INTERCEPT-AD: Understanding the Patient Experience and Expectations for Treatment Through Qualitative Interviews Among Trial Participants with Early Alzheimer's Disease and Their Study Partners

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Introduction

- Incorporation of the patient voice has been recognized as a fundamental component of drug development.
  - Recent legislation has codified the importance of patient experience data in regulatory decision-making.[1]
- Qualitative interviews conducted among clinical trial participants are an established method of ascertaining the patient experience.
- While often administered in later trial phases, qualitative interviews can provide important insight into the patient journey when conducted among participants in early trial phases.
  - Information regarding the symptoms that patients find most bothersome, as well as what would constitute a meaningful treatment benefit, can help inform the measurement of concepts in subsequent trials.
  - It is also important to understand patient expectations regarding treatment.
- As part of a phase 1 study, we conducted semi-structured qualitative exit interviews among a subset of participants with mild cognitive impairment (MCI) or mild Alzheimer's disease (AD) and their study partners; topics included disease experience and expectations for treatment.

Methods

- A subset of trial participants was interviewed as part of the ACU-001 (INTERCEPT-AD) study, a phase 1 study evaluating the safety and tolerability of the monoclonal antibody sabirnetug (ACU193).
  - Interviews occurred within 7 days of the end of study visit, were approximately 90 minutes long, and included both participants and study partners.
- Participants were asked to report their most problematic symptoms, to describe what they would hope to gain from a new AD treatment, and what changes would be meaningful.
  - The interview guide was developed in accordance with FDA Patient Focused Drug Development guidance.[2,3]

Sample Questions: Disease Experience

Participant

"When did you first start noticing any memory or thinking problems? What types of problems did you notice?"

"Of the problems that you mentioned, what are the three most challenging for you?"

"What is a typical day like for you lately, in terms of your memory or thinking? What is a good day like? What is a bad day like?"

Study Partner

"Can you describe any concerns that you had around the time that *[participant's name]* sought medical advice related to memory or thinking problems?"

"Thinking about *[participant's name]* memory or thinking problems, what are the three most challenging aspects for you? Why?"

Sample Questions: Treatment Expectations & Meaningful Change

Participant

"If there were a new treatment for memory or thinking problems like you experience, what would you would most hope to see as a result of the treatment?"

"How would you describe your ideal treatment in terms of how it would affect your memory or thinking?"

Study Partner

"Can you describe any changes in *[participant's name]*'s memory or thinking problems that if they happened, might seem small, but would make a big difference to you or your family?"

"If there were a new treatment for memory or thinking problems like your loved one experiences, what would you hope to see as a result of the treatment? "

- Coding and analysis of the transcripts followed principles of qualitative thematic analysis, conforming to best practices in the field.[4]

References

1.) Eastern Research Group, Inc. *Assessment of the Use of Patient Experience Data in Regulatory Decision-Making*; 2021:1-3.
2.) FDA CDER. *Patient-Focused Drug Development: Methods to Identify What is Important to Patients;* 2022.
3.) FDA CDER: *Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision-Making;* 2023.
4.) Guest G, et al. *Applied Thematic Analysis*. Sage Publication; 2012

Results

Participant Demographics

- Twenty-eight participants and their study partners were interviewed, representing 43% of the total randomized trial population.
- Among interviewees, the mean participant age was 70.8 (SD 7.2) and ranged from 56 to 85.
  - The majority of participants were female (64.3%), White (96.4%) and not Hispanic (96.4%).

Disease Experience

- Participants reported a broad array of problems consistent with AD; the most frequent included difficulty with memory or cognitive functioning (96.4%). **Table 1.**
- Getting lost, either while driving or walking through parking lots, stores, or the neighborhood, was commonly described by participants as a symptom of memory loss (71.4%).
- Notably, the majority of participants reported problems with mood (60.7%) and difficulty communicating (57.1%).
- Within each of these groupings, specific problems varied among participants:
  - For memory and cognitive functioning, higher numbers of participants reported forgetting appointments, names, and losing things (81.4%), while fewer reported experiencing confusion (11.1%).
  - Getting angry or mad and feeling frustrated were the most frequently reported problems with mood (47.1% and 41.2%, respectively); fewer participants reported agitation/anxiety/stress (23.5%) and feeling isolated (5.9%).

Treatment Expectations

- Nearly every participant expressed the desire for a new treatment that would either keep the disease from getting worse (89.3%) or slow the progression down (89.3%); these were equated with the maintenance of functional abilities. **Table 2.**
  - Being able to maintain the ability to recognize loved ones and maintaining or improving communication abilities were also perceived as important benefits of a new treatment.
- Half of the participants stated that a cure or return to their condition before the onset of AD was most desirable.
  - Participants recognized that a cure may not be possible, and they would be satisfied with a new treatment that either stopped progression or slowed down progression.
- Broadly, participants felt that a general improvement in their memory would make a positive difference in their lives.
  - Specifically, being able to follow through with tasks, not getting lost, and being able to have full conversations without losing their train of thought were important.

Table 1. Experience with AD

Problems Due to AD[1]	n (%)
Memory and cognition	**27 (96.4)**
Forgetting appointments, names, losing things	22 (81.4)
Finishing tasks, losing focus	21 (77.8)
General memory difficulties	14 (51.9)
Confusion	3 (11.1)
Getting lost	**20 (71.4)**
While driving	18 (90.0)
While walking	3 (15.0)
Communication	**16 (57.1)**
Repetitive questioning	10 (62.5)
Losing train of thought	7 (43.8)
Word finding	5 (31.3)
Changes in mood	**17 (60.7)**
Getting angry or mad	8 (47.1)
Feeling frustrated	7 (41.2)
Agitation / anxiety / stress	4 (23.5)
Isolated	2 (5.9)
Feeling tired	**3 (10.7)**

AD = Alzheimer's disease
[1]Participants could have provided multiple responses across and within concepts

Participant Quotes

Study Partner ACU12
"The first one would be, obviously, cure it, the second one would be stop it, and the next one would be slow it down."

Participant ACU11
"... I could take a drug and keep me where I am exactly right now, I could live a happy and prosperous life for the rest of my life."

Participant ACU34
"For myself I would hope that I could cut down on some frustrations when I'm in a conversation and can't communicate what I'm trying to say. So that would be probably my biggest wish, or biggest hope."

Study Partner ACU05
"Well, if he was able to do a task that involved more than one step. After one step of anything he cannot retain what I need to do next, so he can turn the phone on, but now what do I do, how do I–he can make a phone call, he can read his email, he can pull up the news, but if it goes further than that, if it involves a password or downloading something, anything with a list, he can't go past the first step."

Study Parnter ACU52
"You know, I just want her to be able to remember me."

Study Partner ACU35
"It was a little bit more than her just forgetting names like she normally did. You know, it was a little more often, and maybe even somebody who she should really know the name, you know, she would have a hard time recalling that. Those kinds of little things."

Study Partner ACU14
"...his personality has changed, he was always planning things, he's the extrovert, I'm in the *[sic]* introvert, and we always had stuff going on, and now he doesn't want to do anything, he sits in his room all day, which is disturbing, and I probably should be doing more like taking him for walks and stuff."

Table 2. Treatment Expectations

Treatment Expectations[1]	n (%)
Slow worsening	25 (89.3)
Keep from getting worse	25 (89.3)
Memory/cognition	20 (71.0)
Reversal/cure	14 (50.0)
Removal of Plaques	7 (25.0)
Maintain functioning	5 (17.9)
Recognize loved ones	4 (14.3)
Maintain communication	3 (10.7)
Improve mood	2 (7.1)

[1]Participants could have provided multiple responses.

CONCLUSIONS

- Overall, the study findings highlight the need to contextualize clinical trial results by incorporating the patient voice.
  - Problems reported by participants were typical to AD, although there was heterogeneity in overall AD experience.
- Many participants reported changes in their mood, including feelings of anger, frustration, anxiety and stress, and depression and isolation.
  - Challenges with communication were also particularly bothersome to participants.
- Being able to maintain the ability to recognize loved ones and maintaining or improving communication abilities were mentioned as desired benefits of a new treatment.
  - Participants also equated stopping or slowing disease progression with being able to maintain functional abilities.