Qualitative Clinical Trial Exit Interviews Evaluating Treatment Benefit, Burden, and Satisfaction in Patients With Schizophrenia

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BACKGROUND

- The complex symptomology of schizophrenia can lead to considerable impairment, with sequelae ranging from quality of life decrements to increases in morbidity and mortality[1-3]
- Qualitative exit interviews conducted during clinical studies that capture the patient's voice may provide important supplemental information about the burden associated with schizophrenia and its treatment[4]
  – These data may include patient perceptions of treatment benefit and risk, expectations of treatment, unmet needs that remain despite treatment, and unanticipated challenges encountered with treatments of interest[4]
- Here, we describe qualitative methodology and report findings from exit interviews conducted to assess patient perceptions of disease burden and previous treatments, along with patient experiences during open-label treatment with OLZ/SAM, an investigational antipsychotic in development for the treatment of schizophrenia and bipolar I disorder

METHODS

Study Design and Patients

- A combination of olanzapine and samidorphan (OLZ/SAM) is in development for the treatment of patients with schizophrenia or bipolar I disorder[5]
- The ENLIGHTEN-2-extension (EXT) study (NCT02873208) enrolled outpatients with schizophrenia who had completed the antecedent 24 week ENLIGHTEN-2 study (NCT02694328)
  – Patients received once-daily OLZ/SAM (10–20 mg/10 mg) for up to 52 weeks
  – Primary results from ENLIGHTEN-2-EXT are presented in a companion poster[6] at this virtual meeting
- At the conclusion of ENLIGHTEN-2-EXT, patients either entered a 4-week safety follow-up period or continued into a long-term OLZ/SAM follow-up study lasting up to 4 years (ongoing; NCT03201757)
- Exit interviews were scheduled within 60 days of completing or discontinuing from the ENLIGHTEN-2-EXT for patients who entered the 4-week safety follow-up; exit interviews for those rolling over into the 4-year safety study could take place at any time following completion of the ENLIGHTEN-2-EXT study
  – Exit interviews were conducted in a subset of patients from ENLIGHTEN-2-EXT who spoke English fluently and were able to participate in a 60-minute interview
- Interviews were conducted by experienced qualitative researchers who used a semi-structured interview guide that was developed based on feedback from experienced clinical investigators (**Figure 1**)

Coding and Analysis

- Interviews were recorded, transcribed, and content coded using NVivo v11.0 (**Figure 1**)
- Once the initial coding was complete, broad content categories were refined and organized by theme according to the principles of grounded theory[7]
- Interviews were conducted until <5% of the information gathered was new (ie, saturation was reached)
  – Results presented in this poster are derived entirely from patient interviews, not from the primary ENLIGHTEN-2-EXT study data

Figure 1. Substudy Process for Patient Exit Interviews

Literature Review and Clinician Interviews
- Targeted literature review and 3 clinician interviews conducted
- Topics included schizophrenia disease state, the patient experience, and relevant trial details

Material Development and Ethics Approval
- A semi-structured interview guide was developed for use with patients
- An independent review board approved the study materials

Recruitment and Screening
- Patients identified and recruited
- Interviews scheduled for patients meeting the inclusion/exclusion criteria

Data Collection
- Exploratory, ≈60-minute interviews conducted in person, by telephone, or via webcam
- Following each interview, proper adverse event reporting procedures were followed

Analysis
- Interview transcripts were content coded and analyzed using NVivo v11.0

RESULTS

Interview Details and Patient Characteristics

- Out of a total of 266 patients, 41 exit interviews were conducted: 24 (58.5%) in person and 17 (41.5%) via telephone or webcam (video conference)
- At the time of the interview, 40 of the patients were continuing on OLZ/SAM and 1 had discontinued treatment
- Interviewed patients had a mean (SD) time since being diagnosed with schizophrenia of 15.0 (8.2) years
- Patients reported various living arrangements, including living with relatives or significant others (n=23; 56.1%), living alone (n=10; 24.4%), living with roommates (n=4; 9.8%), and living in transitional housing (n=4; 9.8%)
- The majority of patients were unemployed (n=30; 73.2%)

Burden of Disease: Schizophrenia Symptoms and Their Impact

Table 1. Schizophrenia Symptoms Experienced (N=41)

Symptom[a]	Experienced During Lifetime, n (%)	Experienced in Previous 30 Days, n (%)
Auditory hallucinations	36 (87.8)	18 (43.9)
Paranoia	24 (58.5)	9 (22.0)
Visual hallucinations	18 (43.9)	8 (19.5)
Anxiety/worry/panic	13 (31.7)	9 (22.0)
Easily mad/mood	11 (26.8)	3 (7.3)
Delusions	6 (14.6)	2 (4.9)
Negative thoughts/urges[b]	5 (12.2)	3 (7.3)
Olfactory hallucinations	1 (2.4)	0 (0)
Flat affect	1 (2.4)	0 (0)
No symptoms reported	0 (0)	9 (22.0)

[a]Patients may have reported >1 symptom. [b]Includes suicidal/self-harm thoughts and negative thoughts toward others.

Figure 2. Domains of Schizophrenia Symptom Impact and Select Patient Perspectives (N=41)

Impact [a]	Experienced During Lifetime, n (%)
Work	34 (82.9)
Hospitalization	30 (73.2)
Relationships	29 (70.7)
Self-esteem	27 (65.9)
Social isolation/avoidance of others	27 (65.9)
Emotional health	25 (61.0)
Daily activities	21 (51.2)
Cognitive or concentration difficulties	13 (31.7)
Physical health	13 (31.7)
Suicidality	13 (31.7)
Sleep	13 (31.7)
Substance use	9 (22.0)

Patient Perspectives

Work

I used to be a dishwasher and worked in restaurants. I used to be a cleaner, cleaned up kitchens, so I miss that. I miss it, but the way my mind is all messed up, **I can't hold a job** with my sickness, but I miss it.

Emotional Health

Emotionally, it's affected me by the voices telling me things that aren't true, or just harassing me and making me cry and **making me feel bad.**

Daily Activities

I don't drive. **I don't get out of the house.** Only to doctors' appointments. That's the only time I go out of the house. I don't bathe every day. I don't do my laundry very often. I don't function very well.

[a]Lifetime occurrence in ≥20% of patients; more than one impact may have been reported by each patient.
More than half of the patients interviewed reported negative lifetime impacts of schizophrenia symptoms with regard to employment, hospitalization, relationships, social activities, emotional health, and daily tasks.

Treatment Effects

- Patients reported being exposed to a variety of pharmacologic agents over the course of their illness
  – These most commonly included antipsychotics (n=39; 95.1%), serotonin modulators (ie, trazodone, n=12; 29.3%), selective serotonin reuptake inhibitors (n=11; 26.8%), benzodiazepines (n=7; 17.1%), and non-benzodiazepine hypnotics (n=6; 14.6%)
  – In patients reporting previous antipsychotic treatment, 26 (63.4%) had been exposed to quetiapine, 22 (53.7%) to risperidone, 20 (48.8%) to olanzapine, 15 (36.6%) to aripiprazole, and 9 (22.0%) to haloperidol at some point during their lifetime
- Most patients (n=32; 78.0%) reported benefits with previous medications, including alleviation of symptoms (eg, auditory/visual hallucinations, anxiety, and depression; n=22; 68.8%), improved sleep (n=11; 34.4%), and feeling more calm (n=8; 25.0%)
- However, patients' experiences with previous medications also included side effects affecting physical health (n=39; 95.1%), emotional or behavioral health (n=17; 41.5%), and cognitive functioning (n=5; 12.2%)
  – Lack of energy/drowsiness (n=23; 56.1%), weight gain (n=19; 46.3%), involuntary movements (n=8; 19.5%), and change in mood (n=8; 19.5%) were the most frequently reported drawbacks of prior medications

Perceptions of OLZ/SAM Treatment

Figure 3. Schizophrenia Symptom Reduction and Select Patient Perspectives Following Treatment With OLZ/SAM (N=41)

Improved Symptom[a]	Respondents n (%)
Auditory hallucinations	26 (63.4)
Concentration	14 (34.1)
Paranoia	13 (31.7)
Anxiety/worry	9 (22.0)
Depression	8 (19.5)
Visual hallucinations	7 (17.1)
Delusions	4 (9.8)
Mood swings	3 (7.3)
Racing thoughts	3 (7.3)
Suicidal thoughts	3 (7.3)
Headaches	2 (4.9)
Violent behavior	2 (4.9)
Irritability/agitation	1 (2.4)
Muscle tension	1 (2.4)
Negative self-talk	1 (2.4)
Personality	1 (2.4)

[a]Patients may have reported more than one symptom.

Patient Perspectives

Auditory Hallucinations

Oh yes, the medication help you out. Even if you hear voices it's to the minimal and then you learn to deal with not listening to it. It don't got complete control over you … **It's less voices and less louder.**

Concentration

I just get up and I do not feel scattered. **I can focus** and accomplish what I need. Before that, I was just kind of like a leaf in a big wind. I just went where the breeze took me. It is getting back to some sense of normality now because of the med so it is cool.

Paranoia

I'm not paranoid that much anymore. Yes, if there's a loud noise or something I'll kind of jump, but other than that it's … I'm actually doing really well lately.

Anxiety

I still have a little bit of anxiety but not as much as I used to have. I can get up and do things that I will be wanting to do.

Figure 4. Domains of Improvement Associated With Schizophrenia Symptom Reduction and Select Patient Perspectives Following OLZ/SAM Treatment (N=41)

Positive Impact[a]	Respondents n (%)
Emotional or mental well-being	26 (63.4)
Self-esteem	25 (61.0)
Social activity	25 (61.0)
Relationships	21 (51.2)
Daily activities	19 (46.3)
Sleep	17 (41.5)
Hospitilization	15 (36.6)
Physical health	15 (36.6)
Weight	11 (26.8)
General quality of life	9 (22.0)
Work	7 (17.1)
Energy	5 (12.2)
School	4 (9.8)
Stability	4 (9.8)
Coping	2 (4.9)
Incarceration	1 (2.4)

[a]Patients may have reported more than one impact.

Patient Perspectives

Emotional or Mental Well-being

- It makes me feel good. **I participate more. I smile more.**
- There's days where I feel good, I'm happy, and some days I feel depressed, so. But basically **it kind of keeps me even**, I think. Like, going straight.

Social Activities

It has helped me be able to enjoy the life. I don't have friends, but **I'm able to go out, like I said, and go to the … out in public** and not worry about people watching me. I don't have to be looking around, make sure nobody's following me home and stuff. I'm able to enjoy that … at least to be able to go out and not be stuck in the house just worrying.

Daily Activities

I can get up and clean my living room, scrub my toilets and stuff, scrub the bathtub and stuff. You know before I wouldn't do none of that stuff … **take out the trash, go shopping, cook.** I couldn't do all that stuff before, because I didn't feel like doing it.

Sleep

I sleep all night now ever since I've been on that medicine. I take my medicine every night at 8:00 and when I wake up I don't have no groggy head. About four or five months ago I missed one day because I work midnight, I woke up with a groggy head, I could see that that medicine really helped me. It keeps me sleep all night.

- In total, 23 patients (56.1%) reported side effects attributed to OLZ/SAM
  – Lack of energy (n=12; 29.3%), dry mouth (n=5; 12.2%), and dizziness (n=2; 4.9%) were most commonly reported
- Among 40/41 (97.6%) patients who provided a rating of their overall experience with OLZ/SAM, all (40/40; 100.0%) reported a positive experience (ie, ratings >3 on a scale ranging from 1 [not satisfied] to 5 [very satisfied])
  – Of these respondents, 60.0% (24/40) were very satisfied with OLZ/SAM treatment
- The majority of patients (n=35; 85.4%) preferred to continue OLZ/SAM vs switching to another medication

LIMITATIONS

- Among the 41/266 patients interviewed in this substudy, 40 (98%) completed the extension. As such, satisfied patients may be overrepresented in this analysis; therefore, the experience of patients in this substudy should not be applied more broadly to that of the ENLIGHTEN-2-EXT study or to the treatment effect of OLZ/SAM
- While the semi-structured format gave interviewers flexibility to ask questions conversationally and to explore patients' responses, this format may have led to missing data, as not every patient was asked the same questions
- Recall bias may have impacted the findings; however, interviewers were trained to establish rapport and were provided a list of common medication names for use during patient interviews to mitigate this potential effect
- Some patients reported difficulty attributing specific health experiences as a symptom, impact, or side effect of their schizophrenia or medication (eg, anxiety)

CONCLUSIONS

- Qualitative exit interviews following an open-label extension study of OLZ/SAM provided valuable insight into patients' perspectives regarding their disease burden and treatment experiences
- Most patients who participated in the exit interviews reported treatment satisfaction with OLZ/SAM that was associated with improvements in symptoms, function, health-related quality of life, and a preference to continue OLZ/SAM treatment
- Patient interview data may complement standard assessments of efficacy and safety, and qualitative assessments of patient experience should be incorporated into pivotal study design

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DISCLOSURES

A. Simmons, J. Carpenter-Conlin, L. Bessonova, and A.K. O'Sullivan are or were employees of Alkermes, Inc. D. McDonnell is an employee of Alkermes Pharma Ireland Limited. C. Saucier, M.K. White, A.M. Foster, and J.B. Bjorner have conducted research sponsored by Alkermes, Inc. O. Lapeyra has no conflicts to disclose. D.P. Walling has received research support from Acadia, Alkermes, Inc., Allergan plc, Astellas, Avanir, Biohaven, Boehringer Ingelheim, CoMentis, Intra-Cellular, J&J PRD, Janssen, Lundbeck, Lupin, Novartis, Noven, Roche, ROVI, Sage, Sunovion, and Takeda; he has also served as a consultant for Janssen and Otsuka.

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