Supplementary Online Content

McEvoy JP, Byerly M, Hamer RM, et al. Effectiveness of Paliperidone Palmitate vs Haloperidol Decanoate for Maintenance Treatment of Schizophrenia: a Randomized Clinical Trial. *JAMA*. doi:10.1001/jama.2014.4310

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Outcome Measures of Effectiveness in the Modified Intent-to-Treat Population

Analysis	Paliperidone palmitate (n=145)	Haloperidol decanoate (n=145)	*P* Value: PP vs HD
Primary Efficacy Outcome: Efficacy failure prior to month 24 (censoring 90 days after last injection)			
Efficacy failure prior to month 24, No. of patients/Total No.	49/145	47/145	
Primary test of effect, site-stratified log rank test [a]			0.90
Kaplan-Meier efficacy failure probability (95% CI), at month 12	0.33 (0.246 to 0.409)	0.34 (0.254 to 0.422)	
Kaplan-Meier efficacy failure probability (95% CI), at month 24 [b]	0.43 (0.323 to 0.529)	0.41 (0.311 to 0.501)	
Site-stratified log rank test [a]			0.90
Reasons for censoring, No. of patients			
Completed follow-up	47	52	
Withdrew early	27	33	
Greater than 90 days since last LAI	22	13	
Secondary Efficacy Analysis			
Unstratified log rank test			0.95
Cox-model treatment comparisons, PP vs. HD [c]			
Adjusted hazard ratio (95% CI)	0.98 (0.65 to 1.47)		0.93
Site by treatment interaction [a]			0.46
Score test for equality of hazard ratios across three predefined time intervals: months 1 to 3, months 4 to 12, and months 13 to 24			0.57
Sensitivity Analysis, without censoring 90 days after last injection			
Efficacy failure prior to month 24, No. of patients, Total No.	51/145	47/145	
Kaplan-Meier efficacy failure probability (95% CI), at month 12	0.33 (0.253 to 0.414)	0.33 (0.249 to 0.415)	
Kaplan-Meier efficacy failure probability (95% CI), at month 24	0.41. (0.319 to 0.507)	0.39 (0.301 to 0.483)	
Site-stratified log rank test [a]			0.93
Reasons for censoring, No. of patients			
Completed follow-up	63	63	
Withdrew early	31	35	
Subgroup Analysis, among those not hospitalized at randomization			

…continued **eTable 1.** Outcome Measures of Effectiveness in the Modified Intent-to-Treat Population

Efficacy failure prior to month 24, No. of patients/Total No.	39/121	35/117	
Kaplan-Meier efficacy failure probability (95% CI), at month 12	0.32 (0.226 to 0.405)	0.30 (0.206 to 0.386)	
Kaplan-Meier efficacy failure probability (95% CI), at month 24	0.41 (0.297 to 0.517)	0.38 (0.273 to 0.483)	
Site-stratified log rank test [a]			0.91

Abbreviations: CI, confidence interval; HD, haloperidol decanoate; LAI, Long-acting injectable; PP, paliperidone palmitate; SE, standard error.

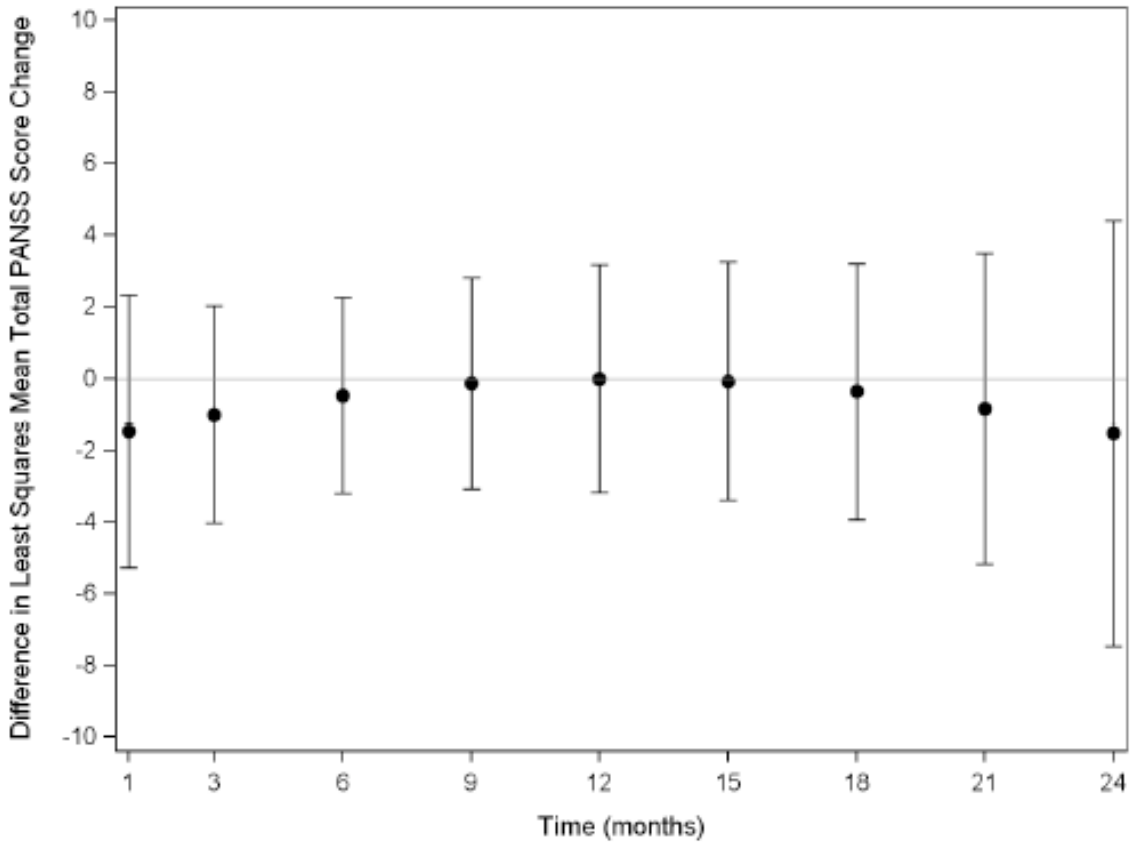
[a] For site-stratified analyses, low enrolling study sites (e.g., sites with fewer than 14 randomized patients) were combined to create one or more "pooled sites" with between 14 and 30 patients prior to examining outcome data by coded treatment group. Pooling was primarily based on the number of patients per site and secondarily on service delivery characteristics and location.

[b] Confidence intervals are calculated using Greenwood's SE formula for the last observed event time and should be interpreted with caution.

[c] The Cox proportional hazards model controlled for baseline PANSS score and pooled site.

eFigure 1. Differences (Paliperidone Palmitate Minus Haloperidol Decnoate) in Least-Square Mean Total PANSS (Positive and Negative Syndrome Scale) With 95% Confidence Intervals for Selected Months Since First Injection

PANSS was analyzed using a mixed effects linear model including fixed effects for treatment, site, baseline PANSS score, time, time^2, and treatment by time (linear and quadratic) interaction (with spatial spherical covariance structure). The response variables for each participant included the change from baseline in total PANSS score at all observed measurement times within 90 days of the patient's last injection. Bars represent 95% confidence intervals. Visits were scheduled quarterly. A few patients who discontinued treatment early contributed data at Month
1.



95% CIs for Differences of Least Squares Means Paliperidone Palmitate minus Haloperidol Decanoate			
Month	Differences of Least Squares Means	Lower 95% boundary	Upper 95% boundary
1	-1.4771	-5.2792	2.3251
3	-1.0041	-4.0360	2.0277
6	-0.4653	-3.1919	2.2614
9	-0.1310	-3.0821	2.8201
12	-0.00142	-3.1873	3.1845
15	-0.07646	-3.3969	3.2440
18	-0.3561	-3.9263	3.2140
21	-0.8404	-5.1850	3.5041
24	-1.5294	-7.4586	4.3998

…continued **eFigure 1.** Differences (Paliperidone Palmitate Minus Haloperidol Decnoate) in Least-Square Mean Total PANSS (Positive and Negative Syndrome Scale) With 95% Confidence Intervals for Selected Months Since First Injection

Number of patients with PANSS at time intervals

Treatment	*Month*	*N*
Haloperidol decanoate	1	5
Paliperidone palmitate	1	4
Haloperidol decanoate	3	131
Paliperidone palmitate	3	136
Haloperidol decanoate	6	103
Paliperidone palmitate	6	105
Haloperidol decanoate	9	87
Paliperidone palmitate	9	82
Haloperidol decanoate	12	73
Paliperidone palmitate	12	77
Haloperidol decanoate	15	59
Paliperidone palmitate	15	53
Haloperidol decanoate	18	46
Paliperidone palmitate	18	44
Haloperidol decanoate	21	42
Paliperidone palmitate	21	38
Haloperidol decanoate	24	26
Paliperidone palmitate	24	19

eTable 2. Reasons for Efficacy Failure Cited by Adjudication Committee Among Those Judged to Have Efficacy Failure (Each Efficacy Failure Could Have Multiple Contributing Reasons)

	Paliperidone Palmitate (N=49)	Haloperidol Decanoate (N=47)
Psychiatric hospitalization	44 (89.8%)	34 (72.3%)
Crisis intervention	16 (32.7%)	16 (34.0%)
Oral antipsychotic could not be discontinued within 8 weeks	9 (18.3%)	6 (12.8%)
Clinician decision to discontinue study medication due to inadequate effect	34 (69.4%)	28 (59.6%)
Clinician decision that ongoing adjunctive oral antipsychotic medication needed	9 (18.4%)	11 (23.4%)