CLT-03

Input From People Living With ALS and Their Caregivers Into Drug Development

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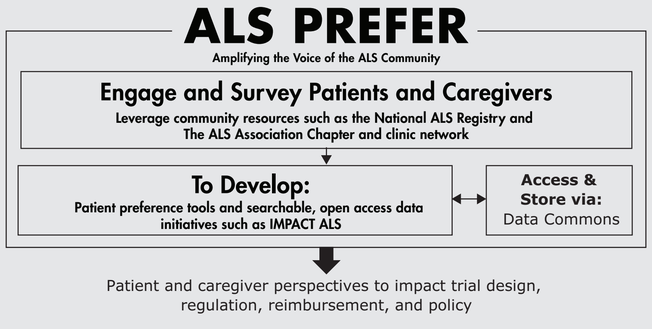
impact ALS
INVESTIGATING AND MEASURING PATIENT AND CAREGIVER TRENDS ABOUT ALS

INTRODUCTION

- There is a rising call for rigorous patient input to key areas of regulatory consideration, such as clinically meaningful outcomes, benefit/risk calculations, and determinations of value for health plan coverage and payment
- A community-developed draft ALS [amyotrophic lateral sclerosis] Drug Development Guidance has recently been docketed by the US Food and Drug Administration (FDA; FDA-2017-D-6503) and is open for public comment
  - The guidance project engaged nearly 40 persons with ALS and their caregivers, more than 10 ALS advocacy organizations, 45 of the world's leading ALS researchers and clinicians from 30 different institutions, 15 representatives from 9 biopharmaceutical companies, and 5 government representatives from the 3 centers at the National Institutes of Health and the Centers for Disease Control and Prevention
- Following the community-led FDA guidance initiative and with support from stakeholders, The ALS Association is developing a patient and caregiver-driven initiative—ALS PREFER—as a cross-sector collaboration intended to help facilitate robust patient experience and preference studies in ALS (**Figure 1**)

Figure 1. Schema for the ALS PREFER platform.



ALS, amyotrophic lateral sclerosis; IMPACT ALS, Investigating and Measuring Patient and Caregiver Trends about ALS.

- Existing information on the burden of disease and patient treatment preferences in ALS is limited and must be gleaned from small or geographically restricted studies[1-6]
- IMPACT ALS, a United States-focused effort, is the first survey initiative within the ALS PREFER platform, which is designed to expand the data available from patient and caregiver experiences and perspectives in order to guide drug development

OBJECTIVES

- The ALS PREFER initiative will provide a research-driven platform for a series of studies of patient experiences and preferences to make trials more attractive to patients and ensure that positive trials produce results that are meaningful to the patient community
- The IMPACT ALS survey aims to gather quantitative and qualitative information regarding the perspective of people with ALS and their caregivers as it relates to burden of disease, functional outcomes, views on treatment, and clinical trial participation

IMPACT-ALS METHODS

Survey Development

- A survey was developed based on collaborative input from The ALS Association and a diverse advisory committee comprising regulatory and methodology experts, ALS clinical thought leaders, a person with ALS, a caregiver for a person with ALS, and representatives from industry partners
- The survey contained 5 modules (disease background, living with ALS, approaches to treating ALS, demographics, and caregiver-specific burden of disease), the first 4 of which concerned persons with ALS; the last was only completed by caregivers about themselves
- The survey was conducted anonymously online through SurveyGizmo between October 10, 2017, and November 2, 2017
- This English-language survey was targeted to US advocacy groups associated with ALS as the first stage of this research

Participants

- Participants self-reported as one of the following: person with ALS, person assisting person with ALS to answer the survey, current caregiver of person with ALS, or past caregiver of person with ALS

Survey Recruitment

- Recruitment for the survey took place online using email and social media, at patient meetings, and at clinical sites
  - Email campaigns and social media notifications were disseminated to members of local patient and caregiver support groups that are partnered with The ALS Association
  - Members of the Northeast Amyotrophic Lateral Sclerosis Consortium, Clinical Research in ALS and Related Disorders for Therapeutic Development Consortium, and National Amyotrophic Lateral Sclerosis Registry were also invited to participate
  - Participants were also invited to participate at various clinical care centers associated with The ALS Association

IMPACT ALS RESULTS

Demographics and Disease Characteristics

- Overall, 1534 people participated; not everyone responded to all modules
  - 813 were persons with ALS, 74 were people assisting persons with ALS to answer the survey, and 647 were caregivers responding from their own point of view (444 self-reported current caregivers, 201 self-reported past caregivers, 2 unknown status)
- 1005 participants offered demographic information for the person with ALS: 78% of persons with ALS were >55 years of age, 60% were male, 91% were white, and 96% were not Hispanic or Latino (**Table 1**)

Table 1. Participant-Reported Patient Demographics and Disease Characteristics

Demographics	Responders (N = 1005)	
Age group, years, n (%)		
18-24	3 (0.3)	
25-34	15 (1.5)	
35-44	46 (4.6)	
45-54	160 (16)	
55-64	368 (37)	
65-74	305 (30)	
75 and older	108 (10.0)	
Male, n (%)	603 (60)	
Race, n (%)		
White	912 (91)	
Black or African American	26 (2.6)	
Asian	16 (1.6)	
Other	44 (4.4)	
Ethnicity, n (%)		
Hispanic or Latino	42 (4.2%)	
Not Hispanic or Latino	963 (96)	
Employment status (n = 1004), n (%)		
Full time	82 (8.2)	
On disability	386 (38)	
Part time	30 (3.0)	
Retired	429 (43)	
Unemployed	35 (3.5)	
Other	42 (4.2)	
Disease Characteristics	**Responders (n = 1524)**	
Time since first symptom or formal diagnosis, n (%)	**First symptom (n = 1523)**	**Formal diagnosis (n = 1463)**
<6 months	59 (3.9)	186 (13)
6 - 12 months	144 (9.5)	267 (18)
12 - 18 months	164 (11)	192 (13)
18 months - 2 years	221 (15)	132 (9.0)
2 - 3 years	211 (14)	168 (12)
3 - 4 years	187 (12)	131 (9.0)
4 - 5 years	111 (7.3)	98 (6.7)
>5 years	426 (28)	289 (20)
Type of ALS, n (%)		
Familial	115 (7.5)	
Sporadic	1083 (71)	
Don't know	326 (21)	
ALSFRS-R score, mean (SD) (n = 242)	32 (13)	
Persons with ALS who had passed away, n (%)	193 (13)	
Disease impact on caregiver financial status,[a] (n = 383), mean rating on a 5-point scale (SD)	3.0 (1.3)	

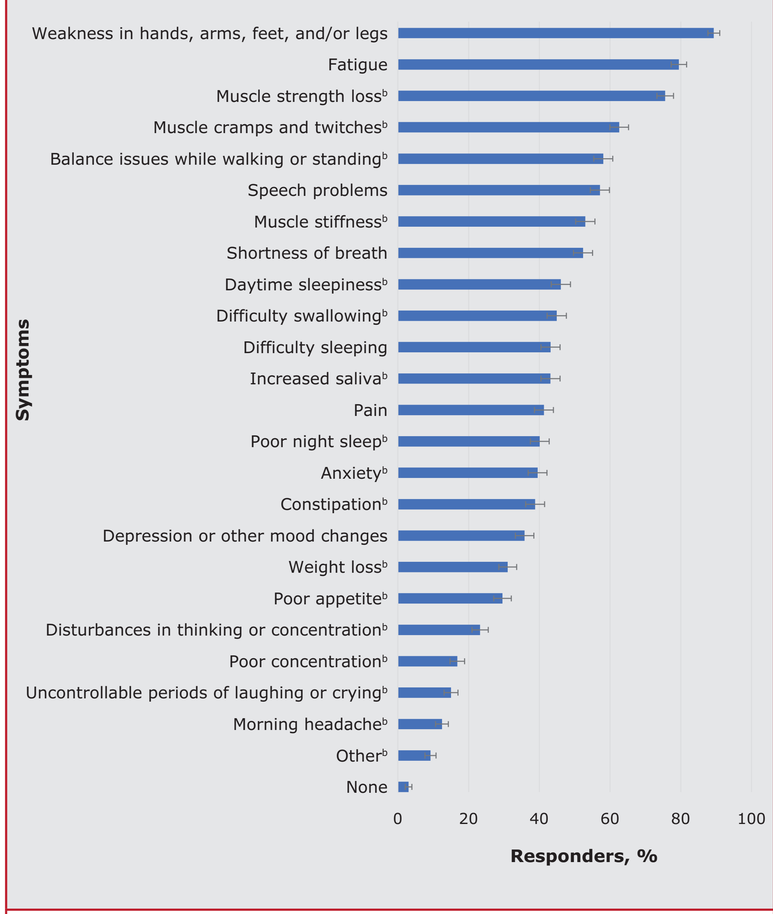
ALS, amyotrophic lateral sclerosis; ALSFRS-R, ALS functional rating score-R; SD, standard deviation.
[a]Financial impact results represent 383 caregivers who rated the effects of caring for a person with ALS on their own financial status from 1 (no effect) to 5 (devastating effect)

- Overall, persons with ALS were living in every state in the United States, and representation was comparable with the proportion of the US population in each state; 31 (3.1%) were living outside the United States
- Among 384 caregivers who took the survey on behalf of a person with ALS and who reported their own demographics, 58% were >55 years of age, 21% were male, 90% were white, and 95% were not Hispanic or Latino

The Burden of Disease

- Within the previous 2 weeks, the majority of responders had experienced muscle-related symptoms, balance issues, speech problems, and shortness of breath (**Figure 2**)
- Only 3% of responders reported having no symptoms in the previous 2 weeks (**Figure 2**)

Figure 2. Participant-reported symptoms experienced by persons with ALS.[a]

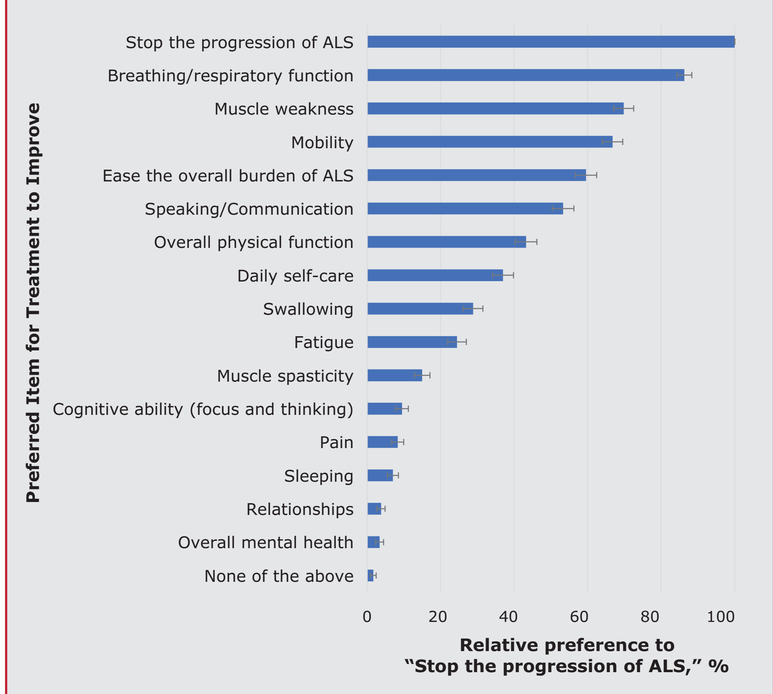


ALS, amyotrophic lateral sclerosis.
[a]Participants were asked to check all symptoms that applied in 2 separate questions. The total number of responders was 1295, unless otherwise specified for the second question.
[b]Total number of responders, N = 1291.

Treatment Preferences

- Of 1107 responders who indicated which outcomes were most preferred in a new treatment, "stop the progression of ALS" was the most commonly chosen item (chosen by 527/1107; 48%)
- Relative to this outcome, responders preferred improvements to breathing/respiratory function at 86%, followed by muscle weakness at 70% and mobility at 67% (**Figure 3**)

Figure 3. Preferred items for future treatments to improve relative to the most noted item "Stop the progression of ALS."[a]

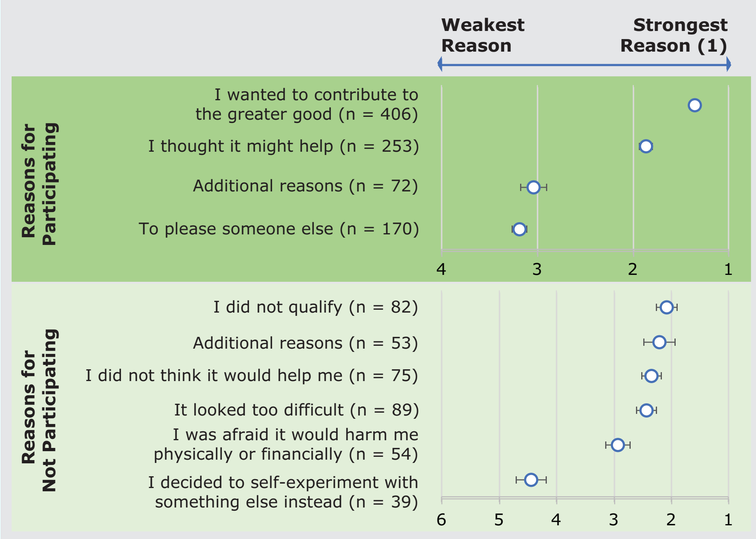


ALS, amyotrophic lateral sclerosis.
[a]Participants were asked to indicate their top 3 choices.

Clinical Trial Perspectives

- Among the 637 (57%) persons with ALS who had been offered participation in a clinical trial, 455 (71%) did participate and 182 (29%) did not
  - Of 454 responders who ranked reasons for participation, the highest ranked reason was "to contribute to the greater good" (ranked first for 66% of responders; **Figure 4**)
  - Of 182 responders who ranked reasons for not participating, the highest ranked reason was "I did not qualify" (ranked first for 31% of responders; **Figure 4**)

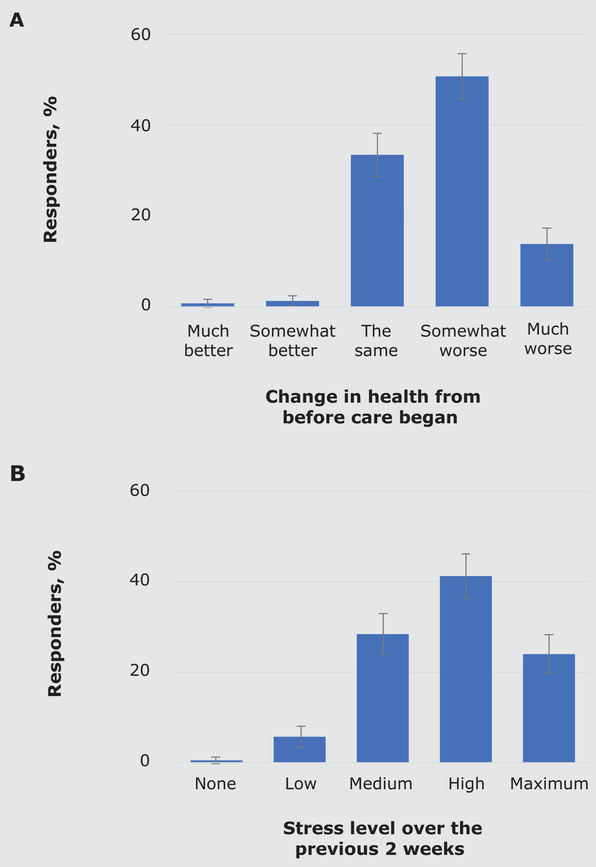
Figure 4. Reasons for or for not participating in a clinical trial that was offered.



Caregiver Burden

- Among 383 caregivers who responded to questions about themselves, 247 (65%) rated their health as somewhat or much worse compared with before they began caring for the person with ALS, and 359 (94%) reported medium, high, or maximum stress levels over the previous 2 weeks (**Figure 5**)

Figure 5. Burden of ALS on caregivers measured as (A) changes in health since care began and (B) stress level over the previous 2 weeks.



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CONCLUSIONS

- As part of ALS PREFER, the IMPACT ALS cross-sectional self-report online survey established the symptom burden associated with ALS, preferences for treatment, perspectives on clinical trials, and caregiver burden
- Nearly every participant reported at least 1 ALS symptom experienced in the previous 2 weeks, suggesting a very high symptom burden for this population
  - Caregivers also reported a particularly high burden of disease on themselves (health decline and stress)
- Preferences for future treatments were skewed towards medical treatment of the disease itself and the impact on physical and bulbar function and less toward symptom management
- Clinical trial participation was largely undertaken for the common good

FUTURE DIRECTIONS

- The ALS PREFER initiative will inform drug development, decision-making by the FDA and health insurers, and other policy issues
- The IMPACT ALS survey of persons with ALS and their caregivers can help inform drug development in areas of greatest patient burden and highest unmet need
- Future analyses will compare caregiver perspectives with patient perspectives on the burden of disease associated with ALS
- A similar European survey is currently in development to characterize patient experiences across Europe and inform global ALS drug development

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ACKNOWLEDGMENTS

We thank the 1534 individuals with ALS and their caregivers who took precious time to respond, in some way, to our lengthy survey. Special thanks to Madeline Kennedy and Brian Kennedy, who provided valuable input to the survey design from a patient and caregiver perspective. We also thank our advisors James Berry, John F. P. Bridges, Zachary Simmons, John Ravits, Richard Bedlack, Miriam Galvin, and Orla Hardiman for expert guidance. This research would not exist without their commitment to supporting ALS research. Financial support for this survey was provided by Cytokinetics, Inc., Biogen Inc., and Ionis Pharmaceuticals, Inc. Medical writing and editorial assistance was provided by ApotheCom (San Francisco, CA) and was funded by The ALS Association.

Presented at the 29th International Symposium on ALS/MND Meeting 2018; 7-9 December 2018; Glasgow Scotland, UK.