

Changes in Cardiac Effort in Pulmonary Hypertension-Interstitial Lung Disease: Insights from the ASCENT Trial

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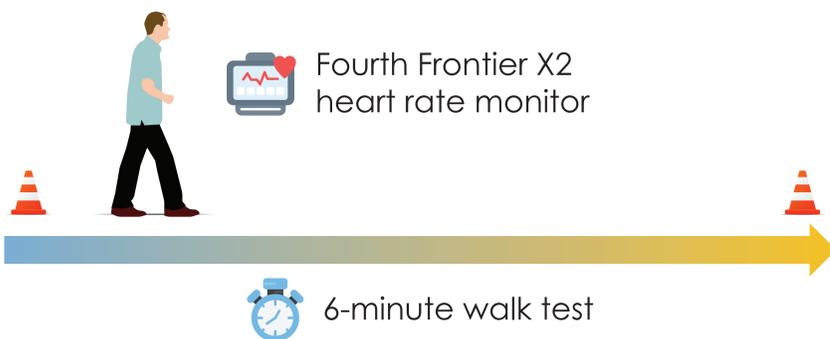
Rationale

- Cardiac Effort (**Figure 1**), defined as number of heartbeats during a 6-minute walk test (6MWT) / 6-minute walk distance (6MWD), is a novel, noninvasive endpoint to characterize physiologic limitations during exercise in patients with pulmonary hypertension-interstitial lung disease (PH-ILD)
- Cardiac Effort:
 - is less variable than 6MWD (less dependent on effort, mood, pain, etc.)
 - tracks with physiologic improvement
 - correlates with stroke volume in patients with Group 1 pulmonary hypertension¹
- Here, we describe Cardiac Effort in patients with PH-ILD, at baseline and after 8 weeks of treatment with LIQ861 (YUTREPIA™) developed by Liquidia Technologies

Methods

- ASCENT (NCT06129240) is a prospective, multicenter, open-label study evaluating the safety, tolerability, and efficacy of LIQ861, an investigational dry powder inhaler formulation of treprostinil, in patients with PH-ILD, including combined pulmonary fibrosis and emphysema
 - Cohort A includes approximately 60 patients with PH-ILD
 - Eligible patients receive open-label LIQ861 with dose titration based on tolerability and clinical response for 52 weeks
- 13 patients had completed their baseline and week 8 visits for this data cut
- Heart rate monitoring during all 6MWTs was performed using the Fourth Frontier X2, a single-lead, dry-electrode electrocardiogram device
- Baseline 6MWD and Cardiac Effort were calculated as the average of screening and baseline values
- 6MWD and Cardiac Effort at week 8 were compared with baseline using nonparametric testing

Figure 1. Cardiac Effort



Results

- One patient was excluded due to study protocol violation
- Study population was recently diagnosed PH in older males with moderate FVC reduction and severe walk impairments (**Table 1**)

Table 1. Baseline Demographics and Clinical Characteristics

Characteristic	Overall (N=13)
Age, median (range), y	74 (53-80)
Sex, n (%)	
Male	8 (62)
Female	5 (39)
Duration of PH diagnosis, y	0.5 (0.6)
Duration of ILD diagnosis, y	4.3 (4.3)
ILD type, n (%)	
Idiopathic interstitial pneumonias	7 (54)
Autoimmune ILDs	3 (23)
Chronic fibrosis with emphysema	3 (23)
Pulmonary function tests	
FEV ₁ , L	1.9 (0.5)
Percent FEV ₁ predicted	72 (22)
FVC, L	2.3 (0.9)
Percent FVC predicted	69 (25)
Corrected DLCO, mmol/min/mm Hg	8.8 (3.7)
Percent DLCO predicted	41 (17)
Hemodynamics	
mPAP, mm Hg	36 (11)
PCWP, mm Hg	9 (4)
PVR, Wood units	6.1 (2.8)
6MWD, m	290 (92)
Cardiac effort, median (range), beats/m	2.3 (1.3-4.6)

Data are mean (SD) unless otherwise noted.
 Abbreviations: 6MWD, 6-minute walk distance; DLCO, diffusing capacity of the lung for carbon monoxide; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; ILD, interstitial lung disease; mPAP, mean pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance.

References

1. Lachant DJ, et al. *Pulm Circ.* 2020;10(4):2045894020972572.

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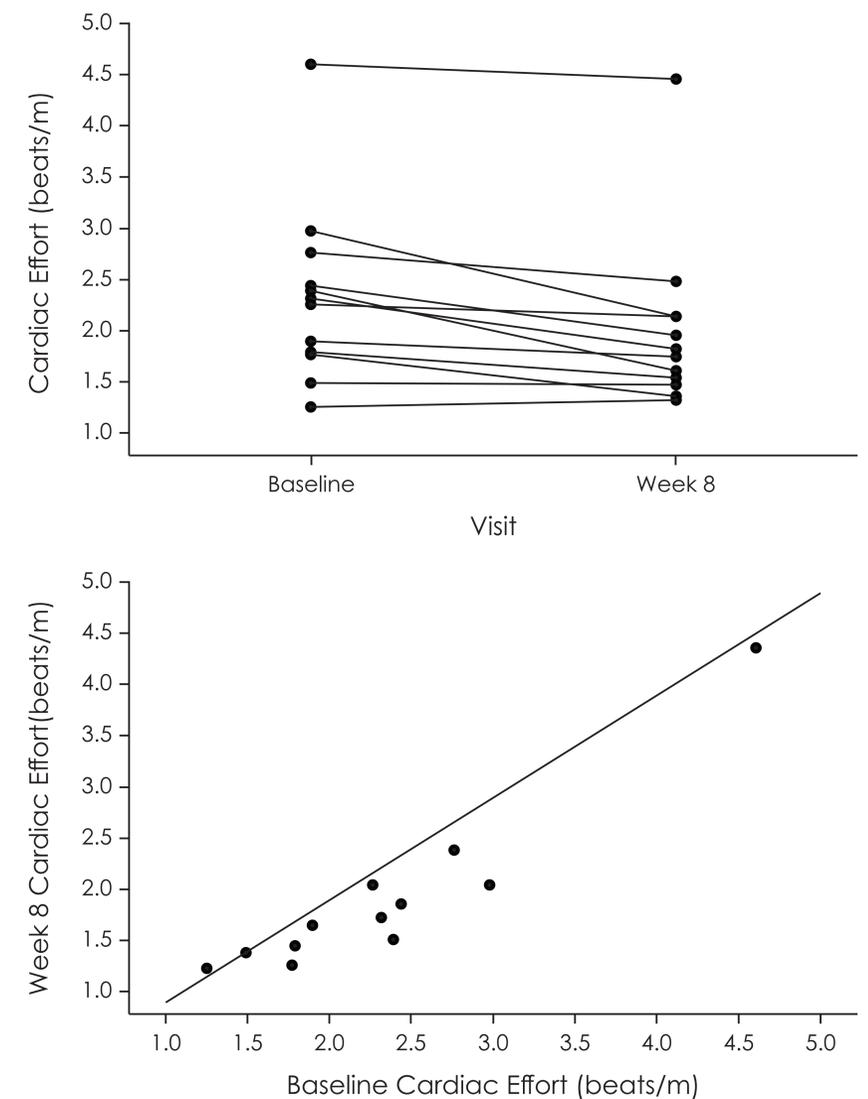
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Author Disclosures

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- Median dose of LIQ861 at week 8 was 132.5 mcg 4x daily
- Median 6MWD increased from 299 m at baseline to 317 m at week 8; median increase of 23 m
- Median Cardiac Effort decreased from 2.3 to 1.8 beats/m (**Figure 2**)
- 7 patients improved Cardiac Effort by >10% from baseline

Figure 2. Change in Cardiac Effort in Response to LIQ861 Treatment



Conclusions

- ASCENT suggests that Cardiac Effort offers early insight into physiologic improvement in PH-ILD following treatment with LIQ861
- Incorporating continuous electrocardiogram-based heart rate monitoring may provide additive and complementary physiologic insight beyond 6MWD alone when evaluating treatment response