CLT-04

Correlation Between Slow Vital Capacity Measured at Home and in the Clinic for Patients With Amyotrophic Lateral Sclerosis

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INTRODUCTION

- Slow vital capacity (SVC) is often used to evaluate ventilatory function in patients with amyotrophic lateral sclerosis (ALS)[1,2]
- However, participation in clinical trials requiring frequent in-clinic visits can prove challenging for patients with ALS, leading to the desire to identify remotely performed outcome measures
- A portable spirometer may allow SVC to be measured at home, thereby reducing the burden of participating in a clinical trial
- In an ongoing phase 2 clinical study, FORTITUDE-ALS, we evaluate SVC measured by patients at home as well as in the clinic

OBJECTIVE

- To assess the reliability of SVC measured at home (hSVC) using SVC measured in clinic (cSVC) as the standard in a phase 2 trial evaluating *reldesemtiv* in patients with ALS

METHODS

FORTITUDE-ALS

- In FORTITUDE-ALS, patients are trained at their Day 1 visit to use portable home spirometers (GoSpiro®, Monitored Therapeutics, Inc., Dublin, OH) to measure hSVC weekly
- cSVCs are measured at screening, Day 1, and Weeks 2, 4, 8, and 12, and the follow-up visit and are paired with hSVC measurements conducted within a 7-day window. No baseline measurement was made for hSVC. Outliers that are lower than 0.5 times or greater than 1.5 times the highest evaluable cSVC are displayed but have been excluded from the analyses
- The Pearson correlation coefficients between hSVC and cSVC are calculated overall and by visit. The differences between the two measures are analyzed using a paired *t* test
- To evaluate the utility of hSVC, change from baseline in percent predicted SVC measured at home and in clinic have been compared by visit, using cSVC prior to the first dose of study drug as baseline

RESULTS

- The current compliance rate of hSVC measures is approximately 70%. While the expected total number of hSVC tests is 16 per patient for those who have completed the study, the average number of tests done is 9.2
- A survey was designed to better understand the lower than expected compliance rate **(Table 1)**
  - Responses were collected from 34/65 sites (52.3%)

Table 1. Site survey to better understand compliance rates

Plays a role in why patients are compliant (defined as performing at least 75% of tests) [Top 3 reasons] 1. Motivated patient (76.5%) 2. Patient technologically savvy (52.9%) 3. Written instructions (41.8%)
Plays a role in why patients are noncompliant [Top 3 reasons] 1. Spirometer and tablet won't sync (55.9%) 2. Tablet won't connect to WiFi (52.9%) 3. Patient forgets (52.9%)
Free-text themes for obstacles to use • Machines are not user-friendly • Solutions not always provided by tech support • Testing may be daunting for some patients • Seen as an added burden for patients and caregivers, particularly for the patients with more severe disease

- SVC and percent predicted SVC measured at home and in the clinic were significantly correlated **(Figure 1)**

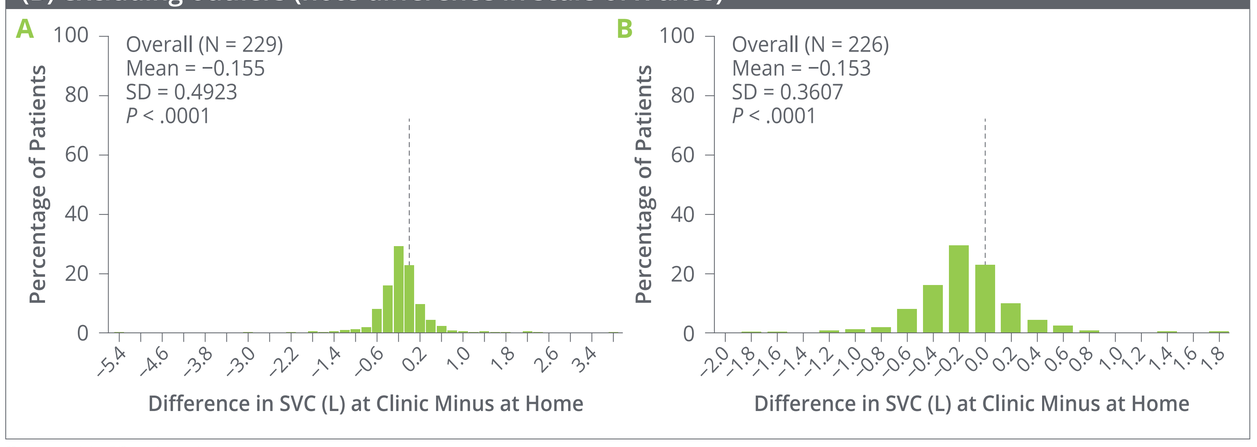
Figure 1. Relationship between SVC in liters measured at home vs in the clinic

	SVC Measured in Clinic (N=695)		SVC Measured at Home (N=695)		Pearson Correlation Between at Home and in Clinic		
	Mean (SD)	Minimum, Maximum	Mean (SD)	Minimum, Maximum	Correlation Coefficient	95% Confidence Interval	Two-Sided *P* Value
SVC (L)	3.4 (1.0)	1.2, 6.0	3.6 (1.0)	0.9, 6.1	0.94	0.93, 0.94	< .0001
Percent predicted SVC	83.7 (17.5)	30.3, 173.2	94.7 (20.1)	24.2, 195.3	0.88	0.86, 0.90	< .0001

SD, standard deviation; SVC, slow vital capacity

- The distributions in differences between hSVC and cSVC are shown in **Figure 2**
  - The mean difference between the results of hSVC and cSVC is 0.153 L (standard deviation, 0.3607; *P* < .0001)

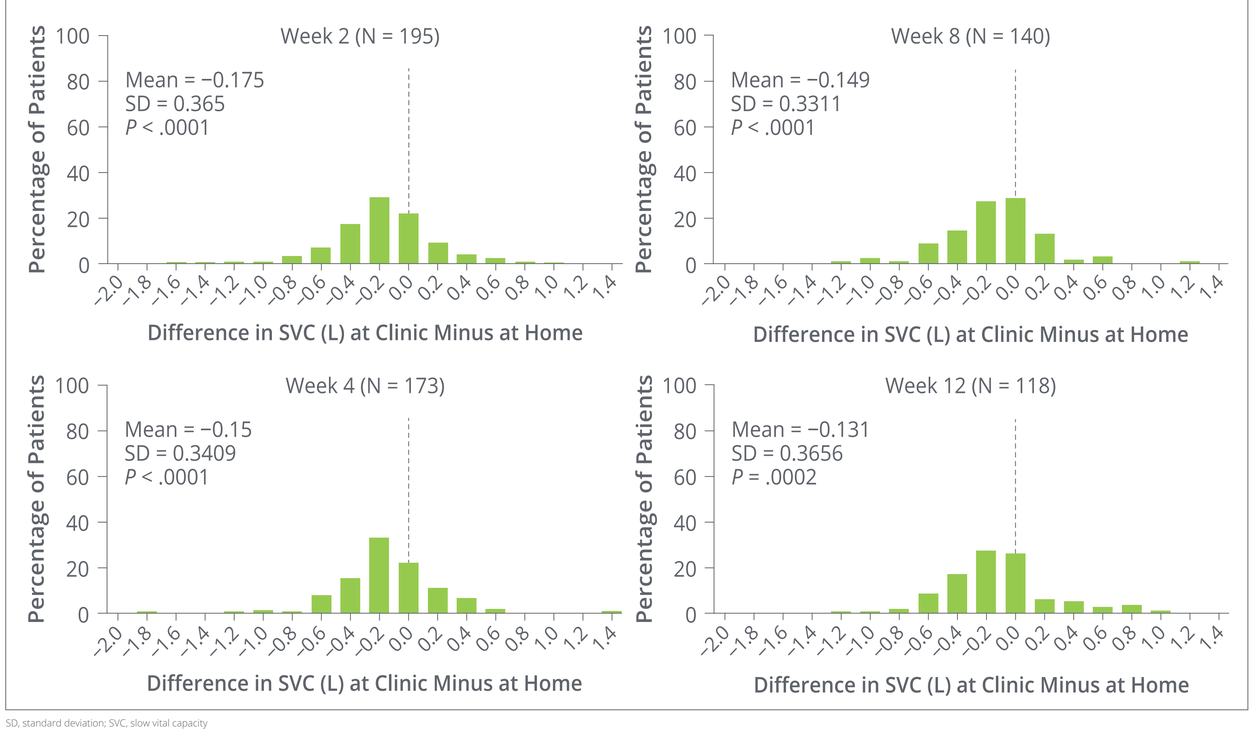
Figure 2. Differences between SVC (liters) measured in the clinic and at home; (A) all data, (B) excluding outliers (note difference in scale of x-axes)



SD, standard deviation; SVC, slow vital capacity

- The difference between SVC measured at home and in the clinic over time is shown in **Figure 3**

Figure 3. Difference in SVC measured in the clinic and at home over time



SD, standard deviation; SVC, slow vital capacity

- The change from baseline in percent predicted SVC measured at home versus in clinic over time is shown in **Table 2**

Table 2. Change from baseline in percent predicted SVC measured in the clinic versus at home

Percent Predicted SVC, percentage points	Baseline	Week 2		Week 4		Week 8		Week 12		Follow-up	
	Clinic as standard	Clinic	Home	Clinic	Home	Clinic	Home	Clinic	Home	Clinic	Home
N	217	192	192	168	168	137	137	114	114	67	67
Mean (SD)	85.64 (15.88)	83.92 (16.38)	95.51 (19.18)	84.63 (16.78)	95.90 (18.62)	83.84 (17.68)	94.70 (20.88)	83.11 (18.32)	93.26 (20.90)	82.05 (21.23)	92.54 (24.35)
Difference (clinic minus home)											
LS mean difference (SE)		−11.59 (0.67)		−11.27 (0.72)		−10.86 (0.79)		−10.15 (0.87)		−10.49 (1.19)	
P value		< .0001		< .0001		< .0001		< .0001		< .0001	

LS, least squares; SD, standard deviation; SE, standard error of the mean; SVC, slow vital capacity

- There was no significant difference in percent predicted SVC measured in the clinic between patients who used a home spirometer to take SVC measurements and those who did not **(Table 3)**

Table 3. Change from baseline in percent predicted SVC measured in the clinic in patients who used a home spirometer (user) and those who did not (non-user)

Percent Predicted SVC, percentage points	Baseline		Week 2		Week 4		Week 8		Week 12		Follow-up	
	User	Non-user	User	Non-user	User	Non-user	User	Non-user	User	Non-user	User	Non-user
N	231	79	216	72	200	66	165	58	143	44	122	41
Mean (SD)	85.28 (16.04)	81.22 (13.79)	84.31 (16.60)	79.86 (14.04)	83.97 (17.29)	79.48 (14.29)	82.78 (18.23)	77.73 (15.75)	82.96 (18.50)	79.60 (15.54)	80.58 (20.04)	76.42 (16.06)
Difference (users minus non-users)												
LS mean difference (SE)			−0.12 (1.20)		0.92 (1.22)		1.43 (1.27)		0.85 (1.36)		1.73 (1.45)	
P value			.9176		.4536		.261		.533		.2314	

LS, least squares; SD, standard deviation; SE, standard error of the mean; SVC, slow vital capacity

- The frequency of home spirometer use did not significantly impact the measurement of percent predicted SVC

CONCLUSIONS

- **The current compliance rate of hSVC measures is suboptimal**
- **Although the correlation between hSVC and cSVC is good, there is a significant discrepancy between them, though this discrepancy decreases slightly over time. Differences in percent predicted SVC change were more than 10 percentage points**
- **There was no significant difference in percent predicted cSVC change from baseline between patients who used a home spirometer and those who did not (baseline measured for cSVC only)**
- **Home measurements could permit more frequent monitoring of ALS ventilatory function, allowing for more timely clinical decisions, including when to initiate noninvasive ventilation. However, the variable patient compliance and the significant discrepancy between hSVC and cSVC may raise concerns regarding the advisability of decreasing the frequency of in-clinic trial visits by substituting hSVC for cSVC**

References

1. Lechtzin N, et al. *Amyotroph Lateral Scler Frontotemporal Degener*. 2018;19:321–30.
2. Andrews JA, et al. *JAMA Neurol*. 2018;75:58–64.

Disclosures

Meng, Rudnicki, Cockroft, Malik, and **Wolff** are employees of and own stock in Cytokinetics, Inc. **Lechtzin** has served as a consultant/advisor for Cytokinetics, Inc., Hill-Rom, PMD Healthcare, and Vertex and lectured and participated at meetings on behalf of Cytokinetics, Inc. and Hill-Rom. **Shefner** has consulted for Biogen, Biohaven, Cytokinetics, Inc., Mitsubishi Tanabe Pharma, and Neurosense, and has received research support from ALS Association, ALS Finding a Cure, Biogen, Biohaven, Cytokinetics, Inc., Neuraltus, and NIH.

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In collaboration with Astellas Pharma, Inc., Cytokinetics is developing *reldesemtiv* as a potential treatment for people living with ALS and certain other debilitating diseases and conditions associated with skeletal muscle weakness and/or fatigue.

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