

# Supplementary Material

## Application of a Novel Endpoint Staging Framework: Proof of Concept in the AMBAR Study

**Supplementary Table 1. Marginal Mean-Based Effects for Cognition at Each Visit (ADAS-Cog 12)**

<b>EFFECT</b>	<b>LSM</b>	<b>LSM LCL</b>	<b>LSM UCL</b>	<b>p</b>	<b>LSM DIF</b>	<b>LCL</b>	<b>UCL</b>	<b>DIF p</b>
PBO Intermediate Visit (Month 2)	1.8	0.4	3.2	0.0100	.	.	.	.
Pooled TX Intermediate Visit (Month 2)	0.6	-0.2	1.4	0.1203	-1.2	-2.8	0.4	0.1347
PBO LVPE 4 (Month 6)	1.3	-0.4	2.9	0.1435	.	.	.	.
Pooled TX LVPE 4 (Month 6)	0.6	-0.3	1.6	0.2040	-0.6	-2.5	1.3	0.5202
PBO LVPE 7 (Month 9)	2.4	0.3	4.4	0.0235	.	.	.	.
Pooled TX LVPE 7 (Month 9)	0.7	-0.5	1.9	0.2522	-1.7	-4.0	0.7	0.1635
PBO LVPE 10 (Month 12)	4.4	2.3	6.4	<0.0001	.	.	.	.
Pooled TX LVPE 10 (Month 12)	1.8	0.6	3.0	0.0040	-2.6	-5.0	-0.2	0.0328
PBO Final Visit (Month 14)	4.9	2.6	7.1	<0.0001	.	.	.	.
Pooled TX Final Visit (Month 14)	2.1	0.8	3.4	0.0020	-2.8	-5.4	-0.2	0.0330
PBO Final Visit (Month 14) in Target Stage	1.5	-0.7	3.7	0.1758	.	.	.	.
Pooled TX Final Visit (Month 14) in Target Stage	-0.1	-1.4	1.3	0.9400	-1.6	-4.1	1.0	0.2284
PBO Final Visit (Month 14) in Non-Target Stage	8.2	4.3	12.2	0.0001	.	.	.	.
Pooled TX Final Visit (Month 14) in Non-Target Stage	4.2	1.9	6.5	0.0004	-4.0	-8.5	0.4	0.0760
Pooled TX versus PBO Final Visit (Month 14) in Non-Target Stage	-4.0	-8.5	0.4	0.0760	.	.	.	.
Pooled TX versus PBO Final Visit (Month 14) in Target Stage	-1.6	-4.1	1.0	0.2284	2.5	-2.7	7.6	0.3456

TX, treatment; PBO, placebo; LSM, least squares means; LCL, Lower 95% confidence limit; UCL, Upper 95% confidence limit; SE, standard error; LSM, Least squares means; LSM DIF, Difference in least squares means; DIF p, p-value for difference in least squares means

**Supplementary Table 2. Marginal Mean-Based Effects for Functional Status at Each Visit (ADCS-ADL)**

<b>EFFECT</b>	<b>LS M</b>	<b>LSM LCL</b>	<b>LSM UCL</b>	<b>p</b>	<b>LSM DIF</b>	<b>LCL</b>	<b>UCL</b>	<b>DIF p</b>
PBO Intermediate Visit (Month 2)	-3.1	-5.2	-1.0	0.0042	.	.	.	.
Pooled TX Intermediate Visit (Month 2)	-1.3	-2.5	-0.1	0.0344	1.8	-0.6	4.1	0.1394
PBO LVPE 4 (Month 6)	-6.4	-8.5	-4.2	<0.0001	.	.	.	.
Pooled TX LVPE 4 (Month 6)	-2.0	-3.3	-0.8	0.0017	4.3	1.9	6.8	0.0006
PBO LVPE 7 (Month 9)	-8.7	-11.4	-6.0	<0.0001	.	.	.	.
Pooled TX LVPE 7 (Month 9)	-4.1	-5.7	-2.5	<0.0001	4.6	1.5	7.7	0.0038
PBO LVPE 10 (Month 12)	-10.9	-14.3	-7.6	<0.0001	.	.	.	.
Pooled TX LVPE 10 (Month 12)	-4.0	-6.0	-2.1	0.0001	6.9	3.0	10.7	0.0005
PBO Final Visit (Month 14)	-12.7	-16.3	-9.0	<0.0001	.	.	.	.
Pooled TX Final Visit (Month 14)	-4.8	-6.9	-2.7	<0.0001	7.9	3.7	12.1	0.0002
PBO Final Visit (Month 14) in Target Stage	-21.6	-28.3	-14.8	<0.0001	.	.	.	.
Pooled TX Final Visit (Month 14) in Target Stage	-7.4	-11.2	-3.6	0.0002	14.2	6.6	21.8	0.0003
PBO Final Visit (Month 14) in Non-Target Stage	-3.8	-6.7	-0.9	0.0115	.	.	.	.
Pooled TX Final Visit (Month 14) in Non-Target Stage	-2.2	-4.0	-0.4	0.0191	1.6	-1.8	5.1	0.3519
Pooled TX versus PBO Final Visit (Month 14) in Non-Target Stage	1.6	-1.8	5.1	0.3519	.	.	.	.
Pooled TX versus PBO Final Visit (Month 14) in Target Stage	14.2	6.6	21.8	0.0003	12.6	4.2	20.9	0.0033

TX, treatment; PBO, placebo; LSM, least squares means; LCL, Lower 95% confidence limit; UCL, Upper 95% confidence limit; SE, standard error; LSM, Least squares means; LSM DIF, Difference in least squares means; DIF p, p-value for difference in least squares means