Clinical Outcomes of YUTREPIA™ Dose in 6MWD and Quality of Life

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Background

The current standard of care for inhaled treatment of pulmonary arterial hypertension (PAH) is a nebulized treprostinil solution administered four times a day (QID). Improved clinical outcomes in PAH treatment have been observed at higher treprostinil doses (Shapiro 2021). However, only 28% of the 5000 patients surveyed reached doses above 9 breaths QID of nebulized treprostinil. The average dose of 9.1 breaths per patient suggests dosing the optimal dosing of inhaled treprostinil has not yet been reached.

Investigational drug, YUTREPIA™ (LIQ861) is a novel dry-powder formulation of treprostinil designed using proprietary PRINT® Technology. The PRINT® process enables the development of drug particles that are precise and uniform in size, shape, and composition. YUTREPIA™ particles are monodisperse and have minimal agglomeration allowing efficient delivery to the lungs by a simple capsule-based, dry powder inhaler (DPI, Plastiape RS00 Model 8).

Patient data was reviewed to understand if patients receiving higher doses of treprostinil, administered as YUTREPIA™, had improved clinical outcomes as observed in the earlier referenced publication.

YUTREPIA™ Inhaler

Methods

The INSPIRE trial was a Phase 3, open-label, multicenter trial (LTI-301) to evaluate the long-term safety and tolerability of YUTREPIA™ in PAH WHO Group 1 patients. Exploratory efficacy measures assessed included changes from baseline in six-minute walking distance (6MWD) and New York Heart Association Functional Class (NYHA FC).

The INSPIRE trial enrolled 121 patients who were naïve to prostacyclin or had been on at least three months of stable nebulized treprostinil dosing. Naïve patients initiated therapy at 26.5 mcg while transition patients began with the corresponding treprostinil dose of YUTREPIA™. Over time, patients titrated dosage at 26.5 mcg per week at investigator discretion to alleviate PAH symptoms, not to maximum tolerability. Post hoc analysis was performed to determine the clinical outcome of patients separated into non-randomized <79.5 mcg, 79.5 mcg, and ≥106 mcg dose groups at Month 2.

Nebulized Treprostinil Breaths to YUTREPIA™ Capsule Dose Conversion

Nebulized Treprostinil Breaths	YUTREPIA™ QID Dose (mcg)	YUTREPIA™ Capsule Combination
≤5	26.5	26.5 mcg per capsule
≥6	53	53 mcg per capsule
≥9	79.5	79.5 mcg per capsule
≥12	106	106 mcg per capsule
≥15	132.5	53 mcg per capsule + 79.5 mcg per capsule
≥18	159	79.5 mcg per capsule + 79.5 mcg per capsule
≥21	185.5	79.5 mcg per capsule + 106 mcg per capsule
≥24	212	106 mcg per capsule + 106 mcg per capsule

Results

Of the 121 patients enrolled in the INSPIRE study, 21 patients were on <79.5 mcg dose, 38 patients were on 79.5 mcg dose, and 51 patients were on ≥106 mcg dose of treprostinil at Month 2. Baseline demographics of functional class and % of patients on dual therapy trended with dose group at Month 2.

INSPIRE: Patient Demographics Before Yutrepia Grouped by Dose at Month 2

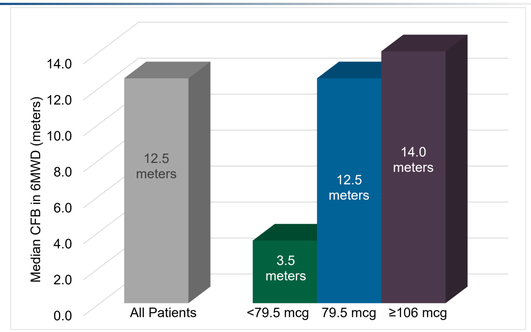
		All Patients (n=121)*	<79.5 mcg (n=21)	79.5 mcg (n=38)	≥106 mcg (n=51)
Sex	Female	99 (81.8%)	16 (76.2%)	30 (78.9%)	44 (86.3%)
Age (years)	Mean ± SD	54.2 ± 14.3	53.3 ± 13.7	49.2 ± 14.7	57.9 ± 14.0
BMI (kg/m²)	Mean ± SD	29.4 ± 7.6	28.4 ± 5.9	32.4 ± 8.1	27.8 ± 7.3
PAH Duration (years)	Mean ± SD	5.79 ± 5.24	6.97 ± 7.20	5.40 ± 4.50	5.94 ± 4.95
NYHA Functional Class†	Class II	78 (64.5%)	20 (95.2%)	25 (65.8%)	29 (56.9%)
	Class III	43 (35.5%)	1 (4.8%)	13 (34.2%)	22 (43.1%)
PAH Therapy†	PDE5i alone	21 (17.4%)	6 (5.0%)	7 (5.8%)	7 (5.8%)
	ERA alone	7 (5.8%)	-	5 (4.1%)	1 (0.8%)
	sGC alone	2 (1.7%)	-	1 (0.8%)	1 (0.8%)
	ERA + PDE5i	81 (66.9%)	13 (10.7%)	22 (18.2%)	38 (31.4%)
	ERA + sGC	5 (4.1%)	-	2 (1.7%)	3 (2.5%)
	None‡	5 (4.1%)	2 (1.7%)	1 (0.8%)	1 (0.8%)

SD, standard deviation; BMI, body mass index; ERA, endothelin receptor agonist; PDE5i, phosphodiesterase 5 inhibitor; sGC, soluble guanylate cyclase stimulator.
*All patients column includes patients who were not on study drug at Month 2.
†NYHA FC and PAH Therapy information from Baseline visit rather than Screening visit.
‡Five patients transitioned from nebulized treprostinil and did not have any additional PAH specific background medications.

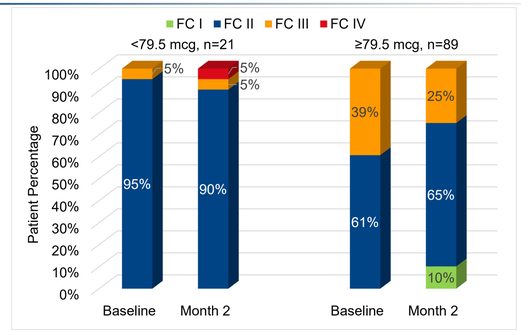
In every dose group, the median Month 2 6MWD improved. Patients receiving doses ≥79.5 mcg showed greater improvements in 6MWD at Month 2 compared to patients receiving <79.5 mcg doses, suggesting that higher doses correlated to larger increases in 6MWD.

Patients receiving ≥79.5 mcg dose showed greater improvements in NYHA Functional Class (FC) than patients receiving <79.5 mcg. At Month 2, percent of patients in FC II or better increased to 75% from 61% at Baseline in the groups receiving ≥79.5 mcg, compared to a decrease to 90% from 95% in the <79.5 mcg dose group.

Median 6MWD Change From Baseline (CFB) in Each Dose Group



% of Patients in Each NYHA Functional Class at Baseline and Month 2



Conclusion

Increasing YUTREPIA™ dose trends with improvements in 6MWD and NYHA Functional Class. Patients treated with <79.5 mcg (26.5 mcg and 53 mcg) showed stable 6MWD and FC while patients at doses ≥79.5 mcg displayed improvement signals in 6MWD and FC suggesting titration to higher YUTREPIA™ doses by Month 2 may improve clinical outcomes.

1. Hill, NS, Feldman, JP, Sahay, S, Benza, RL, Preston, IR, Badesch, D, Frantz, RP, Patel, S, Galloway, A, Bull, TM. INSPIRE: Safety and tolerability of inhaled Yutrepia (treprostinil) in pulmonary arterial hypertension (PAH). *Pulm Circ*. 2022; 12:e12119.
2. Shapiro S, Mandras S, Restrepo-Jaramillo R, et al. Survival and drug persistence in patients receiving inhaled treprostinil at doses greater than 54 µg (nine breaths) four times daily. Pulm Circ. 2021;11(4):20458940211052228. Published 2021 Oct 29.