<u>Supplementary Material</u>

Article Title: Efficacy and Safety of a Combination of Olanzapine and Samidorphan in Adult Patients With an Acute Exacerbation of Schizophrenia: Outcomes From the Randomized, Phase 3 ENLIGHTEN-1 Study

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<u>List of Supplementary Material for the article</u>

<u>Disclaimer</u>

SUPPLEMENTARY MATERIAL

Supplementary Table 1. Summary of prior antipsychotic medications (≥5% of patients overall; Safety Population)

	OLZ/SAM n = 134	Olanzapine n = 133	Placebo n = 134	All N = 401
Patients who took at least 1 prior antipsychotic medication, n (%)	**121 (90.3)**	**119 (89.5)**	**117 (87.3)**	**357 (89.0)**
Risperidone	45 (33.6)	45 (33.8)	34 (25.4)	124 (30.9)
Haloperidol	37 (27.6)	40 (30.1)	45 (33.6)	122 (30.4)
Quetiapine	18 (13.4)	18 (13.5)	24 (17.9)	60 (15.0)
Aripiprazole	13 (9.7)	13 (9.8)	11 (8.2)	37 (9.2)
Amisulpride	6 (4.5)	2 (1.5)	14 (10.4)	22 (5.5)

Abbreviation: OLZ/SAM, olanzapine/samidorphan.

Supplementary Table 2. Summary of extrapyramidal symptom scores from baseline to last on-treatment assessment

Measure	OLZ/SAM n = 134	Olanzapine n = 133	Placebo n = 134
AIMS total score, mean (SD)			
Baseline	0.2 (0.51)	0.2 (0.80)	0.4 (1.40)
Last on-treatment assessment	0.2 (0.91)	0.1 (0.75)	0.2 (0.78)
Change from baseline	0.1 (0.80)	0.0 (0.99)	−0.2 (1.27)
BARS (sum of objective and subjective scores), mean (SD)			
Baseline	0.3 (0.77)	0.3 (0.98)	0.4 (1.15)
Last on-treatment assessment	0.3 (0.86)	0.3 (0.72)	0.3 (0.97)
Change from baseline	0.0 (0.78)	−0.1 (1.04)	−0.1 (0.89)
BARS (global clinical assessment), mean (SD)			
Baseline	0.2 (0.43)	0.2 (0.57)	0.2 (0.64)
Last on-treatment assessment	0.1 (0.39)	0.2 (0.42)	0.2 (0.52)
Change from baseline	0.0 (0.47)	0.0 (0.61)	−0.1 (0.49)
SAS total score, mean (SD)			
Baseline	0.5 (1.02)	0.8 (2.43)	0.8 (2.21)
Last on-treatment assessment	0.4 (0.83)	0.6 (1.46)	0.7 (1.89)
Change from baseline	0.0 (0.78)	−0.3 (1.65)	−0.2 (1.45)

Abbreviations: AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; OLZ/SAM, olanzapine/samidorphan; SAS, Simpson-Angus Scale.

Supplementary Figure 1. Change from Baseline in PANSS Subscales by Week (MMRM; Efficacy population)
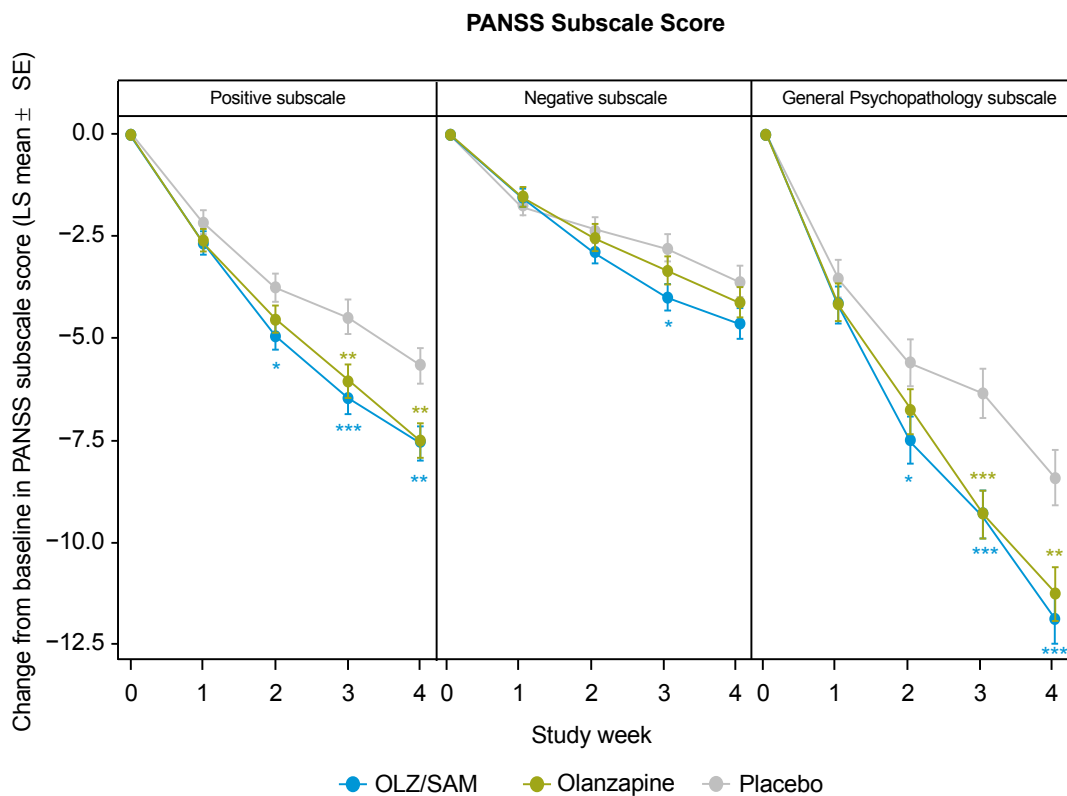
P values vs placebo: *P<0.05; **P<0.01; ***P<0.001.

Abbreviations: LS, least squares; MMRM, mixed model with repeated measurements; OLZ/SAM, olanzapine/samidorphan; PANSS, Positive and Negative Syndrome Scale; SE, standard error.

Supplementary Figure 2. PANSS (≥30% improvement from baseline) (A) and CGI-I (score of ≤2) (B) Responders by Week (LOCF; efficacy population)

A)
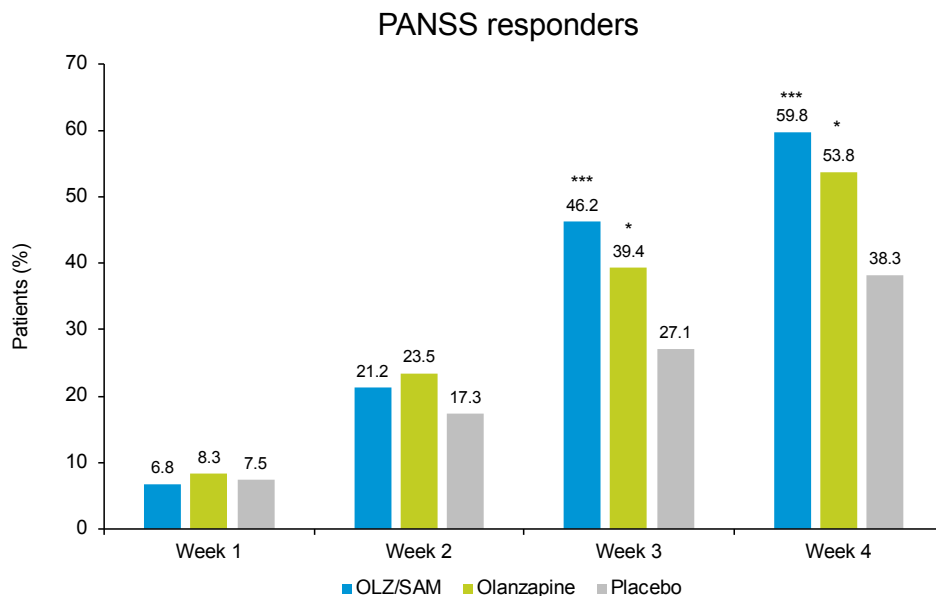
B)

P value vs placebo: *P<0.05; **P≤0.01; ***P<0.001.

Abbreviations: CGI-I, Clinical Global Impression–Improvement; LOCF, last observation carried forward; OLZ/SAM, olanzapine/samidorphan; PANSS, Positive and Negative Syndrome Scale.

Supplementary Figure 3. Change from Baseline in PANSS Total Score at Week 4 in the Overall Efficacy Population and Key Subgroups for A) OLZ/SAM and olanzapine vs placebo and B) OLZ/SAM vs olanzapine (MMRM approach)

A)

Demographic subgroup categorical value	Forest plot	LS mean difference (95% CI)
Age (years)		
<55 OLZ/SAM vs Placebo (n = 222)		−9.2 (−13.1, −5.3)
Olanzapine vs Placebo (n = 229)		−7.7 (−11.5, −3.8)
≥55 OLZ/SAM vs Placebo (n = 43)		9.8 (0.7, 18.9)
Olanzapine vs Placebo (n = 36)		10.6 (1.0, 20.2)
Gender		
Male OLZ/SAM vs Placebo (n = 161)		−6.7 (−11.3, −2.2)
Olanzapine vs Placebo (n = 158)		−4.9 (−9.5, −0.3)
Female OLZ/SAM vs Placebo (n = 104)		−6.2 (−12.2, −0.3)
Olanzapine vs Placebo (n = 107)		−6.0 (−11.8, −0.1)
Race		
White OLZ/SAM vs Placebo (n = 176)		−9.5 (−13.6, −5.4)
Olanzapine vs Placebo (n = 188)		−8.0 (−12.0, −4.0)
Black OLZ/SAM vs Placebo (n = 79)		3.0 (−4.1, 10.1)
Olanzapine vs Placebo (n = 71)		4.8 (−2.9, 12.4)
Other OLZ/SAM vs Placebo (n = 10)		−12.4 (−36.7, 11.8)
Olanzapine vs Placebo (n = 6)		−5.6 (−42.4, 31.1)
Baseline PANSS Total Score		
<95 OLZ/SAM vs Placebo (n = 72)		−2.8 (−9.2, 3.5)
Olanzapine vs Placebo (n = 81)		−1.7 (−7.8, 4.4)
≥95 OLZ/SAM vs Placebo (n = 193)		−7.9 (−12.3, −3.5)
Olanzapine vs Placebo (n = 184)		−7.2 (−11.7, −2.6)
Overall		
OLZ/SAM vs Placebo (n = 265)		−6.4 (−10.0, −2.8)
Olanzapine vs Placebo (n = 265)		−5.3 (−8.9, −1.7)

−45 −40 −35 −30 −25 −20 −15 −10 −5 0 5 10 15 20 25 30 35 40 45 50

← Favors Active   Favors Placebo →

■ OLZ/SAM vs Placebo   ■ Olanzapine vs Placebo

B)

Demographic subgroup categorical value	Forest plot	LS mean difference (95% CI)
Age (years)		
<55 OLZ/SAM vs olanzapine (n = 219)		−1.5 (−5.4, 2.4)
≥55 OLZ/SAM vs olanzapine (n = 45)		−0.7 (−9.4, 7.9)
Gender		
Male OLZ/SAM vs olanzapine (n = 163)		−1.8 (−6.4, 2.7)
Female OLZ/SAM vs olanzapine (n = 101)		−0.3 (−6.1, 5.6)
Race		
White OLZ/SAM vs olanzapine (n = 184)		−1.5 (5.5, 2.5)
Black OLZ/SAM vs olanzapine (n = 74)		−1.8 (−9.1, 5.5)
Baseline PANSS total score		
<95 OLZ/SAM vs olanzapine (n = 87)		−1.1 (−6.9, 4.6)
≥95 OLZ/SAM vs olanzapine (n = 177)		−0.7 (−5.3, 3.8)
Overall		
OLZ/SAM vs olanzapine (n = 264)		−1.2 (−4.7, 2.4)

−20 −15 −10 −5 0 5 10 15 20

← Favors OLZ/SAM   Favors olanzapine →
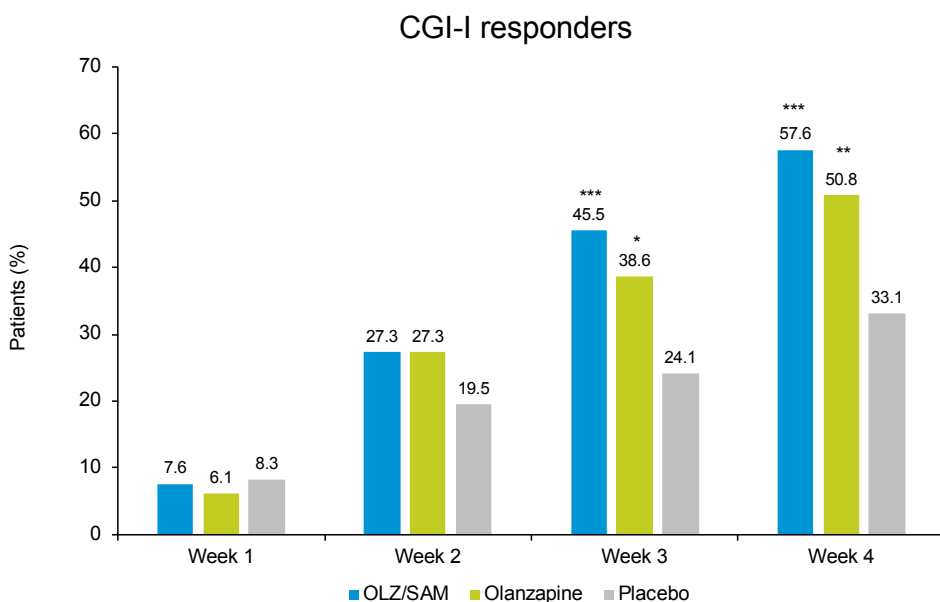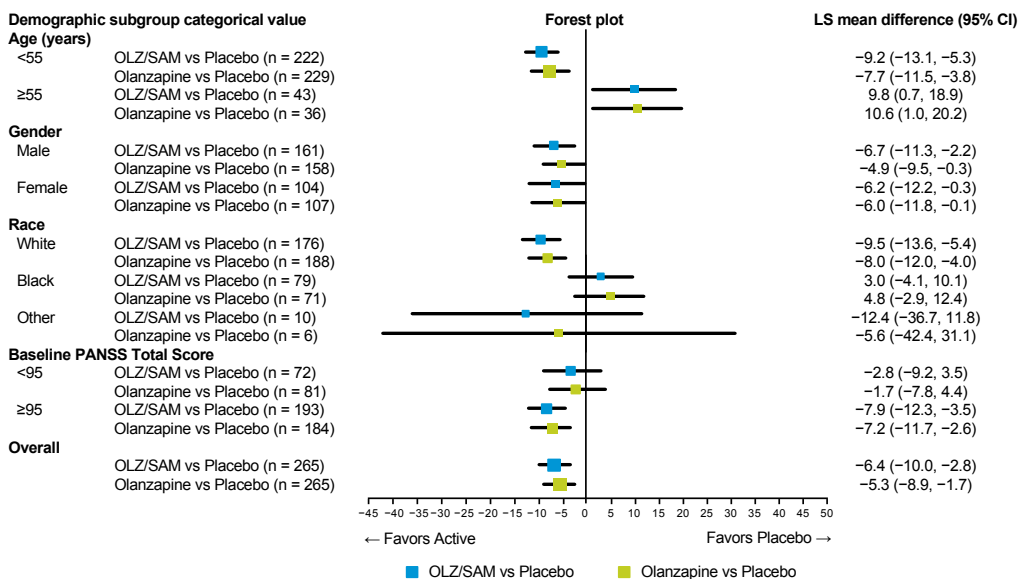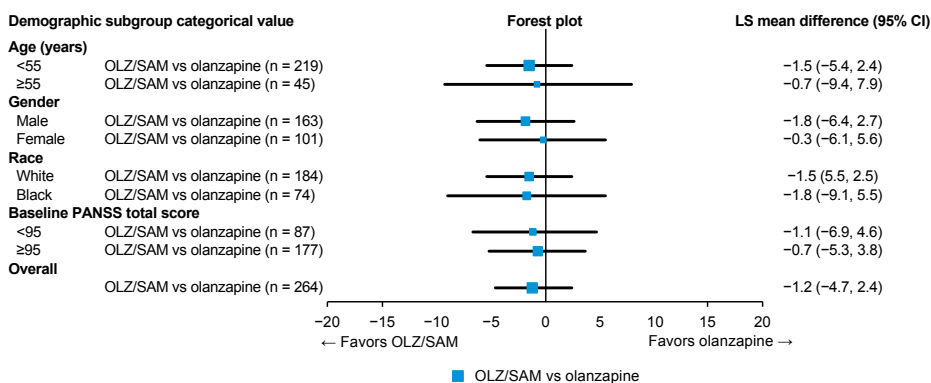
■ OLZ/SAM vs olanzapine

Abbreviations: CI, confidence interval; LS, least squares; MMRM, mixed-effects model for repeated measures;

OLZ/SAM, olanzapine/samidorphan; PANSS, Positive and Negative Syndrome Scale.