Lipid and Glycemic Profile of Olanzapine and Samidorphan: A Patient Subgroup Analysis of a 4-Year Open-Label Study

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BACKGROUND

- A combination of olanzapine and samidorphan (OLZ/SAM) is approved in the US for the treatment of adults with schizophrenia or bipolar I disorder (BD-I)[1]
- In a 4-year open-label study, OLZ/SAM treatment maintained symptom control and was associated with small changes in body weight and minimal changes in waist circumference in patients with schizophrenia, schizophreniform disorder, or BD-I who had previously completed an antecedent study[2]

OBJECTIVE

- To analyze lipid and glycemic parameters across patient subgroups in a 4-year open-label study of OLZ/SAM in adults with schizophrenia, schizophreniform disorder, or BD-I

METHODS

- The study (NCT03201757) was a phase 3, 2- to 4-year, multicenter, open-label study assessing the safety, tolerability, and durability of treatment effect of OLZ/SAM
- Eligible patients enrolled ≤7 days after completing 1 of 3 antecedent studies in the ENLIGHTEN clinical trial program
- Patients could receive ≥2 and up to 4 years of additional OLZ/SAM treatment
- Prespecified subgroup analyses were conducted by age (<30 or ≥30 years), sex (male or female), race (Black/African American or non-Black/African American), baseline body mass index (BMI; <25 or ≥25 kg/m^2), and geographic region (US or non-US)
- Changes from baseline in lipid (total, high-density lipoprotein [HDL], and low-density lipoprotein [LDL] cholesterol and triglycerides) and glycemic (glycosylated hemoglobin [HbA_{1c}] and fasting glucose) parameters were assessed

RESULTS

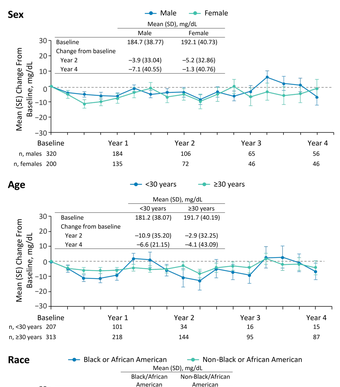
- Overall, 524 patients were enrolled, and 523 received ≥1 dose of study drug (**Table 1**)
- Of these patients, 72 discontinued due to the Ukraine-Russia conflict; 242/451 (53.7%) and 109/335 (32.5%) completed 2 and 4 years of treatment, respectively
- Across subgroups, OLZ/SAM treatment was associated with minimal changes from baseline in total cholesterol (**Figure 1**), triglycerides (**Figure 2**), and HbA_{1c} (**Figure 3**) at 2 and 4 years
- Similarly, minimal changes in HDL and LDL cholesterol and fasting glucose (**Table 2**) were observed after 2 and 4 years of OLZ/SAM treatment across subgroups
- Most adverse events were mild or moderate in severity (**see poster #75**)

Table 1. Demographics and Baseline Clinical Characteristics[a]

Characteristics	Subgroups									
	Sex		Age[b]		Race		Baseline BMI		Geographic region	
	Male (n=322)	Female (n=201)	<30 years (n=205)	≥30 years (n=314)	Black/ African American (n=130)	Non-Black/ African American (n=393)	<25 kg/m^2 (n=241)	≥25 kg/m^2 (n=282)	US (n=206)	Non-US (n=317)
Age,[c] mean (SD), years	33.2 (11.7)	38.1 (12.4)	23.4 (3.2)	42.9 (9.2)	37.1 (12.1)	34.4 (12.1)	33.1 (11.9)	36.8 (12.2)	35.9 (12.4)	34.6 (12.0)
Sex, n (%)										
Male	322 (100)	NA	154 (75.1)	167 (53.2)	86 (66.2)	236 (60.1)	160 (66.4)	162 (57.4)	144 (69.9)	178 (56.2)
Female	NA	201 (100)	51 (24.9)	147 (46.8)	44 (33.8)	157 (39.9)	81 (33.6)	120 (42.6)	62 (30.1)	139 (43.8)
Race, n (%)										
White	226 (70.2)	154 (76.6)	153 (74.6)	226 (72.0)	NA	380 (96.7)	174 (72.2)	206 (73.0)	68 (33.0)	312 (98.4)
Black or African American	82 (25.5)	44 (21.9)	40 (19.5)	83 (26.4)	126 (96.9)	NA	55 (22.8)	71 (25.2)	125 (60.7)	1 (0.3)
Asian	6 (1.9)	2 (1.0)	7 (3.4)	1 (0.3)	NA	8 (2.0)	6 (2.5)	2 (0.7)	5 (2.4)	3 (0.9)
Other[d]	8 (2.5)	1 (0.5)	5 (2.4)	4 (1.3)	4 (3.1)	5 (1.3)	6 (2.5)	3 (1.1)	8 (3.9)	1 (0.3)
Region, n (%)										
US	144 (44.7)	62 (30.8)	81 (39.5)	121 (38.5)	128 (98.5)	78 (19.8)	87 (36.1)	119 (42.2)	206 (100)	NA
Non-US	178 (55.3)	139 (69.2)	124 (60.5)	193 (61.5)	2 (1.5)	315 (80.2)	154 (63.9)	163 (57.8)	NA	317 (100)
Weight, mean (SD), kg	81.1 (15.7)	71.5 (13.1)	76.6 (15.1)	78.0 (15.8)	78.5 (16.8)	77.0 (15.0)	66.8 (9.1)	86.4 (14.0)	79.4 (16.9)	76.1 (14.4)
BMI, mean (SD), kg/m^2	25.8 (4.1)	26.3 (4.7)	25.3 (4.0)	26.5 (4.5)	26.1 (4.2)	26.0 (4.4)	22.4 (2.0)	29.1 (3.3)	26.4 (4.3)	25.8 (4.3)
CGI-S score, mean (SD)	3.11 (0.85)	2.98 (0.89)	3.03 (1.00)	3.08 (0.77)	3.00 (0.70)	3.08 (0.91)	3.08 (0.84)	3.04 (0.89)	2.95 (0.75)	3.14 (0.93)

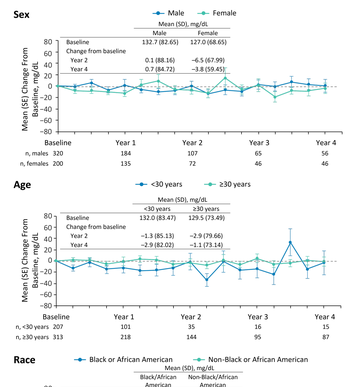
[a]All patients who received ≥1 dose of OLZ/SAM.
[b]Excluding 4 patients <18 years old.
[c]Age is based on data collected at the time of screening in the patient's initial randomized controlled trial.
[d]"Other" includes patients who were American Indian or Alaska Native individuals, those reporting multiple races, and those responding "other."
BMI, body mass index; CGI-S, Clinical Global Impression–Severity; NA, not applicable; OLZ/SAM, combination olanzapine and samidorphan.

Figure 1. Changes From Baseline in Total Cholesterol



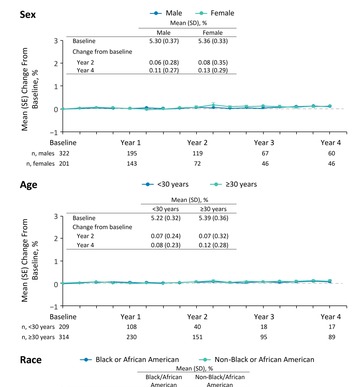
BMI, body mass index.

Figure 2. Changes From Baseline in Triglycerides



BMI, body mass index.

Figure 3. Changes From Baseline in HbA_{1c}



BMI, body mass index; HbA_{1c}, glycosylated hemoglobin.

Table 2. Changes From Baseline in HDL and LDL Cholesterol and Fasting Glucose

	Subgroups									
	Sex		Age		Race		Baseline BMI		Geographic region	
	Male	Female	<30 years	≥30 years	Black/ African American	Non-Black/ African American	<25 kg/m^2	≥25 kg/m^2	US	Non-US
HDL cholesterol, mean (SD), mg/dL										
Baseline	50.2 (14.56)	58.1 (16.37)	50.3 (13.35)	55.2 (16.89)	57.1 (18.26)	51.9 (14.60)	56.2 (16.99)	50.8 (14.18)	54.7 (16.97)	52.3 (14.84)
Year 2	−3.4 (11.37)	−1.6 (11.40)	−6.2 (8.54)	−1.8 (11.82)	−3.3 (13.17)	−2.4 (10.65)	−2.8 (13.54)	−2.6 (9.58)	−3.3 (11.86)	−2.2 (11.06)
Year 4	−3.3 (15.36)	−5.0 (10.48)	−2.5 (5.74)	−4.4 (14.26)	−5.0 (18.81)	−3.8 (11.43)	−5.2 (15.13)	−3.0 (11.51)	−4.5 (15.77)	−3.9 (11.88)
LDL cholesterol, mean (SD), mg/dL										
Baseline	121.6 (36.73)	122.4 (37.66)	119.2 (34.88)	123.7 (38.37)	105.4 (35.03)	127.4 (36.11)	116.5 (38.73)	126.4 (35.01)	111.8 (36.20)	128.5 (36.17)
Year 2	−0.9 (30.62)	−4.2 (32.65)	−2.1 (35.89)	−2.2 (30.39)	4.1 (31.67)	−4.6 (31.08)	−2.3 (29.97)	−2.1 (32.56)	2.5 (31.78)	−5.6 (30.85)
Year 4	5.1 (38.80)	10.2 (38.68)	7.0 (23.37)	7.4 (40.80)	0.7 (37.12)	9.3 (39.09)	2.6 (40.45)	11.8 (36.72)	6.4 (40.76)	7.9 (37.69)
Fasting glucose, mean (SD), mg/dL										
Baseline	94.9 (13.26)	95.7 (15.26)	92.5 (11.88)	97.0 (15.07)	94.5 (16.35)	95.4 (13.21)	94.1 (14.33)	96.1 (13.76)	95.2 (16.73)	95.2 (12.02)
Year 2	−0.5 (12.70)	3.3 (16.04)	−1.1 (11.93)	1.5 (14.71)	−2.7 (16.18)	2.5 (13.21)	1.5 (13.12)	0.8 (15.06)	−1.8 (14.65)	3.1 (13.65)
Year 4	−3.6 (12.05)	−2.0 (15.50)	−2.6 (11.31)	−2.9 (14.13)	−4.3 (13.33)	−2.5 (13.88)	−1.8 (14.50)	−3.9 (12.99)	−3.3 (12.51)	−2.6 (14.39)

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

LIMITATIONS

- The lack of a comparator arm may limit interpretation of these lipid and glycemic data
- Missing data due to patients who discontinued may have affected the results; patients with a less favorable outcome may have dropped out of the antecedent trial, creating potential selection bias
- The baseline characteristics of patients in this study may have varied due to differences in the inclusion and exclusion criteria of the 3 antecedent studies
- Fasting status was based on self-report and not confirmed by the investigator

CONCLUSIONS

- Treatment with OLZ/SAM was associated with minimal changes in lipid and glycemic parameters after up to 4 years of additional treatment; these changes were similar across age, sex, race, BMI, and geographic subgroups
- These outcomes were generally consistent with the previously published overall study results[2]

REFERENCES

1. Lybalvi [package insert]. Waltham, MA: Alkermes, Inc.; 2025.
2. Ballon JS, et al. *J Clin Psychiatry*. 2025;86(1):24m15511. DOI: 10.4088/JCP.24m15511

DISCLOSURES

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CA and **AL** are or were employees of Alkermes, Inc., and may own stock/options in the company.
CUC has been a consultant and/or advisor for or has received honoraria from AbbVie, Acadia, Alkermes, Allergan, Angelini, Aristo, Autobahn, Biogen, Boehringer-Ingelheim, Cardio Diagnostics, Cerevel, CNX Therapeutics, Compass Pathways, Darnitsa, Denovo, Gedeon Richter, Hikma, Holmusk, Intra-Cellular Therapies, Jamjoom Pharma, Janssen/Johnson & Johnson, Karuna, LB Pharma, Lundbeck, MedAvante-ProPhase, MedinCell, Merck, MindPax, Mitsubishi Tanabe Pharma, Mylan, Neurelis, Neurocrine, NeuShen, Newron, Noven, Novo Nordisk, Otsuka, Pharmabrain, PPD Biotech, Recognify Life Science, Recordati, Relmada, Reviva, Rovi, Seqirus, Servier, SK Life Science, Sunovion, Sun Pharma, Supernus, Takeda, Teva, and Viatris; has provided expert testimony for Janssen and Otsuka; has served on a data safety monitoring board for Compass Pathways, Denovo, Intra-Cellular Therapies, Lundbeck, Relmada, Reviva, Rovi, Supernus, and Teva; has received grant support from Janssen and Takeda; has received royalties from UpToDate; and is a stock option holder of Cardio Diagnostics, Küleon Biosciences, LB Pharma, MedLink, MindPax, Quantic, and Terran.

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Key Contributors
All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the poster; gave final approval of the version to be presented; and agree to be accountable for all aspects of the work.

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