An ASCENT to Week 8: Initial Safety and Exploratory Efficacy Data on LIQ861 Dry Powder Inhaled Treprostinil in PH-ILD Patients

Poster #1404

Liquidia®

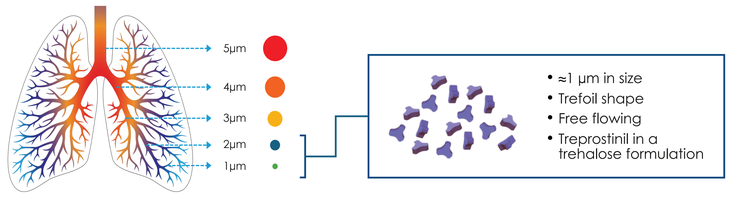
Rajan Saggar,[1] Ashwin Ravichandran,[2] Naomi Habib,[3] Savan Patel,[4] Ashley Galloway,[4] Rajeev Saggar,[4] Jeremy Feldman[5]

[1]UCLA David Geffen School of Medicine/UCLA Medical Center, Los Angeles, CA; [2]St. Vincent Medical Group, Indianapolis, IN; [3]Arizona Pulmonary Specialists, Phoenix, AZ; [4]Liquidia Technologies, Morrisville, NC; [5]Summit Health, Bend, OR

Rationale

- Pulmonary hypertension (PH) is a frequent complication of interstitial lung disease (ILD), and PH-ILD is associated with reduced exercise capacity and substantially increased morbidity and mortality[1]
- Nebulized treprostinil has demonstrated improvements in 6-minute walk distance (6MWD), especially at doses above 9 breaths per session (54 mcg)[2]
- LIQ861 (YUTREPIA™) is an investigational dry powder inhaled formulation of treprostinil developed by Liquidia Technologies (**Figure 1**)
  - LIQ861 particles are designed to enhance deep-lung delivery[3, 4]
  - PRINT® technology produces uniformity of particle size, shape, and composition, for deep-lung delivery[4-6]

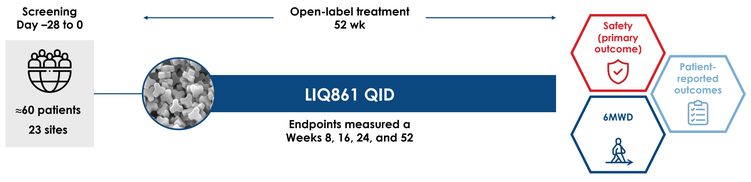
Figure 1. LIQ861 particles



Methods

- ASCENT (NCT06129240) is a prospective, multicenter, open-label study evaluating the safety and tolerability of LIQ861 in patients with PH-ILD, including combined pulmonary fibrosis and emphysema (CPFE)
  - Cohort A will include approximately 60 patients with World Health Organization Group 3 PH-ILD (**Figure 2**)
  - Eligible patients will receive LIQ861 with dose titration based on tolerability and clinical response for 52 weeks (**Figure 3**)
- Here, we present data for the 6MWD exploratory endpoint and the Dyspnea-12,[7] EmPHasis-10,[8] and simplified cough score[9] patient-reported outcome questionnaires from the first 20 patients who completed their Week 8 visit, including only data collected up to that timepoint

Figure 2. Study Design (Cohort A)



Abbreviations: 6MWD, 6-minute walk distance; QID, 4 times daily.

Figure 3. Dose Comparison Between TYVASO® and LIQ861

Number of TYVASO® (nebulized) QID breaths	LIQ861 QID dose (mcg)	LIQ861 capsule combination
≤5	26.5	1 Yellow (26.5 mcg)
6 to 8	53	1 Green (53 mcg)
9 to 11	79.5	1 Blue (79.5 mcg)
12 to 14	106	1 Purple (106 mcg)
15 to 17	132.5	1 Green (53 mcg) + 1 Blue (79.5 mcg)
≥18	159	2 Blue (79.5 mcg)
≥21	185.5	1 Blue (79.5 mcg) + 1 Purple (106 mcg)
≥24	212	2 Purple (106 mcg)

Abbreviation: QID, 4 times daily.

Results

- Two patients had protocol violations and were excluded from the exploratory endpoints analyses
- Among the first 20 patients, the average age was 71.8 years, and 50.0% of the cohort was female (**Table 1**)
- The mean (SD) duration since diagnosis of PH and ILD was 0.4 (0.48) years and 4.2 (3.70) years, respectively
- ILD types included idiopathic interstitial pneumonias (60.0%), autoimmune ILDs (25.0%), and CPFE (15.0%)
- Baseline mean (SD) pulmonary arterial pressure, pulmonary vascular resistance, and pulmonary capillary wedge pressure were 34.2 (8.71) mm Hg, 6.2 (2.42) Wood units, and 8.8 (3.29) mm Hg, respectively

Table 1. Baseline Demographics and Clinical Characteristics

Characteristic	Overall (N=20)
Age, y	71.8 (6.96)
Sex, n (%)	
Male	10 (50.0)
Female	10 (50.0)
Duration of PH diagnosis, y	0.4 (0.48)
Duration of ILD diagnosis, y	4.2 (3.70)
ILD type, n (%)	
Idiopathic interstitial pneumonias	12 (60.0)
Autoimmune ILDs	5 (25.0)
Chronic fibrosis with emphysema	3 (15.0)
Pulmonary function tests	
FEV_1, L	1.8 (0.49)
Percent FEV_1 predicted	75.6 (19.9)
FVC, L	2.2 (0.76)
Percent FVC predicted	72.5 (22.9)
Corrected DLCO, mmol/min/mm Hg	8.1 (3.4)
Percent DLCO predicted	40.1 (16.7)
PIFR, min-max, L/min	65-120
Hemodynamics	
mPAP, mm Hg	34.2 (8.71)
PCWP, mm Hg	8.8 (3.29)
PVR, Wood units	6.2 (2.42)

Data are mean (SD) unless otherwise noted.

Abbreviations: 6MWD, 6-minute walk distance; DLCO, diffusing capacity of the lung for carbon monoxide; FEV_1, 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; PIFR, peak inspiratory flow rate; PVR, pulmonary vascular resistance.

- At Week 8, the median dose of LIQ861 was 132.5 mcg 4 times daily (QID), ranging from 79.5 mcg to 238.5 mcg QID (**Figure 4**)
- The mean (SD) 6MWD increased from 302.7 (100.3) m at baseline to 329.1 (94.0) m at week 8 (**Figure 5A**)
  - The median (min-max) 6MWD increased from 298.8 (148-502) m at baseline to 317.0 (164-513) m at week 8
- The mean (SD) Dyspnea-12 score improved from 13.3 (7.3) to 11.4 (8.8) (**Figure 5B**), and the mean (SD) EmPHasis-10 score had limited improvement from 24.9 (11.2) to 24.1 (12.7)
- The mean (SD) simplified cough score was 1.2 (0.65) at baseline and 1.3 (0.75) at week 8 (**Figure 5C**)

Figure 4. LIQ861 Dose at Week 8

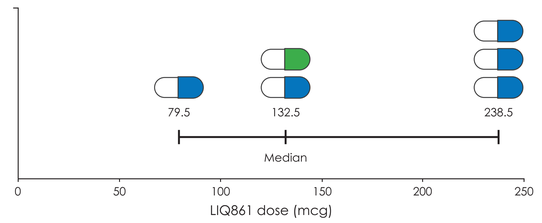
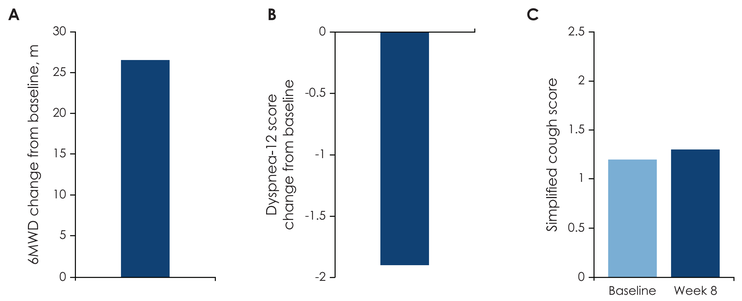


Figure 5. Change in Exercise Capacity, Dyspnea-12 Score, and Simplified Cough Score in Response to LIQ861 Treatment



Abbreviation: 6MWD, 6-minute walk distance.

- With a single exception, all treatment-related treatment-emergent adverse events (TEAEs) were mild, and none were dose dependent
  - The most common treatment-related TEAEs (**Table 2**) were cough (45.0%), headache (10.0%), chest discomfort (10.0%), diarrhea (10.0%), and oropharyngeal pain (10.0%)
  - 1 patient had severe respiratory tract irritation

Table 2. Summary of TEAEs

	Overall (N=20)
Patients with ≥1 TEAE, n (%)	20 (100)
Patients with ≥1 treatment-related TEAE, n (%)	16 (80.0)
Treatment-related TEAEs occurring in >1 patient, n (%)	
Cough	9 (45.0)
Diarrhea	2 (10.0)
Chest discomfort	2 (10.0)
Headache	2 (10.0)
Oropharyngeal pain	2 (10.0)

Abbreviation: TEAE, treatment-emergent adverse event.

Conclusions

- Inhaled LIQ861 was well tolerated for 8 weeks in the first 20 patients
- The median dose was 132.5 mcg QID, and 33.3% of patients achieved a dose of ≥159 mcg QID (equivalent to ≥18 breaths of TYVASO®)
- Improvements in patient-reported outcome measures and exercise capacity were also observed
- The simplified cough score at week 8 was relatively unchanged from baseline
- Early safety, dosing, and efficacy data in the ASCENT Cohort A study are encouraging
  - Continued enrollment and long-term follow-up are needed to confirm these findings

References
1. Waxman AB, et al. *Eur Respir Rev.* 2022;31(165):210220; **2.** Waxman A, et al. *N Engl J Med.* 2021;384(4):325-334; **3.** Hill NS, et al. *Pulm Circ.* 2022;12(3):e12119; **4.** Rosigno RF, et al. *Vascul Pharmacol.* 2021;138:106840; **5.** Garcia A, et al. *J Drug Deliv.* 2012;2012:941243; **6.** Hengo MP, et al. *Int J Environ Res Public Health.* 2020;17(19); **7.** Yorke J, et al. *Chest.* 2011;139(1):159-164; **8.** Yorke J, et al. *Eur Respir J.* 2014;43(4):1106-1113; **9.** Wang Z, et al. *J Thorac Dis.* 2019;11(10):4379-4388.

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