Study Retention Rates in the OLZ/SAM Phase 3 Clinical Program

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BACKGROUND

- The combination of olanzapine and samidorphan (OLZ/SAM) is used for the treatment of adults with schizophrenia or bipolar I disorder[1]
- The ENLIGHTEN clinical program included 6 phase 3 studies that assessed the efficacy and safety of OLZ/SAM[2-7]
- Based on results of these studies, OLZ/SAM provides the established antipsychotic efficacy of olanzapine while mitigating olanzapine-associated weight gain
- Findings from real-world studies[8,9] indicate that OLZ/SAM initiation may result in clinically meaningful reductions in real-world disease burden (as evidenced by decreases in hospital-based healthcare resource utilization) and that longer treatment retention is associated with improved effectiveness (see Posters #62 and #63)

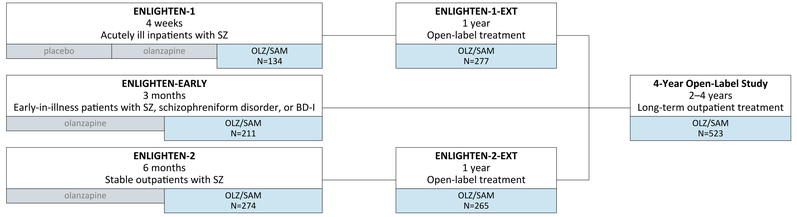
OBJECTIVE

- To summarize retention rates for patients on OLZ/SAM in the phase 3 clinical program

METHODS

- Retention data from 3 randomized controlled trials and 3 open-label extension studies were included (**Figure 1**)
- Demographics and clinical characteristics were summarized
- Proportions of patients who completed the OLZ/SAM treatment period were assessed descriptively for each study separately, as were reasons for discontinuation

Figure 1. Studies in the ENLIGHTEN Phase 3 Clinical Program



BD-I, bipolar I disorder; EXT, extension; OLZ/SAM, combination olanzapine and samidorphan; SZ, schizophrenia.

RESULTS

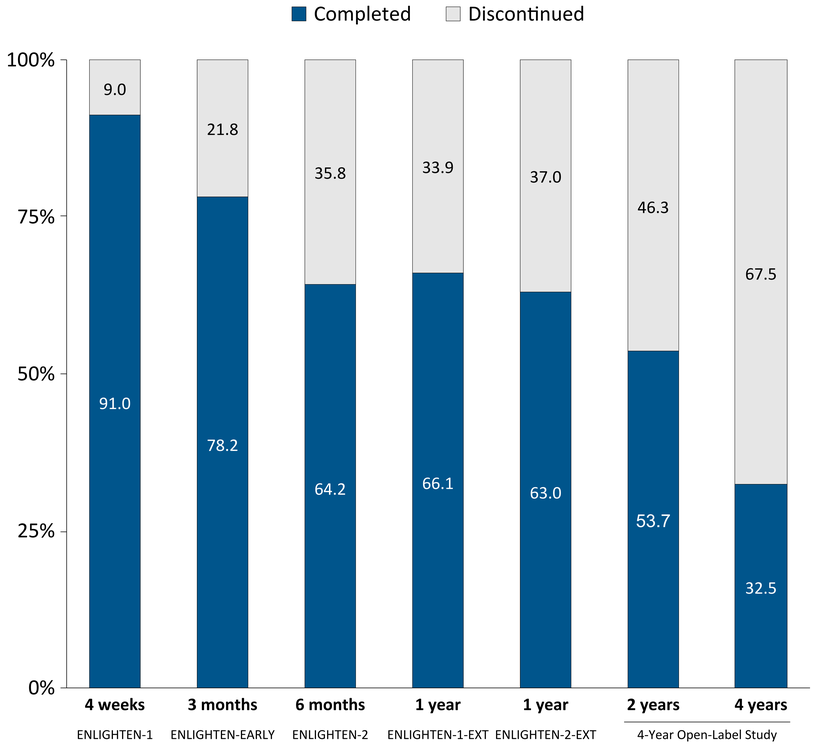
Table 1. Demographics and Clinical Characteristics at Baseline in Each Study

Characteristics	4 weeks ENLIGHTEN-1 (N=134)	3 months ENLIGHTEN-EARLY (N=211)	6 months ENLIGHTEN-2 (N=274)	1 year ENLIGHTEN-1-EXT (N=277)	1 year ENLIGHTEN-2-EXT (N=265)	4 years Open-Label Study (N=523)
Age, mean (SD), years	40.8 (12.6)	26.0 (6.1)	40.3 (9.8)	41.4 (11.3)	40.7 (9.7)	35.1 (12.2)
Male, n (%)	85 (63.4)	142 (67.3)	193 (70.4)	161 (58.1)	192 (72.5)	322 (61.6)
Race, n (%)						
White	87 (64.9)	139 (65.9)	63 (23.0)	218 (78.7)	64 (24.2)	380 (72.7)
Black	42 (31.3)	62 (29.4)	199 (72.6)	52 (18.8)	187 (70.6)	126 (24.1)
Weight, mean (SD), kg	77.9 (15.4)	71.6 (13.3)	77.2 (13.7)	79.1 (17.8)	80.6 (14.7)	77.4 (15.5)
BMI, mean (SD), kg/m^2	26.3 (4.5)	23.8 (3.3)	25.4 (3.1)	26.9 (5.1)	26.8 (3.8)	26.0 (4.3)
CGI-S,[a] mean (SD)	5.1 (0.7)	3.9 (0.8)	3.5 (0.6)	3.9 (1.0)	3.1 (0.7)	3.1 (0.9)

[a]From the full analysis set for ENLIGHTEN-1 (N=132), ENLIGHTEN-EARLY (N=202), ENLIGHTEN-2 (N=266), and ENLIGHTEN-1-EXT (N=248) and the safety population for ENLIGHTEN-2-EXT and the 4-Year Open-Label study.
BMI, body mass index; CGI, Clinical Global Impressions–Severity; EXT, extension.

Retention rates across the OLZ/SAM phase 3 clinical program

Figure 2. Retention Rates of Patients on OLZ/SAM Treatment



OLZ/SAM, combination olanzapine and samidorphan; EXT, extension.

Table 2. Reasons for Discontinuation Among Patients on OLZ/SAM Treatment

	4 weeks ENLIGHTEN-1 (N=134)	3 months ENLIGHTEN-EARLY (N=211)	6 months ENLIGHTEN-2 (N=274)	1 year ENLIGHTEN-1-EXT (N=277)	1 year ENLIGHTEN-2-EXT (N=265)	4 years Open-Label Study (N=523)
Reasons for discontinuation, n (%)						
Withdrawal by patient	8 (6.0)	20 (9.5)	23 (8.4)	43 (15.5)	36 (13.6)	133 (25.4)
Adverse event	2 (1.5)	10 (4.7)	33 (12.0)	16 (5.8)	15 (5.7)	44 (8.4)
Lack of efficacy	1 (0.7)	0	2 (0.7)	5 (1.8)	1 (0.4)	1 (0.2)
Lost to follow-up	1 (0.7)	11 (5.2)	22 (8.0)	19 (6.9)	22 (8.3)	37 (7.1)
Noncompliance with study drug	0	NA	8 (2.9)	8 (2.9)	12 (4.5)	0
Not determined[a]	NA	NA	NA	NA	NA	5 (1.0)
Pregnancy	0	0	1 (0.4)	1 (0.4)	2 (0.8)	2 (0.4)
Protocol deviation	0	3 (1.4)	1 (0.4)	1 (0.4)	8 (3.0)	20 (3.8)
Study terminated by sponsor	0	0	0	0	0	1 (0.2)
Other	0	2 (0.9)	8 (2.9)	1 (0.4)	2 (0.8)	92 (17.6)[b]

[a]Patients discontinued treatment, but their reasons for doing so were not collected. [b]Overall, 72 patients discontinued the study due to the Ukraine-Russia conflict.
EXT, extension; NA, not applicable; OLZ/SAM, combination olanzapine and samidorphan.

LIMITATIONS

- Please see the primary publications for the limitations inherent to each study[2-7]
- Differences in retention could be related to the different designs of the individual studies (eg, double-blind versus open label)
- These results may not be generalizable to all patients with schizophrenia or bipolar I disorder

CONCLUSIONS

- Overall, 70% of dosed patients completed studies ≤1 year in duration
- In the 4-year open-label study, retention rates were 53.7% at 2 years and 32.5% at 4 years
- Withdrawal by subject was the most common reason for discontinuation from each study, except for the 6-month trial (adverse event)

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AUTHOR DISCLOSURES

RSK has served as a consultant for and/or has received grants or speaking fees from Alkermes, Janssen-Cilag, Lundbeck, Merck, Minerva Neuroscience, Otsuka, Roche, Sunovion, and Teva. **CA** and **MEH** are or were employees of Alkermes, Inc., and may own stock/options in the company. **DM** is or was an employee of Alkermes Pharma Ireland Ltd. and may own stock/options in the company.

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