INTERCEPT-AD: A Gender Analysis of the Phase 1 Experience Among Trial Participants with Early Alzheimer's Disease and Their Study Partners

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Introduction

- Participant recruitment and retention pose significant challenges to the completion of Alzheimer's disease (AD) clinical trials, particularly regarding adequate representation of affected groups.[1,2]
  - Women are disproportionately burdened by AD compared to men, although it is uncertain whether the proportion of female AD trial participants adequately reflects that of the AD population.[3-5]
- Maintaining gender balance is presently of most relevance, as the quantity and nature of current AD trials now require a greater number of and more commitment among participants.[6]
- Understanding motivations surrounding the decision to enroll in AD trials and the positive and negative aspects of the trial experience can provide insight into the study participant journey.
  - Previous research has reported that AD trial participants expressed altruistic motivations and a desire for personal benefit as reasons for trial participation.[7]
  - Evaluating findings by participant characteristics, including gender, can illuminate differences that may be applied to later trial stages to aid in both study recruitment and retention.
- As part of a phase 1 study for mild cognitive impairment (MCI) or mild Alzheimer's disease (AD), we conducted semi-structured qualitative exit interviews among a subset of participants and their study partners to obtain feedback on topics that included the decision-making process preceding trial enrollment and the overall trial experience; results were then examined by participant gender.

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.
- Study participant/study partner dyads were defined as female or male according to the gender of the study participant as it was captured in the main study protocol; study partner gender was not obtained.
- 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.

Sample Questions:
Decision to Enroll in the Trial

"Why did you choose to participate in this clinical trial?"

"Who helped you make the decision to participate in the trial? How did they help you make the decision?"

"When you were deciding whether or not to participate in the clinical trial, did you have any concerns about participating in the trial? What were those concerns?"

Sample Questions:
Clinical Trial Experience

"Can you describe what it was like to be a participant in the clinical trial?"

"What was the most rewarding aspect of participating in the clinical trial?"

"What was the most challenging aspect of participating in the clinical trial?"

- Coding and analysis of the transcripts followed principles of qualitative thematic analysis.[8]
- Results between genders were highlighted when: 1) the percentages of male and female dyads reporting a concept differed by at least 15%, and 2) the number of dyads reporting a concept was at least five for one or both gender groups.

References

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Results

Participant Demographics
- Twenty-eight participants (64.3% female) and their study partners were interviewed, representing 43.1% of the total randomized trial population (n=65; 53.8% female).
- Among interviewees, the mean participant age was 70.8 (SD 7.2) and ranged from 56 to 85.
- The majority of participants were White (96.4%) and not Hispanic (96.4%).
- Demographic characteristics were similar to the overall INTERCEPT-AD cohort in terms of age and race, although the percentage of female and Hispanic representation were higher and lower, respectively, among the interview study cohort (64.3% female and 3.6% Hispanic for the interview study cohort vs. 53.8% and 15.4% for INTERCEPT-AD overall).

Overall Concepts Reported
- Participants and their study partners 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. (Table 1)

Decision to Participate in a Clinical Trial
- Reasons for participation centered around benefiting others and self, taking early action about AD, and getting more information about their condition.
- More dyads with female participants reported the desire to obtain more information about AD (33% vs. 10% of dyads with male participants) and the desire to benefit others as reasons for study participation (50% vs. 30% of dyads with male participants).
- Dyads with female study participants accounted for 100% of those that stated they independently made the decision to enroll.
  - More dyads with male participants reported receiving help from family when deciding to enroll (50% vs. 33.3% of dyads with female participants.

Participation in INTERCEPT-AD
- Burdens of trial participation were related to: Distance to clinics, time commitment required to participate, study procedures, and desiring more information about the study medication.
  - For study procedures, reservations were around the cognitive tests, blood draws/needles, and lumbar punctures.
- More dyads with female participants reported being burdened by cognitive tests (55.6% vs. 20% of dyads with male participants) and blood draws (38.9% vs. 20% of dyads with male participants).
- More dyads with male participants reported being burdened by the length of study visits (70% vs. 50% of dyads with female participants) and expressed a desire to receive study results (60% vs. 33.3% of dyads with female participants).

Table 1. Trial Participation Factors: Overall and by Gender

	Overall N = 28	Female N = 18	Male N = 10	% Difference (Female – Male)[2]
Referral Source[3]				
Doctor or Physician	35.7 (%) 10 (n)	38.9 (%)[1] 7 (n)	30.0 (%) 3 (n)	8.9
Social Media	46.4 13	44.4 8	50.0 5	-5.6
Friends/Family	17.9 5	11.1 2	30.0 3	-18.9
Pre-Trial Reasons for Participation				
Getting more information about AD	**25.0** **7**	**33.3** **6**	**10.0** **1**	**23.3**
Benefit to Others	**42.9** **12**	**50.0** **9**	**30.0** **3**	**20.0**
Benefit to Self	71.4 20	72.2 13	70.0 7	2.2
Taking action about AD early	28.6 8	22.2 4	40.0 4	-17.8
Physician advised	14.3 4	11.1 2	20.0 2	-8.9
Source of Help in Participation Decision-Making				
No one or Self	**25.0** **7**	**38.9** **7**	**0** **0**	**38.9**
Family	**39.3** **11**	**33.3** **6**	**50.0** **5**	**-16.7**
Doctor	7.1 2	5.6 1	10.0 1	-4.4
Pre-Trial Concerns				
Side effects (any)	25.0 7	27.8 5	20.0 2	7.8
Taking more medication	3.6 1	5.6 1	0 0	5.6
Concerns of study procedures	7.1 2	5.6 1	10.0 1	-4.4
Getting placebo	7.1 2	11.1 2	0 0	11.1
Time commitment	7.1 2	11.1 2	0 0	11.1
Study Likes				
Site Staff	64.3 18	61.1 11	70.0 7	-8.9
Uber to Visits	3.6 1	5.6 1	0 0	5.6
Post-trial Reported Burdens				
Distance to clinics	60.7 17	55.6 10	70.0 7	-14.0
Study Procedures				
Cognitive tests	**42.9** **12**	**55.6** **10**	**20.0** **2**	**35.6**
Blood draws	**32.1** **9**	**38.9** **7**	**20.0** **2**	**18.9**
Scans	14.3 4	11.1 2	20.0 2	-8.9
Lumbar punctures	25.0 7	16.7 3	40.0 4	-23.3
Time commitment issues				
Length of visits	**57.1** **16**	**50.0** **9**	**70.0** **7**	**-20.0**
Scheduling difficulties	25.0 7	22.2 4	30.0 3	-7.8
Prefer more information				
More information about study drug	10.7 3	11.1 2	10.0 1	1.1
Not knowing if on drug or placebo	**42.9** **12**	**33.3** **6**	**60.0** **6**	**-26.7**

[1]%= n/N, the percentage of dyads with participants in each gender (n) who mentioned the concept out of all dyads in each gender (N)
[2]**Bold**=The difference between genders in the percentage of dyads who mentioned the concept is ≥ 15.0%; Negative values=More dyads with male participants mentioned concept
[3]Dyads could mention more than one concept within each category

Participant Quotes

Participant, ACU28 - *female*
"I'm hoping that they can come up with a drug not just for me, but for a lot of other people that are suffering with this."

Participant, ACU40 - *female*
"I think the most rewarding aspect of it is that at least we were trying to do something Instead of just sitting we were doing something. And to me that was the most rewarding aspect of it. The scans, the different–the things that they did there, I can't remember right now, but they were–but just the overall experience of it is–was so rewarding. At least–like I said, at least we were doing something and they were doing something."

Participant, ACU34 - *female*
"Well, I just wanted to throw the computer out the window a few times but other than that or, you know, [laughs] get up and walk out. I know they were necessary but they were–frustrating."

Participant, ACU09 - *male*
"After the trial, you know, tell me what is happening. You know, did we have the drug or did not and stuff like that, but I know that you can't do that."

CONCLUSIONS

- A broad array of factors related to participation in the INTERCEPT-AD study were reported among study participants and partners.
- Certain factors differed more than others by participant gender, including motivations for participation and perceived burden of some study procedures.
  - More dyads with female participants reported independent decision-making surrounding trial enrollment and also burdens surrounding cognitive tests and blood draws.
  - More dyads with male participants were burdened by the length of study visits and expressed a desire to obtain study results.
- Gender-based analyses were exploratory in nature; a larger sample size is needed to fully ascertain any differences between groups.
- Results from the overall sample align with those reported in previous research, while findings around potential gender differences provide additional context