M247

Understanding the Spectrum of SCA1, SCA2, SCA3, and SCA6: Self-Reported Functional Status and Quality of Life

Lauren C Seeberger, MD[1], Melissa Wolfe Beiner, MD[2], Michele Potashman, PhD[2], Anne Neumann, RN, BSN[2], Skyler Jackson, BA[3], Austin R Letcher, MS[3], Patti A Engel, BSN[3], Lauren Moore, PhD[4], Julie Greenfield, PhD[5], Giovanni Ristori, MD[6], Laura Heller, PharmD[2]

1. Boise VA Medical Center, Department of Neurology, Boise, Idaho, 2. Biohaven Pharmaceuticals, Inc., 3. Engage Health, Inc., 4. National Ataxia Foundation, 5. Ataxia UK, 6. Department of Neurosciences, Mental Health and Sensory Organs, Sant'Andrea Hospital, Sapienza University of Rome and Neuroimmunology Unit, Fondazione Santa Lucia IRCCS, Rome, Italy

CONCLUSIONS

- Data from the quantitative self-reported component of this global, cross-sectional, mixed-methods study involving PWSCA (including SCA1, SCA2, SCA3, and SCA6) demonstrate that most participants are aware of family members who either are suspected to have SCA or have a confirmed SCA diagnosis.
- PWSCA reported difficulty walking and reported greater physical and mental morbidity than is reported in the general population.
- PWSCA3 consistently scored markedly below population norms and had the lowest SF-36 scores among the 4 SCA subtypes included in this study.
- The symptoms of SCAs — a group of ultra-rare, dominantly inherited, neurodegenerative disorders — impact all aspects of patients' quality of life.

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PURPOSE

- This study aims to capture burden-of-disease experiences of persons with spinocerebellar ataxia (PWSCA) and their caregivers; and to identify disease aspects that are paramount to them.

BACKGROUND

- Spinocerebellar ataxias (SCAs) are a dominantly inherited group of ultra-rare, progressively debilitating, neurodegenerative disorders with no available treatments to slow or halt disease progression.[1-5]
- PWSCA experience gait disturbances, lack of motor coordination, loss of balance and associated falls, challenges with speech and swallowing, and cognitive impairment, all of which worsen over time.[1-4,6-9]
- Furthermore, SCA can significantly impact mental and social well-being and overall quality of life.
- There are more than 40 distinct SCA genotypes, with genotypes 1, 2, 3, and 6 being the most common worldwide.[2,10]
- Lived experiences of PWSCA offer essential insights regarding care and treatment. More data regarding the lived experiences of PWSCA are needed, not only to understand the impact of disease progression over time but also to identify potential therapies and optimal modalities for care provision.[11]
- This global study captures experiences of PWSCA who have genotypes SCA1, SCA2, SCA3, and SCA6, with a focus on functional status and quality of life (QOL) as determined by quantitative responses gathered via online questionnaires.

METHODS

- Individuals with symptomatic SCA1, SCA2, SCA3, or SCA6, and proof of disease were eligible to participate in the study.
  - Proof of SCA was confirmed by laboratory testing (68.8%), medical record (14.0%), or physician communication (17.2%).
- Surveys were conducted in English, French, German, or Portuguese with patients or caregivers. Caregivers and spouses were invited to participate if PWSCA either had passed away within the 2 years prior to study initiation or were currently living but had difficulty speaking.
- The Coordination of Rare Diseases at Sanford (CoRDS) Registry, the National Ataxia Foundation, Ataxia UK, and Engage Health (using the Engage Health EnCompass® database) were responsible for global recruitment, with a focus on participants from Australia, Brazil, Canada, France, Germany, the UK, and the US.
- For this study phase, which focuses on quantitative responses gathered via online questionnaires, the targeted total sample size was 100.
- Using a secure, HIPAA/508/GDPR-compliant online portal, participants were directed to provide demographic data, complete a modified Klockgether questionnaire (a physician-administered tool that assesses SCA functional status, modified with patient-friendly language), and complete the SF-36 QOL measure.
  - The SF-36v2 utilizes norm-based scoring with a linear T-score transformation method such that each of the health domain scores and summary components have a mean of 50. Scores below or above 50 are reflective of scores below and above the 2009 US general population, respectively.[12]
  - A post-hoc analysis of SF-36 scores was performed to calculate nominal *P* values comparing values between SCA types, where *P* <.05 indicated a significant difference (Excel).
  - Linear correlation coefficients were calculated between Klockgether and SF-36 scores to evaluate the relationship between participants' self-assessment of functioning using the modified Klockgether scale and physical health measured by the SF-36 (Excel).
- Institutional review board (IRB) and ethics approval from WCG IRB was granted prior to study initiation. Participants utilized the online portal to provide consent in their native language prior to initiating any study activities.

RESULTS

Participant Disposition

- Of the 347 individuals who accessed the online site and provided preliminary information, including consent, 161 were excluded due to failure to complete the SF-36 assessment or the modified Klockgether questionnaire, lack of proof of disease, or proof of disease that was deemed insufficient for study enrollment.
- 186 individuals participated; this included caregivers for 2 PWSCA who died and a caregiver who was a parent of an individual with SCA, resulting in a total of 183 PWSCA and 3 caregivers.
- Due to the self-reported nature of the SF-36 assessment, only the 183 PWSCA were invited to complete this measurement; caregivers were excluded.

Table 1. Participant Disposition

	n
Total number of people who visited the reservation site, gave consent, and provided some information	347
People excluded because they did not complete the SF-36 or modified Klockgether, did not provide proof of disease, or lacked proof of disease sufficient for enrollment (eg, missing patient name or SCA type)	161
Completed quantitative assessments*	186
• Caregivers	3
• Patients	183

* The SF-36 questionnaire was only completed by patients.

How Participants Became Aware of Study

- The majority of participants (n = 92; 49.5%) became aware of the study through the CoRDS registry or a patient association (n = 56; 30.1%), with other participants becoming aware through social media, a family member or friend, their health care provider, or through the Engage Health EnCompass® Database, which characterizes health care providers and patients in the rare disease space.

Figure 1. How Participants Became Aware of Study

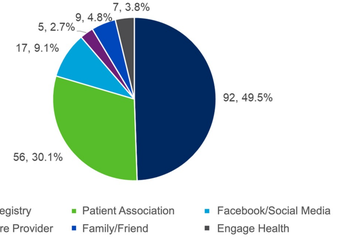


Table 2. Demographic Data

	Phase 1			
	SCA1 (n = 26)	SCA2 (n = 37)	SCA3 (n = 61)	SCA6 (n = 62)
Female / male	17 / 9	22 / 15	33 / 28	38 / 24
Mean age (yrs) (range)	49.6 (28.0–74.2)	47.7* (26.9–71.3)	50.1** (26.6–73.9)	64.5 (43.2–85.9)
Geography				
Americas	19	28	47	49
Europe & UK	7	6	10	9
Asia	0	2	3	0
Africa/Middle East	0	1	0	0
Australasia	0	0	1	4
Family members with confirmed SCA	60	84	128	99
Family members with suspected SCA	30	47	64	78

* Excludes 1 deceased person (74.1 years).
** Excludes 1 deceased person (66.1 years).

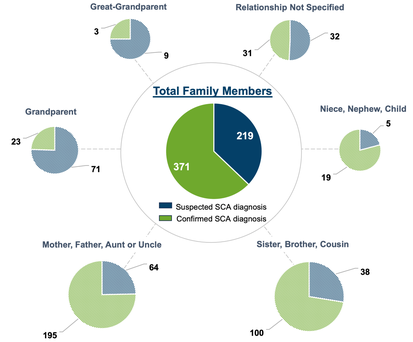
Demographics

- Participants with SCA3 (n = 61) or SCA6 (n = 62) were represented more than participants with SCA1 (n = 26) or SCA2 (n = 37).
- Females were a combined 59% of participants across all SCA types.
- Ages of the PWSCA ranged from 26.6 to 85.9 years, with the oldest population represented by PWSCA6, among whom the mean age was 64.5 years. PWSCA2 represented the youngest population, with a mean age of 47.7 years.
- The majority of participants were from North or South America, with 65.6% of participants across all SCA types being from the US.

Family History

- Of the 186 study participants, 175 (94.1%) reported a family member with either confirmed or suspected SCA.
- Participants reported a total of 371 family members who were diagnosed with SCA and an additional 219 family members in whom SCA was suspected (**Table 2**). PWSCA3 reported the greatest number of family members affected, with 128 confirmed and 64 suspected of having SCA. PWSCA6, PWSCA2, and PWSCA1 reported a total of 177, 131, and 90 family members with confirmed or suspected SCA respectively.
- Among the study group as a whole (N = 186), participants reported more relatives of the previous generation (mother, father, aunt, uncle) or same generation (sister, brother, cousin) having either confirmed or suspected SCA compared to relatives of other generations (**Figure 2**). For the older generations, lack of diagnosis may have been confounded by lack of medical knowledge and technology, such as genetic testing, at the time.

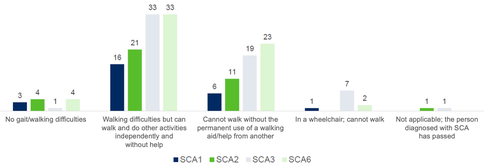
Figure 2. Family History of SCA; Relationship to Participant



Modified Klockgether and SF-36

- Functional status, as measured by the modified Klockgether questionnaire, was chronicled for all 186 PWSCA (**Figure 3**): 6.5% (n = 12) reported no difficulties with gait or walking; 55.4% (n = 103) experienced difficulty walking but engaged in other activities independently; 31.7% (n = 59) were unable to walk unaided; 5.4% (n = 10) could not walk at all; and for the 2 patients who were deceased (1.1%), functional status was not applicable.

Figure 3. Modified Klockgether



- PWSCA2 and PWSCA6 had mean SF-36 scores <50 on every scale (general health, physical functioning, physical and emotional role limitations, vitality, social functioning, and mental health) except bodily pain (52.2 and 52.0, respectively).
- There were statistically significant differences in SF-36 scores across SCA types for the physical component summary, physical role limitations, and bodily pain, with the lowest scores among PWSCA3 in each of these 3 areas. Furthermore, mean SF-36 scores in PWSCA3 were <50 on every scale and highest in the mental component summary (47.9); thus, PWSCA3 consistently scored well below general population norms.
- Leveraging the SF-36 First Stage Positive Depression Screen, as derived from the mental component items, 35% of PWSCA3 were identified as at risk for depression, which is nearly twice the prevalence among the general population (18%).[12,13] Also, 24% of PWSCA1, 22% of PWSCA2, and 17% of PWSCA6 in this cohort were found to be at risk for depression.

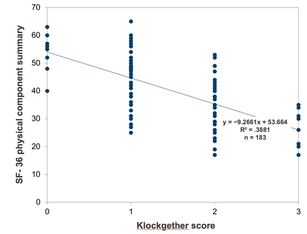
Table 3. SF-36

SF-36 scale	Phase 1 | SF-36*				*P* value
	SCA1 (n = 25)	SCA2 (n = 36)	SCA3 (n = 60)	SCA6 (n = 62)	
SF-36 Physical Summary	46.6	42.0	37.9	41.5	**.002**
SF-36 Mental Summary	47.3	49.8	47.9	49.9	.65
Physical Functioning	41.7	37.5	35.8	37.0	.17
Role, Physical	45.8	43.0	36.5	40.2	**.003**
Bodily Pain	54.8	52.2	46.2	52.0	**<.001**
General Health	44.7	43.8	42.6	46.0	.32
Vitality	48.6	45.4	44.9	47.3	.41
Social Functioning	45.1	45.6	41.1	44.1	.20
Role, Emotional	46.4	47.7	44.0	46.3	.44
Mental Health	46.8	48.8	47.3	49.3	.69

*Excludes caregivers representing 1 PWSCA, 1 PWSCA2, and 1 PWSCA3

- The participants' self-assessment of functioning using the modified Klockgether scale was correlated with physical health measured by the SF-36 (y = −9.2661x + 53.664; R^2 = .3881).

Figure 4. Relationship Between SF-36 Physical Component Summary and Modified Klockgether



Limitations

- Study limitations include the use of data derived from a convenience sample of patients and findings that may not be representative of the entire spectrum of SCA for each genotype.