=60] -76.9 (9.0)	0.018	0.887
<i>Annualized change***, LS mean (SE)</i>	[N=58] -86.4 (10.6)	[N=38] -124.4 (13.0)	[N=60] -86.6 (10.4)	0.026	0.989
Entorhinal cortex, left					
<i>Baseline, mean (SD)</i>	[N=58] 1330.5 (416.9)	[N=38] 1283.8 (393.7)	[N=60] 1449.5 (381.0)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -49.1 (13.8)	[N=15] -57.3 (9.8)	[N=12] -67.6 (10.9)	0.640	0.307
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -42.0 (56)	[N=38] -53.9 (7.2)	[N=60] -39.1 (5.5)	0.202	0.716
<i>Annualized change***, LS mean (SE)</i>	[N=58] -46.3 (6.3)	[N=38] -58.9 (7.8)	[N=60] -42.7 (6.2)	0.211	0.685
Entorhinal cortex, right					
<i>Baseline, mean (SD)</i>	[N=58] 1290.7 (399.6)	[N=38] 1384.5 (457.4)	[N=60] 1329.6 (330.3)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -39.4 (12.2)	[N=15] -83.7 (8.8)	[N=12] -67.5 (9.9)	0.006	0.089
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -36.9 (5.4)	[N=38] -62.0 (6.9)	[N=60] -37.6 (5.2)	0.006	0.922
<i>Annualized change***, LS mean (SE)</i>	[N=58] -40.1 (6.5)	[N=38] -65.5 (8.0)	[N=60] -43.9 (6.3)	0.015	0.671
Hippocampus, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 6082.7 (1081.7)	[N=38] 6029.6 (1216.8)	[N=60] 6174.0 (1188.4)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -116.9 (36.5)	[N=15] -209.3 (25.2)	[N=12] -197.0 (29.2)	0.047	0.110
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -102.7 (12.9)	[N=38] -157.9 (16.5)	[N=60] -158.3 (12.6)	0.011	0.002
<i>Annualized change***, LS mean (SE)</i>	[N=58] -119.8 (15.5)	[N=38] -169.5 (19.1)	[N=60] -178.9 (15.2)	0.046	0.007
Hippocampus, left					
<i>Baseline, mean (SD)</i>	[N=58] 2985.8 (591.5)	[N=38] 2912.9 (636.4)	[N=60] 3053.7 (626.4)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -60.4 (24.5)	[N=15] -91.0 (16.9)	[N=12] -90.8 (19.3)	0.317	0.355
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -49.1 (7.1)	[N=38] -78.9 (9.1)	[N=60] -75.4 (6.9)	0.013	0.009
<i>Annualized change***, LS mean (SE)</i>	[N=58] -57.9 (8.1)	[N=38] -83.2 (10.0)	[N=60] -87.4 (8.0)	0.053	0.011
Hippocampus, right					
<i>Baseline, mean (SD)</i>	[N=58] 3096.9 (538.5)	[N=38] 3116.7 (640.0)	[N=60] 3120.3 (614.1)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8]	[N=15]	[N=12]		

Volume (mm ³)	Placebo	LY3202626 3 mg	LY3202626 12 mg	Pairwise p-values	
				3 mg versus PBO	12 mg versus PBO
<i>Change at last observation**</i> , LS mean (SE)	-54.3 (18.3) [N=58]	-117.5 (12.8) [N=38]	-108.7 (14.8) [N=60]	0.008	0.033
<i>Annualized change***</i> , LS mean (SE)	-53.9 (7.8) [N=58]	-79.0 (9.9) [N=38]	-82.6 (7.6) [N=60]	0.055	0.009
	-62.3 (9.5)	-86.4 (11.8)	-91.1 (9.3)	0.114	0.032
Inferior parietal lobe, bilateral					
<i>Baseline, mean (SD)</i>	[N=58]	[N=38]	[N=60]		
	19,865 (3619.4)	21,493 (3402.8)	20,364 (2874.5)		
<i>Change at week 52*</i> , LS mean (SE)	[N=8]	[N=15]	[N=12]		
	-324.4 (88.8)	-435.6 (62.8)	-546.3 (69.7)	0.325	0.061
<i>Change at last observation**</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-319.1 (32.7)	-367.8 (41.9)	-438.2 (31.7)	0.375	0.009
<i>Annualized change***</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-378.3 (37.8)	-396.9 (47.0)	-523.2 (36.9)	0.760	0.007
Inferior parietal lobe, left					
<i>Baseline, mean (SD)</i>	[N=58]	[N=38]	[N=60]		
	9088.6 (1752.9)	9543.9 (1573.0)	9240.6 (1558.8)		
<i>Change at week 52*</i> , LS mean (SE)	[N=8]	[N=15]	[N=12]		
	-174.7 (54.5)	-246.3 (38.9)	-278.3 (42.8)	0.305	0.146
<i>Change at last observation**</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-158.2 (16.7)	-174.1 (21.3)	-217.6 (16.2)	0.569	0.011
<i>Annualized change***</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-181.6 (19.1)	-190.3 (23.6)	-253.2 (18.7)	0.776	0.008
Inferior parietal lobe, right					
<i>Baseline, mean (SD)</i>	[N=58]	[N=38]	[N=60]		
	10,776 (2022.8)	11,949 (1995.7)	11,124 (1611.8)		
<i>Change at week 52*</i> , LS mean (SE)	[N=8]	[N=15]	[N=12]		
	-148.2 (48.8)	-190.1 (34.4)	-268.0 (38.5)	0.496	0.068
<i>Change at last observation**</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-160.8 (19.9)	-193.8 (25.5)	-220.7 (19.2)	0.324	0.031
<i>Annualized change***</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-196.0 (23.1)	-207.9 (28.8)	-269.9 (22.4)	0.751	0.023
Isthmuscingulate, bilateral					
<i>Baseline, mean (SD)</i>	[N=58]	[N=38]	[N=60]		
	3799.0 (567.7)	4091.3 (799.9)	4013.1 (641.6)		
<i>Change at week 52*</i> , LS mean (SE)	[N=8]	[N=15]	[N=12]		
	-91.2 (27.6)	-134.5 (20.2)	-96.9 (22.2)	0.224	0.871
<i>Change at last observation**</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-80.6 (9.1)	-106.0 (11.5)	-101.4 (8.7)	0.095	0.100
<i>Annualized change***</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-88.8 (10.8)	-112.0 (13.2)	-121.2 (10.5)	0.179	0.033
Isthmuscingulate, left					
<i>Baseline, mean (SD)</i>	[N=58]	[N=38]	[N=60]		
	1947.7 (314.4)	2082.4 (420.7)	2057.1 (344.1)		
<i>Change at week 52*</i> , LS mean (SE)	[N=8]	[N=15]	[N=12]		
	-53.1 (14.5)	-63.4 (10.5)	-48.1 (11.6)	0.578	0.787
<i>Change at last observation**</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-42.5 (5.6)	-52.1 (7.1)	-51.2 (5.4)	0.306	0.262
<i>Annualized change***</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-45.0 (6.9)	-56.5 (8.5)	-61.8 (6.8)	0.303	0.088
Isthmuscingulate, right					
<i>Baseline, mean (SD)</i>	[N=58]	[N=38]	[N=60]		
	1851.3 (307.1)	2008.9 (444.6)	1956.1 (381.5)		
<i>Change at week 52*</i> , LS mean (SE)	[N=8]	[N=15]	[N=12]		
	-38.2 (15.9)	-71.1 (11.9)	-48.7 (13.1)	0.115	0.615
<i>Change at last observation**</i> , LS mean (SE)	[N=58]	[N=38]	[N=60]		
	-38.6 (5.1)	-53.5 (6.5)	-50.0 (4.9)	0.083	0.110

Volume (mm ³)	Placebo	LY3202626 3 mg	LY3202626 12 mg	Pairwise p-values	
				3 mg versus PBO	12 mg versus PBO
<i>Annualized change***, LS mean (SE)</i>	[N=58] -44.3 (6.0)	[N=38] -54.9 (7.4)	[N=60] -59.2 (5.8)	0.267	0.076
Lateral parietal lobe, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 57,960 (8208.9)	[N=38] 60,622 (6763.6)	[N=60] 59,395 (6196.3)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -1014.9 (199.8)	[N=15] -1227.0 (141.8)	[N=12] -1529.0 (157.6)	0.402	0.055
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -869.4 (84.0)	[N=38] -996.6 (107.1)	[N=60] -1173.0 (81.3)	0.365	0.010
<i>Annualized change***, LS mean (SE)</i>	[N=58] -1008.2 (98.3)	[N=38] -1088.5 (121.3)	[N=60] -1383.3 (95.8)	0.610	0.007
Lateral parietal lobe, left					
<i>Baseline, mean (SD)</i>	[N=58] 28,380 (4264.0)	[N=38] 29,344 (3142.7)	[N=60] 28,787 (3162.8)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -569.3 (126.0)	[N=15] -672.4 (90.0)	[N=12] -804.2 (99.6)	0.518	0.156
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -452.5 (44.0)	[N=38] -481.7 (56.2)	[N=60] -593.8 (42.6)	0.691	0.022
<i>Annualized change***, LS mean (SE)</i>	[N=58] -512.0 (50.6)	[N=38] -535.7 (62.6)	[N=60] -684.4 (49.5)	0.770	0.016
Lateral parietal lobe, right					
<i>Baseline, mean (SD)</i>	[N=58] 29,579 (4256.4)	[N=38] 31,278 (3913.9)	[N=60] 30,607 (3476.2)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -457.9 (95.9)	[N=15] -553.0 (67.8)	[N=12] -718.6 (75.7)	0.432	0.044
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -415.7 (46.5)	[N=38] -515.6 (59.2)	[N=60] -579.9 (45.0)	0.199	0.012
<i>Annualized change***, LS mean (SE)</i>	[N=58] -493.7 (54.5)	[N=38] -555.4 (67.2)	[N=60] -699.8 (53.0)	0.481	0.008
Medial temporal lobe, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 14,023 (2530.4)	[N=38] 14,187 (2550.3)	[N=60] 14,470 (2265.7)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -413.1 (77.2)	[N=15] -599.9 (53.3)	[N=12] -521.6 (61.1)	0.058	0.296
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -337.9 (25.6)	[N=38] -476.4 (32.5)	[N=60] -411.8 (24.8)	0.001	0.039
<i>Annualized change***, LS mean (SE)</i>	[N=58] -386.0 (29.3)	[N=38] -511.1 (36.1)	[N=60] -467.7 (28.7)	0.008	0.049
Medial temporal lobe, left					
<i>Baseline, mean (SD)</i>	[N=58] 6987.1 (1333.2)	[N=38] 6929.8 (1343.0)	[N=60] 7229.3 (1227.3)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -230.4 (50.8)	[N=15] -268.8 (35.1)	[N=12] -245.1 (39.7)	0.546	0.826
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -174.8 (14.3)	[N=38] -239.2 (18.2)	[N=60] -204.1 (13.9)	0.007	0.141
<i>Annualized change***, LS mean (SE)</i>	[N=58] -200.3 (15.8)	[N=38] -254.8 (19.5)	[N=60] -233.9 (15.5)	0.032	0.133
Medial temporal lobe, right					
<i>Baseline, mean (SD)</i>	[N=58] 7036.3 (1294.8)	[N=38] 7256.7 (1347.5)	[N=60] 7241.2 (1185.5)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -177.8 (36.6)	[N=15] -330.3 (25.7)	[N=12] -280.9 (29.5)	0.002	0.043
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -163.8 (14.6)	[N=38] -237.5.7 (18.6)	[N=60] -206.9 (14.1)	0.003	0.035
<i>Annualized change***, LS mean (SE)</i>	[N=58] -186.5 (17.2)	[N=38] -256.3 (21.2)	[N=60] -232.9 (16.8)	0.012	0.056

Volume (mm ³)	Placebo	LY3202626 3 mg	LY3202626 12 mg	Pairwise p-values	
				3 mg versus PBO	12 mg versus PBO
Precuneus, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 15,383 (2485.2)	[N=38] 15,694 (2042.9)	[N=60] 15,469 (1771.2)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -399.1 (75.6)	[N=15] -437.6 (53.7)	[N=12] -516.6 (59.5)	0.687	0.236
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -389.9 (31.4)	[N=38] -373.8 (40.1)	[N=60] -441.4 (30.4)	0.759	0.237
<i>Annualized change***, LS mean (SE)</i>	[N=58] -471.6 (38.2)	[N=38] -396.7 (47.2)	[N=60] -521.7 (37.4)	0.221	0.352
Precuneus, left					
<i>Baseline, mean (SD)</i>	[N=58] 7498.9 (1199.2)	[N=38] 7639.7 (1044.0)	[N=60] 7436.1 (880.5)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -221.6 (40.5)	[N=15] -220.8 (29.0)	[N=12] -255.7 (32.3)	0.986	0.519
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -198.6 (16.7)	[N=38] -180.4 (21.4)	[N=60] -215.2 (16.2)	0.515	0.473
<i>Annualized change***, LS mean (SE)</i>	[N=58] -237.6 (20.0)	[N=38] -192.3 (24.8)	[N=60] -254.1 (19.6)	0.159	0.559
Precuneus, right					
<i>Baseline, mean (SD)</i>	[N=58] 7884.2 (1360.8)	[N=38] 8054.2 (1069.5)	[N=60] 8032.6 (1105.8)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -178.0 (39.4)	[N=15] -215.8 (27.8)	[N=12] -261.9 (30.6)	0.451	0.106
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -191.5 (16.6)	[N=38] -193.9 (21.2)	[N=60] -225.8 (16.1)	0.932	0.139
<i>Annualized change***, LS mean (SE)</i>	[N=58] -234.4 (20.5)	[N=38] -204.2 (25.4)	[N=60] -267.3 (20.1)	0.357	0.255
Prefrontal lobe, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 49,327 (6616.3)	[N=38] 50,798 (5687.8)	[N=60] 49,590 (5676.2)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -546.3 (195.4)	[N=15] -1159.8 (137.5)	[N=12] -1232.8 (155.1)	0.017	0.011
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -741.4 (87.0)	[N=38] -964.1 (111.2)	[N=60] -884.3 (84.4)	0.127	0.237
<i>Annualized change***, LS mean (SE)</i>	[N=58] -876.0 (105.1)	[N=38] -989.8 (130.1)	[N=60] -1073.2 (102.9)	0.500	0.182
Prefrontal lobe, left					
<i>Baseline, mean (SD)</i>	[N=58] 24,856 (3328.8)	[N=38] 25,411 (2881.8)	[N=60] 24,753 (2785.8)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -290.8 (106.4)	[N=15] -624.9 (74.7)	[N=12] -663.5 (83.9)	0.017	0.011
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -401.0 (45.5)	[N=38] -461.5 (58.1)	[N=60] -457.4 (44.1)	0.424	0.369
<i>Annualized change***, LS mean (SE)</i>	[N=58] -464.8 (53.5)	[N=38] -481.7 (66.3)	[N=60] -543.9 (52.5)	0.844	0.294
Prefrontal lobe, right					
<i>Baseline, mean (SD)</i>	[N=58] 24,471 (3479.3)	[N=38] 25,387 (2997.9)	[N=60] 24,837 (3119.1)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -257.7 (97.6)	[N=15] -535.7 (69.1)	[N=12] -566.8 (78.0)	0.028	0.022
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -339.6 (45.4)	[N=38] -503.7 (58.0)	[N=60] -427.3 (44.0)	0.032	0.165
<i>Annualized change***, LS mean (SE)</i>	[N=58] -409.4 (56.4)	[N=38] -510.0 (69.7)	[N=60] -529.8 (55.1)	0.266	0.129

Volume (mm ³)	Placebo	LY3202626 3 mg	LY3202626 12 mg	Pairwise p-values	
				3 mg versus PBO	12 mg versus PBO
Superior temporal lobe, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 19,175 (2697.0)	[N=38] 18,838 (2449.9)	[N=60] 19,293 (2234.9)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -280.5 (90.0)	[N=15] -654.6 (62.8)	[N=12] -571.2 (68.1)	0.003	0.016
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -371.0 (30.7)	[N=38] -471.1 (39.3)	[N=60] -418.5 (29.9)	0.052	0.266
<i>Annualized change***, LS mean (SE)</i>	[N=58] -438.3 (35.3)	[N=38] -495.8 (43.6)	[N=60] -488.2 (34.6)	0.309	0.315
Superior temporal lobe, left					
<i>Baseline, mean (SD)</i>	[N=58] 9624.6 (1502.6)	[N=38] 9547.3 (1429.0)	[N=60] 9709.4 (1210.8)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -150.3 (52.9)	[N=15] -344.0 (38.0)	[N=12] -299.3 (41.3)	0.007	0.034
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -189.3 (17.7)	[N=38] -222.8 (22.6)	[N=60] -220.4 (17.2)	0.257	0.207
<i>Annualized change***, LS mean (SE)</i>	[N=58] -219.3 (19.7)	[N=38] -237.5 (24.3)	[N=60] -250.4 (19.3)	0.563	0.263
Superior temporal lobe, right					
<i>Baseline, mean (SD)</i>	[N=58] 9550.1 (1315.3)	[N=38] 9290.9 (1154.8)	[N=60] 9583.1 (1235.0)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -140.0 (44.4)	[N=15] -307.3 (29.9)	[N=12] -269.5 (32.8)	0.006	0.030
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -181.4 (16.7)	[N=38] -248.1 (21.4)	[N=60] -198.7 (16.2)	0.018	0.457
<i>Annualized change***, LS mean (SE)</i>	[N=58] -281.4 (20.3)	[N=38] -258.3 (25.1)	[N=60] -238.4 (19.9)	0.220	0.485
Ventricles, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 48.1 (20.1)	[N=38] 56.7 (34.3)	[N=60] 46.4 (19.1)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] 4.9 (0.6)	[N=15] 5.1 (0.5)	[N=12] 5.5 (0.5)	0.825	0.484
<i>Change at last observation**, LS mean (SE)</i>	[N=58] 4.3 (0.3)	[N=38] 3.6 (0.4)	[N=60] 4.2 (0.3)	0.216	0.862
<i>Annualized change***, LS mean (SE)</i>	[N=58] 4.9 (0.4)	[N=38] 4.1 (0.5)	[N=60] 4.7 (0.4)	0.162	0.753
Whole brain, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 962.1 (110.5)	[N=38] 994.7 (113.8)	[N=60] 968.9 (91.2)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -16.6 (3.2)	[N=15] -18.3 (2.3)	[N=12] -18.0 (2.6)	0.678	0.741
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -13.2 (1.1)	[N=38] -13.8 (1.4)	[N=60] -15.5 (1.1)	0.755	0.130
<i>Annualized change***, LS mean (SE)</i>	[N=58] -14.8 (1.3)	[N=38] -15.6 (1.6)	[N=60] -17.3 (1.2)	0.670	0.149
Whole temporal lobe, bilateral					
<i>Baseline, mean (SD)</i>	[N=58] 79,488 (11,912)	[N=38] 82,445 (10,061)	[N=60] 82,016 (8157.4)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -2088.2 (321.1)	[N=15] -2901.9 (229.2)	[N=12] -2655.4 (254.9)	0.051	0.180
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -1856.5 (122.0)	[N=38] -2164.1 (155.0)	[N=60] -2018.0 (117.8)	0.132	0.342
<i>Annualized change***, LS mean (SE)</i>	[N=58] -2170.4 (144.3)	[N=38] -2301.4 (177.4)	[N=60] -2354.1 (140.4)	0.571	0.365

Volume (mm ³)	Placebo	LY3202626 3 mg	LY3202626 12 mg	Pairwise p-values	
				3 mg versus PBO	12 mg versus PBO
Whole temporal lobe, left^a					
<i>Baseline, mean (SD)</i>	[N=58] 39,588 (6177.5)	[N=38] 40,908 (5377.0)	[N=60] 40,979 (3969.1)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -1138.2 (175.9)	[N=15] -1560.3 (126.2)	[N=12] -1382.7 (139.6)	0.065	0.287
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -935.6 (62.3)	[N=38] -1092.5 (79.1)	[N=60] -1047.3 (60.2)	0.132	0.198
<i>Annualized change***, LS mean (SE)</i>	[N=58] -1075.2 (73.3)	[N=38] -1172.6 (90.0)	[N=60] -1205.7 (71.4)	0.406	0.207
Whole temporal lobe, right					
<i>Baseline, mean (SD)</i>	[N=58] 39,901 (6105.0)	[N=38] 41,537 (5378.5)	[N=60] 41,037 (4750.6)		
<i>Change at week 52*, LS mean (SE)</i>	[N=8] -956.6 (167.7)	[N=15] -1342.0 (119.4)	[N=12] -1267.8 (133.6)	0.074	0.162
<i>Change at last observation**, LS mean (SE)</i>	[N=58] -914.5 (67.7)	[N=38] -1075.6 (86.2)	[N=60] -974.3 (65.4)	0.156	0.525
<i>Annualized change***, LS mean (SE)</i>	[N=58] -1086.4 (79.9)	[N=38] -1135.4 (98.5)	[N=60] -1152.7 (77.9)	0.703	0.555

ANCOVA, analysis of covariance; LS, least-squares; N, number of randomized patients; PBO, placebo; SD, standard deviation; SE, standard error; vMRI, volumetric magnetic resonance imaging.

^aUnits of volume for whole brain presented as cm³.

*The changes from baseline in vMRI parameters were compared among treatment groups using ANCOVA adjusting for baseline volume and age.

**Adjusted for between-scan time as covariate in ANCOVA model.

*** Annualized change was calculated by extrapolating observed change based on time between scans.

Supplementary Table 2. LS mean (SE) change from baseline as measured by plasma NfL change

Plasma NfL Concentration (pg/mL)	Placebo	LY3202626 3mg	LY3202626 12mg	Pairwise p-values	
				PBO versus 3 mg	PBO versus 12 mg
<i>Baseline, mean (SD)</i>	[N=129] 22.99 (11.43)	[N=53] 25.81 (22.45)	[N=126] 21.60 (9.72)		
<i>Change at week 52*, LS mean (SE)</i>	[N=15] -1.21 (2.22)	[N=8] 1.17 (3.03)	[N=15] 4.17 (2.16)	0.541	0.095
<i>Change at last observation**, LS mean (SE)</i>	[N=38] 0.68 (1.63)	[N=35] 1.73 (1.70)	[N=40] 1.57 (1.59)	0.654	0.696
<i>Annualized change***, LS mean (SE)</i>	[N=38] -0.19 (2.25)	[N=35] 1.91 (2.34)	[N=40] 1.54 (2.19)	0.518	0.583

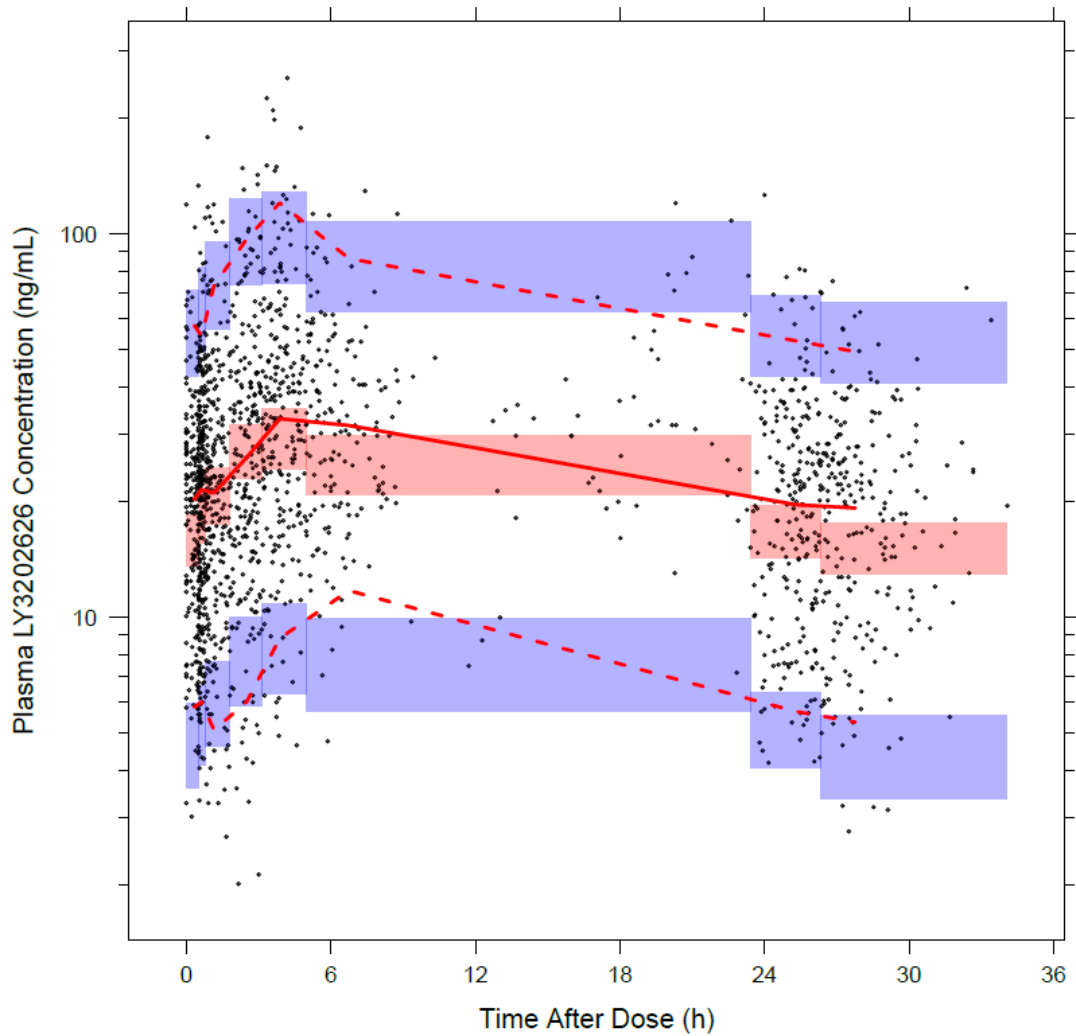
ANCOVA, analysis of covariance; LS, least-squares; N, number of randomized patients; NfL, neurofilament light chain; PBO, placebo; SD, standard deviation; SE, standard error

* The default model for treatment comparison on change from baseline in NfL is ANCOVA adjusting for baseline value and age.

** Adjusted for elapsed time between baseline and post-baseline laboratory samples in ANCOVA model.

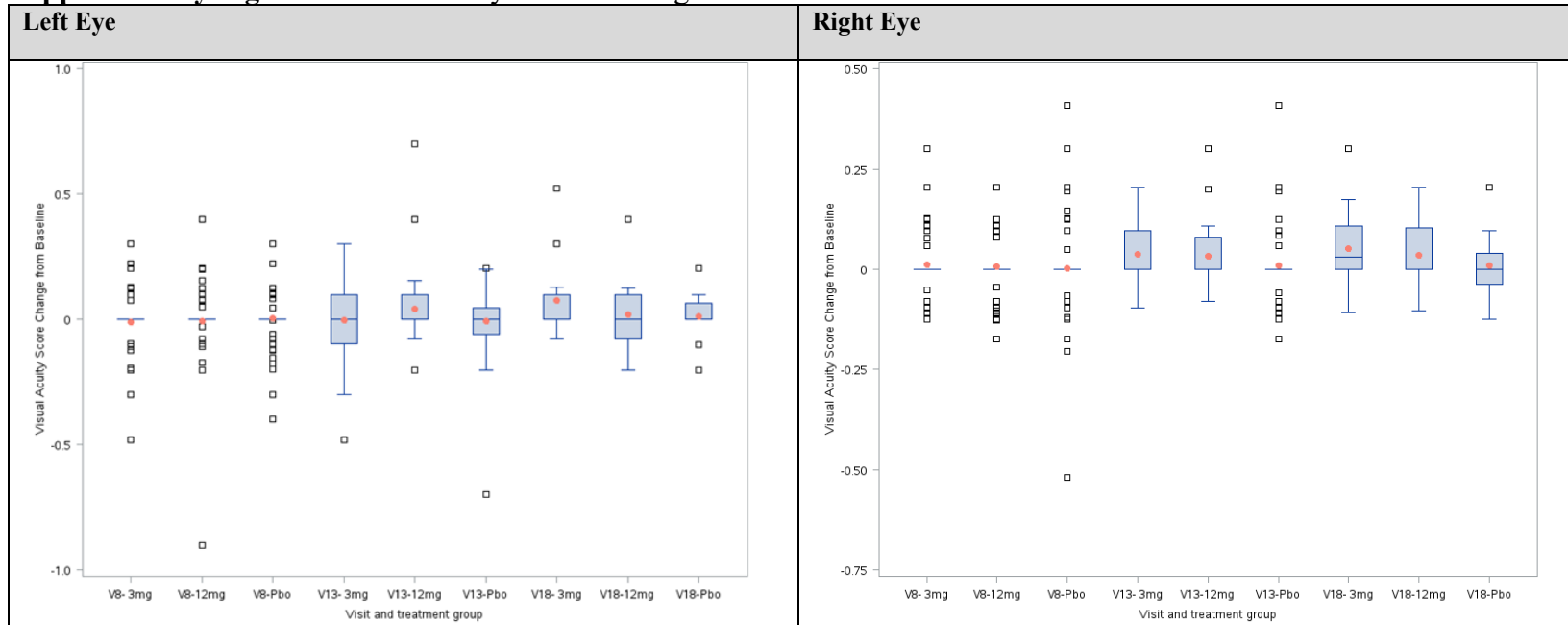
*** Annualized change was calculated by extrapolating observed change based on time between scans.

Supplementary Figure 1. Visual assessment of population-derived PK parameters and patient plasma concentrations of LY3202626.



Black dots represent observed data. Solid red line represents the median of the observed data, while the red dashed lines represent the 10th and 90th percentiles of the observed data. Red shaded regions represent the 90% CI of the median = model predicted concentration, while blue regions represent the 90% CI for the model-predicted 10th and 90th percentile concentrations. All data in the plot are normalized for the typical population prediction, thus, accounting for difference in dose or other model covariates. CI, confidence interval; PK, pharmacokinetic.

Supplementary Figure 2. Visual acuity score – Change from baseline



Supplementary Figure 3. Retinal thickness grid – Total volume (mm³) change from baseline

