Incorporating the Study Participant's Voice into Early Development of ACU193 for Early Alzheimer's Disease: A Qualitative Interview Study Following Participation in the INTERCEPT-AD Study

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Background

- Patient experience data is becoming increasingly recognized as a crucial component of clinical trials.
  - The importance of incorporating the patient voice into drug development has been codified by recent legislation[1]
- Qualitative interviews conducted among clinical trial participants are an established method of ascertaining the patient experience.
  - Interview topics often include disease and treatment experience, assessment of meaningful change, and clinical outcome assessment score interpretation[2,3]
- Interviews conducted early in development are not commonly reported, although they can provide valuable participant perspective.
  - Study participants can provide insight into the trial experience and decision-making regarding their enrollment
- 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 to obtain feedback on disease experience, treatment expectations, trial experience, and the decision-making process preceding trial enrollment. Results pertaining to decision-making regarding trial participation and the subsequent trial experience are presented.

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 ACU193.
  - Interviews occurred within 7 days of the end of study visit, were approximately 90 minutes long, and included both participants and study partners, the latter of whom were interviewed separately
- Trial participation topics included referral source, motivations for participating, individuals involved in the decision-making, and concerns regarding study medication and procedures.
- Questions regarding trial experience assessed the positive and negative aspects of participation.
- The semi-structured interview guide was developed in accordance with FDA Patient Focused Drug Development guidance.[3,4]
- Coding and analysis of the transcripts followed principles of qualitative thematic analysis, with additional features drawn from grounded theory, conforming to best practices in the field.[5-8]
- Sample size was based on concept saturation of the factors of trial participation (i.e., pre-trial concerns and post-trial reported burdens). Concept saturation is the point at which no new relevant information is elicited in the data collection process.[8,9]

Results

- A total of 28 participant and study partner dyads took part in the exit interview study. The mean (SD) age was 70.8 (7.2); patient age ranged from 56 to 85 (median = 71). Most patients were female (64.3%), White (96.4%), and not Hispanic (96.4%).

Decision-Making Regarding Trial Participation

- Participants and their caregivers reported 34 unique concepts related to factors surrounding participation in INTERCEPT-AD, including referral sources, decision-making resources and factors, and burdens experienced during the study. Saturation of concepts was reached within 24 interviews (**Table 1**)
- Interviewed participants first heard about INTERCEPT-AD primarily from social media (n = 13; 46.4%) or their physicians (n = 10; 36.0%).
  - A few (n = 5; 17.9%) noted they heard about the trial from friends or family.
  - When deciding whether to enroll in the study, several participants (n = 11; 39.3%) sought help from family members while others (n = 7; 25.0%) decided independently. Physicians were less commonly reported as a resource (n = 2; 7.1%).
- Participants were motivated to enroll not only to benefit themselves (n = 20; 71.4%), but because doing so could potentially benefit others in similar situations (n = 12; 42.9%).
  - Several participants mentioned the added benefit of taking early action about AD (n = 8; 28.6%) and getting more information about their condition (n = 7; 25.0%).

> "I can't idly sit by and watch the memory issue deteriorate. So now, of course, there's nothing that's available now prescribed by physicians. So, the only other recourse was to go through a clinical trial for an experimental drug. And so I wasn't satisfied just to sit by and watch her memory deteriorate without making some effort."
> [Caregiver, ACU40]

> "...we were excited with the possibility of her getting the medicine–nobody knowing for sure–of it possibly helping her or stopping it and if nothing else helping other people. That was the one thing that we were all excited about. She's here to offer herself to help out other people as well if possible and we left with that same feeling."
> [Caregiver, ACU01]

- 12 (42.9%) participants expressed concerns about enrolling in INTERCEPT-AD; pre-trial apprehensions revolved primarily around potential side-effects (n = 7; 25.0%)

Clinical Trial Experience

- A majority (n = 18; 64.8%) expressed appreciation for the care and attention received from the site staff.
- Burdens of trial participation were largely related to four challenges: 1) distance to clinics, 2) time commitment required to participate, 3) issues with study procedures, and 4) a desire for more information about the study medication (**Figure 1**)

> "The worst thing was the need for bloodwork and–which in itself was not a problem, but I had a few nurses who had these big needles and they got blood out of me. It was a horrendous thing. I complained about it. Why–why so much bloodwork, you know? And the needles were big."
> [Patient, ACU07]

> "I think it would be nice [laughs] to, now that we've done everything, at least give us the information, did anything work, did we get a drop in the amyloid, did the MRI show any improvement? We'd like to get some results, that was the only frustrating thing."
> [Caregiver, ACU05]

Table 1. Saturation Table of Trial Participation Factors

	Transcript Group						
Concept / Factor	1 (n = 4)	2 (n = 4)	3 (n = 4)	4 (n = 4)	5 (n = 4)	6 (n = 4)	7 (n = 4)
Referral Source							
Doctor / Physician	X	X	X		X	X	X
Friends or Family member	X	X	X				X
Social Media		X	X	X		X	X
Other				X	X		
Source of Help with Trial Participation Decision-Making							
Family	X	X		X	X		
No one / Self	X		X	X	X	X	X
Doctor / Physician		X			X		
Other			X	X		X	
Pre-Trial Reasons for Trial Participation							
Benefit to others	X	X	X	X	X	X	X
Benefit to self	X	X	X	X	X	X	X
Taking action about AD early	X	X			X	X	X
Getting more information about AD		X	X		X	X	X
Physician advised		X	X			X	X
Pre-trial Concerns							
Side effects							
Brain bleed	X					X	
General side effects		X				X	
Blood clots					X		
Taking more medication			X				
Concerns of study procedures							
Lumbar punctures			X				
Blood draws			X				
Scans (PET / MRI)			X				
Getting placebo				X			X
Time commitment						X	
Post-trial Reported Burdens							
Distance to clinics	X	X	X	X	X	X	X
Study Procedures							
Cognitive tests	X	X	X	X	X	X	X
Scans (MRI / PET)		X			X	X	
Lumbar punctures		X	X	X	X	X	
Blood draws		X	X		X	X	X
Preference for pill over IV administration			X				
Time commitment							
Length of stay of visits	X	X	X	X	X	X	X
Scheduling difficulties		X	X	X		X	X
Prefer more information							
More information about study drug	X	X	X	X		X	X
Not knowing if on study drug or placebo	X		X				
No improvement in symptoms			X	X			
Preferred a longer trial time period						X	
# of New Concepts	13	9	7	2	1	2	0
% of New Concepts (N = 34 Unique Concepts)	38.2	26.5	20.6	5.9	2.9	5.9	0.0
Cumulative % of New Concepts	38.2	64.7	85.3	91.2	94.1	100.0	100.0

Figure 1. Burdens of Trial Participation

Distance to Clinics

A majority of participants discussed driving distances to the clinics (n = 17; 60.7%).

Time Committement

Other participants discussed challenges with the length of inpatient stay or visits which often included long waits between procedures (n = 15; 53.6%).

Issues with Study Procedures

Participants also expressed some reservations around some of the study procedures, including the cognitive tests (n = 12; 42.9%), blood draws/needles (n = 9; 32.1%), and lumbar punctures (n = 7; 25.0%).

Desire for More Information on Study Medication

Participants also mentioned a desire for more information on the study medication, particularly which treatment group they were in, as well as receiving results of the scans (n = 12; 42.9%).

Conclusions

- Participants and their study partners reported a broad array of factors related to participation in the INTERCEPT-AD study
- Findings regarding burdens of participation can be used to inform operational aspects of subsequent trial phases of ACU-193
- The desire among study participants for more information should also be considered

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References

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