CLT-05

Noninvasive Ventilation Use in Patients Enrolled in VITALITY-ALS

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INTRODUCTION

- Noninvasive ventilation (NIV) has been shown to improve survival in patients with amyotrophic lateral sclerosis (ALS)[1]
- A recent survey of ALS experts, however, found wide variability in NIV prescribing patterns with differences notably present between US and European physicians[2]
- Published guidelines vary regarding the ideal criteria for initiating NIV
- VITALITY-ALS was a phase 3 study that enrolled patients with ALS in the United States, Canada, and 9 European countries and evaluated the efficacy and tolerability of *tirasemtiv*; primary results have been reported previously[3]
  - Information regarding NIV use was recorded throughout the trial

OBJECTIVE

- To evaluate the prescribing practices for NIV and patient compliance with its use during the VITALITY-ALS trial

METHODS

- VITALITY-ALS enrolled patients with ALS not using NIV and a slow vital capacity (SVC) ≥70% of predicted at screening
- After randomization, physicians prescribed NIV without restriction
- Dates NIV was prescribed and initiated, and NIV use, were recorded, as well as reason(s) NIV was prescribed
- NIV use was recorded as prescribed but never initiated, used >2 hours/24 hours for ≥5 consecutive days, used >4 hours/24 hours for ≥5 consecutive days, or used >22 hours/24 hours for ≥10 consecutive days
- Among other outcome measures, SVC and the revised ALS Functional Rating Scale were performed at all clinic visits
- Patients were followed for up to 56 weeks

RESULTS

- 565 patients were randomized and dosed with placebo or *tirasemtiv* in VITALITY-ALS
- No significant differences in baseline demographics or symptoms of sialorrhea, dyspnea, and orthopnea at the time NIV was prescribed were noted between patients who used and did not use NIV or used it for <4 hours/24 hours **(Table 1)**

Table 1. Baseline demographics and symptoms of sialorrhea, dyspnea, and orthopnea at time NIV prescribed

	Never Used/Used NIV <4 Hours per 24 Hours[a]	Used NIV at Least 4 Hours per 24 Hours	*P* Value
Number of patients	55	139	
Age[b]			
n	55	139	
Mean (SD), y	57.2 (11.3)	58.7 (9.7)	.3958
Sex[c]			
Female, n (%)	17 (30.9)	41 (29.5)	.5385
Male, n (%)	38 (69.1)	98 (70.5)	
Site of onset[c]			
Bulbar, n (%)	11 (20.0)	22 (15.8)	.3537
Extremity, n (%)	44 (80.0)	116 (83.5)	
ALSFRS-R Q2[b,d]			
n	54	135	
Mean (SD)	2.94 (1.28)	3.24 (0.95)	.3566
ALSFRS-R Q10[b,d]			
n	54	135	
Mean (SD)	2.87 (1.08)	2.89 (1.08)	.9527
ALSFRS-R Q11[b,d]			
n	54	135	
Mean (SD)	3.07 (1.08)	3.21 (1.07)	.5802

Note: One patient who was prescribed NIV did not provide an answer to NIV use and was excluded from the analysis

[a]Patients who never initiated NIV or who used it ≥2 hours for 5 days and never increased use to 4 hours for 5 days or 22 hours for 10 days. [b]*P* value was obtained from an ANCOVA model with treatment (pooled *tirasemtiv* or placebo), riluzole use or non-use, and indicator of NIV used (never used/<4 hours, or used at least 4 hours) as fixed effects comparing patients who never used/used <4 hours vs patients who used NIV for at least 4 hours. Baseline was included in the model when applicable. [c]*P* value was obtained from Cochran-Mantel-Haenszel general association test stratified by riluzole use or non-use, pooled *tirasemtiv* and placebo comparing patients who never used/used NIV <4 hours vs patients who used it at least 4 hours. Last ALSFRS-R assessment prior to NIV prescription was included in the analysis. [d]At time NIV prescribed

ALSFRS-R, revised ALS Functional Rating Scale; ANCOVA, analysis of covariance; NIV, noninvasive ventilation; Q, question; SD, standard deviation

- Overall, 195 patients (34.5%) were prescribed NIV during the study **(Table 2)**
- The proportion of patients prescribed NIV was similar between North America and Europe (35.0% and 33.1%, respectively)
- No geographic difference was noted in the value of SVC at time NIV was prescribed and the proportion of patients with SVC <50% who were or were not prescribed NIV

Table 2. Summary of SVC in patients prescribed NIV by region

	Total (n = 565)	North America (n = 426)	Europe (n = 139)	*P* Value (North America vs Europe)
Number of patients prescribed NIV, n (%)[a]	195 (34.5)	149 (35.0)	46 (33.1)	.4507
SVC value at time NIV prescribed, mean (SD)[b]	(n = 190) 63.14 (19.70)	(n = 144) 63.12 (19.28)	(n = 46) 63.21 (21.15)	.2307
Patients with SVC <50% and NIV not prescribed/patients with SVC <50%, n/N (%)	57/179 (31.8)	38/133 (28.6)	19/46 (41.3)	.2095

[a]Three patients who were prescribed NIV prior to the study start and 1 patient who answered no to NIV prescription but recorded NIV start date were also treated as patients prescribed NIV. *P* value was obtained from Cochran-Mantel-Haenszel general association test stratified by riluzole use or non-use, pooled *tirasemtiv* and placebo comparing North America vs Europe. [b]*P* value was obtained from an ANCOVA model with baseline, region (North America or Europe), treatment group (pooled *tirasemtiv* or placebo), and riluzole use or non-use as fixed effects comparing North America vs Europe. Last SVC assessment prior to NIV prescription was included in the analysis

ANCOVA, analysis of covariance; NIV, noninvasive ventilation; SVC, slow vital capacity

- In patients prescribed NIV, 9.7% never initiated treatment, 78.5% used NIV for >2 hours/24 hours, and 71.3% >4 hours/24 hours **(Table 3)**

Table 3. Details of NIV use

Patients Prescribed NIV, n (%)	Total (n = 195)	North America (n = 149)	Europe (n = 46)	*P* Value (North America vs Europe)
NIV never initiated	19 (9.7)	18 (12.1)	1 (2.2)	.0494[a]
NIV used >2 hours/24 hours[b]	153 (78.5)	114 (76.5)	39 (84.8)	.2262
NIV used >4 hours/24 hours[b]	139 (71.3)	106 (71.1)	33 (71.7)	.9317
NIV used >22 hours/24 hours[c]	23 (11.8)	17 (11.4)	6 (13.0)	.6416

[a]*P* value derived from Fisher exact test. [b]For ≥5 consecutive days. [c]For ≥10 consecutive days

NIV, noninvasive ventilation

- SVC measurements were the main reason NIV was prescribed in North America, while in Europe respiratory symptoms were the most common reason **(Table 4)**
  - Statistically significant differences were noted between North America and Europe in vital capacity, respiratory symptoms, and overnight pulse oximetry as reasons for NIV prescription

Table 4. Reasons for prescription of NIV

Reasons NIV Prescribed, n (%)	Total (n = 195)	North America (n = 149)	Europe (n = 46)	*P* Value (North America vs Europe)
Vital capacity	105 (53.8)	87 (58.4)	18 (39.1)	.0397
Respiratory symptoms	90 (46.2)	60 (40.3)	30 (65.2)	.0036
Sleep-related symptoms	46 (23.6)	37 (24.8)	9 (19.6)	.4737
Sniff nasal inspiratory pressure	6 (3.1)	5 (3.4)	1 (2.2)	1.000[a]
Overnight pulse oximetry	20 (10.3)	8 (5.4)	12 (26.1)	.0002
Blood gas pCO_2	8 (4.1)	5 (3.4)	3 (6.5)	.3954[a]
Other	13 (6.7)	8 (5.4)	5 (10.9)	.1328

Note: Totals are > than number for whom NIV was prescribed because investigators could choose more than 1 reason it was prescribed

[a]*P* value derived from Fisher exact test

NIV, noninvasive ventilation

CONCLUSIONS

- **Despite allowing for NIV initiation at any point following randomization in VITALITY-ALS, only 2 of every 3 patients whose SVC fell below 50% were prescribed NIV**
- **The nationwide insurance coverage in many European countries for NIV use in patients with ALS was expected to result in a greater percentage of European patients being prescribed NIV and having higher SVC at the time it was prescribed compared with North American patients, but that was not observed**
- **The top 3 reasons for prescribing NIV in VITALITY-ALS were consistent with results of the recent survey of ALS specialists in the United States and Europe**
- **No differences were seen in baseline demographics or in responses to questions regarding sialorrhea, dyspnea, or orthopnea at the time NIV was prescribed in patients who used NIV at least 4 hours/24 hours and those who never used it or used it fewer hours**
- **71.3% of patients who were prescribed NIV used it at least 4 hours/24 hours**
- **NIV prescribing habits in VITALITY-ALS may help inform future ALS study design**

References

1. Bourke SC, et al. *Lancet Neurol.* 2006;5:140–7.
2. Heiman-Patterson TD, et al. *Amyotroph Lateral Scler Frontotemporal Degener.* 2018;19;331–41.
3. Shefner JM, et al. Presentation at Motor Neurone Disease Association; 28th International Symposium on ALS/MND; 8–10 December 2017. Boston, MA.

Disclosures

Rudnicki, **Bian**, **Cockroft**, **Malik**, **Meng**, and **Wolff** are employees of and own stock in Cytokinetics, Inc. **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.

The study was funded by Cytokinetics, Inc. Editorial support was provided by Karen Pemberton on behalf of Evidence Scientific Solutions, Inc, Southport, CT, and was funded by Cytokinetics, Inc.

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