

Supplementary Material

Article Title: Esmethadone (REL-1017) in Patients with Major Depressive Disorder and Antidepressant Tachyphylaxis: An Exploratory Post Hoc Analysis from a Phase 3 Randomized Controlled Trial

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

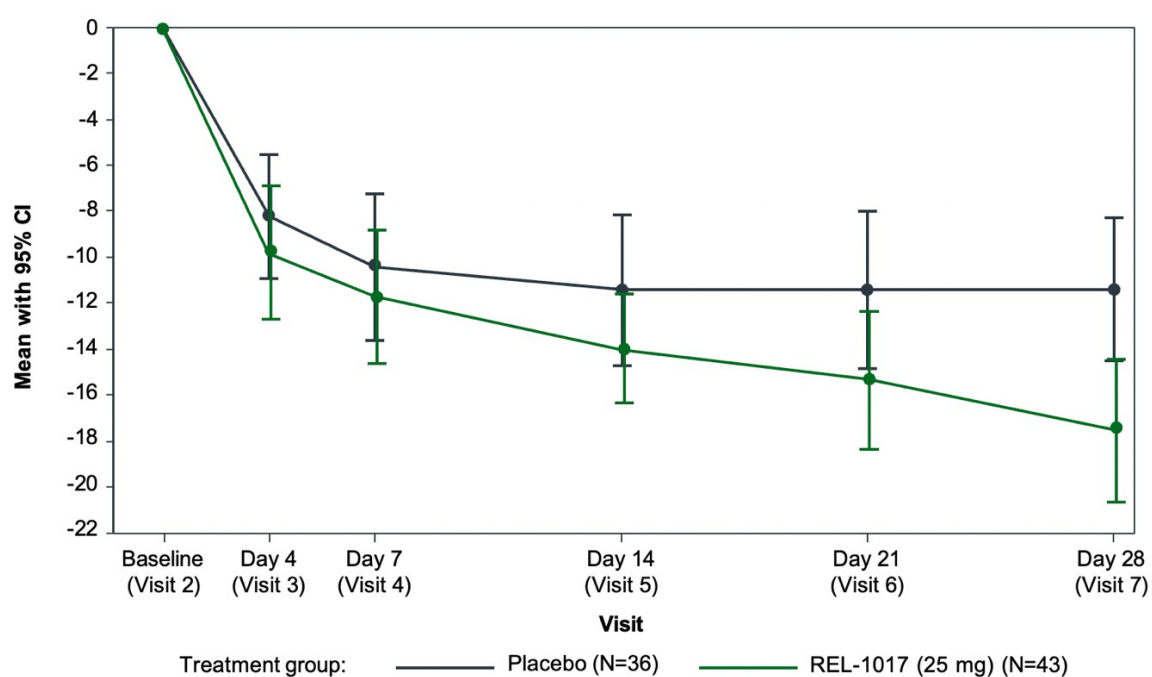
1. [Figure 1](#) Mean Difference (MD) Change From Baseline in MADRS Total Score Over Time for Placebo and for Esmethadone (REL-1017) in the Subgroup Analysis of ATPP
2. [Table 1](#) Mixed Model for Repeated Measures (MMRM) Analyses for Placebo and for Esmethadone (REL-1017) for AT-ITT Subgroup and for AT-PP Subgroup at Primary Endpoint (Day 28)

DISCLAIMER

This Supplementary Material has been provided by the authors as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplemental Figures and Tables

Supplementary Figure 1. Mean difference (MD) change from baseline in MADRS total score over time for placebo and for esmethadone (REL-1017) in the subgroup analysis of AT-PP.



Supplementary Table 1. Mixed model for repeated measures (MMRM) analyses for placebo and for esmethadone (REL-1017) for AT-ITT subgroup and for AT-PP subgroup at primary endpoint (Day 28).

	Placebo	Esmethadone	LS Mean Difference (esmethadone - placebo)
Intent to Treat	N=41	N=46	
Value at Day 28, Mean (SD)	23.1 (11.0)	17.4 (9.6)	
LS Mean (SE)	-13.27 (1.74)	-17.33 (1.60)	-4.06 (2.3)
95% CI	(-16.73, -9.82)	(-20.51, -14.15)	(-8.76, 0.64)
p-value			0.0892
Effect size			-0.38
	Placebo	Esmethadone	LS Mean Difference (esmethadone – placebo)
Per Protocol	N=32	N=42	
Value at Day 28, Mean (SD)	23.8 (10.5)	17.4 (9.7)	
LS Mean (SE)	-11.80 (1.72)	-17.44 (1.57)	-5.64 (2.33)
95% CI	(-15.24, -8.37)	(-20.57, -14.32)	(-10.29, -1.00)
p-value			0.0180
Effect size			-0.56