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Participant satisfaction with learning Alzheimer's disease clinical trial results

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Abstract

To achieve the national agenda of developing improved therapies for Alzheimer's disease (AD), greater community engagement and public trust are needed. Ensuring satisfaction among those enrolling in studies is one means to facilitate these goals. We performed telephone interviews to assess satisfaction with the disclosure of study results among thirteen individuals who were enrolled as participants or study partners in a Phase 3 clinical trial for mild AD. Most participants were at least somewhat satisfied with the manner of disclosure. Two participants were dissatisfied; these participants learned results through the media. Most participants indicated that their preference would have been to learn results through the site study team. Ten participants indicated that they wished to learn randomization assignment and several indicated a desire to learn more details about study data. Future trials should undertake a systematic approach to disclosing study results and assessing participant satisfaction with the process.

Introduction

Clinical trials face consistent barriers to recruitment, due in part to skepticism and distrust toward research.[1, 2] Improving public trust in research may be essential to expediting achievement of the national goal of developing effective therapies for Alzheimer's disease (AD).[3] One mechanism to improve trust is to ensure positive experiences by study participants.

Providing aggregate study results to participants at the conclusion of a trial represents a minimal ethical standard and is an important aspect of trial conduct that improves public

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trust in the research enterprise.[4] Yet, the consistency with which results are shared with participants and their satisfaction with this process are largely unstudied. To address this need and to better understand how participant satisfaction relates to the manner in which trial results are disclosed, we interviewed participants from a recently completed clinical trial for mild Alzheimer's disease (AD).

Methods

The purpose of this study was to better understand how AD trial participants and study partners learn trial results, whether they are satisfied with this experience, and whether this experience affects their attitudes toward AD clinical research. To do so, we performed a telephone interview study with participants in a recent Phase 3 industry-sponsored clinical trial. The UC Irvine Institutional Review Board (IRB) approved this study. Verbal informed consent was performed by telephone and acknowledged in writing by the investigator performing the interview.

The Progress of Mild Alzheimer's Disease in Participants on Solanezumab Versus Placebo, EXPEDITION-3, study enrolled mild AD patients (Mini Mental State Exam score range 20-26) to an 18-month study of the monoclonal antibody against amyloid beta, solanezumab, or placebo (https://clinicaltrials.gov/ct2/show/NCT01900665). Participants received monthly infusions of study medication and underwent routine examination including neuropsychological assessment of study outcome measures. All participants were required to enroll with a knowledgeable informant, or study partner.

Individual participants who completed their 18-month double blind period were invited to rollover into an open-label extension. The final participants in EXPEDITION-3 completed the double-blind portion in October 2016. The open-label extension period continued until November 23, 2016, when a press release announced that development of solanezumab in mild AD would be halted because it did not meet the primary efficacy outcome of the study (https://investor.lilly.com/releasedetail.cfm?ReleaseID=1000871). Several media outlets, including scientific publications, popular press television, radio, and print outlets, and Internet websites, released stories about the announcement.

Immediate formal communication of trial results to study participants was not instructed by the trial protocol or through communication from the sponsor. At our site, we called each of the 11 participants (of whom 10 had enrolled in the open-label study) and their study partners within one week of the press release to inform them of the available trial results. Blinding assignments were not available at the time of these notification phone calls.

To recruit to the current study, we mailed an invitation letter or invited participants verbally at an in-person study closure visit. Additionally, an IRB-approved flyer for the interview study was shared with colleagues at two nearby EXPEDITION-3 sites. Information about the number of participants at these sites was not available.

A single member of the research team (HN)conducted the interviews separately with participants and their study partners. After a brief description of the EXPEDITION-3 study, participants' knowledge and participation in the study were confirmed. We outlined the

timeline of events for the announcement of the EXPEDITION-3 results and used forced choice questions to assess the approximate timing and manner through which participants learned results. We examined participants' satisfaction with the manner through which they learned results, preferences for the manner of learning results, overall desire to learn results and randomization assignment, and likelihood of participating in future AD trials. In total, the survey included 16 forced choice questions. Four additional questions collected brief participant demographic information including age, race, ethnicity, and years of education. Completion of the survey took approximately 15 minutes. A copy of the interview guide is available by emailing the corresponding author. Study data were collected and managed using Research Electronic Data Capture (REDCap).[5]

Results

We interviewed five trial participants and eight trial study partners (Table 1). Two study partners had participated in the trial at outside institutions. Interviews were conducted between February 1, 2017 and September 12, 2017 (approximately 2-10 months after the sponsor press release). One participant stopped the interview prior to completion; their available data were included in analyses.

Each study partner, but only one participant, acknowledged being aware of the trial results prior to the study interview. Two study partners indicated that they learned the results through direct interaction with the study site. Five study partners and one participant learned the results by seeing a news story on traditional media (television, radio, or print). One study partner learned the results by seeing a news story on the web or social media.

As shown in Table 2, among those who acknowledged being aware of the results, three study partners were very satisfied, three study partners and one participant were somewhat satisfied, and two study partners were very dissatisfied with the manner in which they learned the study results. Dissatisfied study partners learned the results through traditional media (n=1) or through the web or social media (n=1).

Two participants who learned the study results through direct communication from the study team indicated that this was their preferred method. Each of the six participants who learned the results through the media indicated that they would have preferred to learn the results directly from the study team (two would have preferred in-person visit, one by letter, one by email, and two by a telephone call). One study partner would have preferred to learn the results directly from the sponsor.

Two study partners and one participant indicated that they had no preference around learning the participant's randomization assignment. Six study partners and four participants strongly desired to learn the randomization assignment.

When asked how likely they would be to enroll in another AD trial of a drug targeting amyloid, five study partners and three participants indicated they would be extremely likely, one participant was somewhat likely, two study partners were somewhat unlikely, and one study partner was extremely unlikely. When asked how likely they would be to enroll in an AD trial of a drug targeting something other than amyloid, five study partners and two

participants indicated they would be extremely likely, two study partners and two participants were somewhat likely, and one study partner was extremely unlikely.

Discussion

We report data from a small number of participants and study partners in a Phase 3 clinical trial that indicate 1) patients and family members involved in clinical trials desire to learn study results,2) that they prefer to do so through the site staff,[6-8] and 3) that learning trial results through the media may risk dissatisfaction and the degradation of public trust.[4] Those dissatisfied with the manner in which they learned results, nevertheless, remained willing to consider enrolling in future trials.

We endorse the assertion that participants should be first to know trial results.[9] Arranging this communication through participant-preferred modalities may present challenges to sponsors. Systematic contact with participants, especially for large trials or if in-person sessions are held to disclose trial results, has cost. Complications may arise when participants have died, including determining with whom results should be shared. Delays in acquiring IRB approval for the disclosure of completed trial results could interfere with media release timelines for industry-sponsored research and cause participants to learn results in a less formalized manner. None of these barriers are insurmountable. We propose that trial protocols should outline a plan for sharing topline results and randomization assignments. Plans should include timelines and potential adjustments for early trial stopping as well as open-label extension. Planning for results dissemination during protocol development would alleviate any delays related to IRB review and ensures consistent practices across sites.

Most participants wanted more information than was made available to them. Ten out of thirteen participants (including both patients and study partners) wished to learn the patient's randomization assignment in the double-blind portion of the study. During the study interviews, multiple participants voiced their desire to know more than the top line results of the study,[10] including "*the statistics of how much it helped…even though it wasn't significant enough to pursue FDA marketing*." Thus, brief presentations of at least top line safety and efficacy data may be essential to ensure participant satisfaction.

These results represent the experiences of only a few participants in a single trial. Other limitations of this study include that the interviews were performed by a member of the study site staff, potentially biasing responses toward the site as a preferred method of disclosure. Participants self-selected enrollment and the timing of the interviews, relative to the public announcement of results, was variable and lengthy in some cases. This creates the potential for error in recollection or change in attitude over time. A more systematic approach of sharing results but also assessing participant satisfaction with the process should be undertaken. AD trial networks, especially those funded by the National Institutes of Health, are poised to instruct this important ethical issue that may also improve public perception of the research enterprise.

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Table 1

Description of the interview participants.

Characteristic	Participants	Study partners
n	5	8
Female, n	3	4
Age, mean (SD)	72.8 (9.6)	74.8 (10.5)
Education, mean (SD)	14.4 (2.8)	15.6 (2.0)
Race		
Caucasian, n	4	7
Asian American, n	1	1
Latino ethnicity, n	0	1

Table 2

Participants' and study partners' manner of disclosure, satisfaction, and preference

Subject	Type	Actual Manner of Disclosure	Level of Satisfaction with Disclosure	Preferred method of Disclosure
1	Study partner	Traditional news media	Very satisfied	In-person meeting with study team
2	Study partner	Traditional news media	Somewhat satisfied	Telephone call from the study team
3	Study partner	Traditional news media	Somewhat satisfied	In-person meeting with the study team
4	Study partner	Traditional news media	Somewhat satisfied	Letter from the study team
5	Study partner	Internet news/social media	Very dissatisfied	Email from the study team
6	Study partner	Traditional news media	Very dissatisfied	Directly from study sponsor
7	Study partner	Telephone call from the study team	Very satisfied	As was disclosed
8	Study partner	Telephone call from the study team	Very satisfied	As was disclosed
9	Participant	Traditional news media	Somewhat satisfied	Telephone call from the study team
10	Participant	Study interview		As was disclosed
11	Participant	Study interview		In-person meeting with study team
12	Participant	Study interview		In-person meeting with study team
13	Participant	Study interview		Email from the study team