Exploratory Efficacy Analysis of INSPIRE Open-Label Extension Study With Inhaled Treprostinil (YUTREPIA™)

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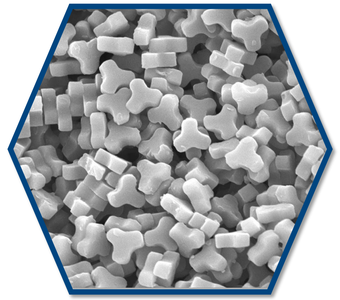
Background

YUTREPIA™ is a dry-powder formulation of treprostinil, as observed in the open-label extension (OLE) of the INSPIRE trial. INSPIRE is a Phase 3, open-label, multicenter study that focuses on patients with pulmonary arterial hypertension (PAH). The study includes patients belonging to the World Health Organization (WHO) Group I classification and are in modified WHO functional class (FC) II or III.

The INSPIRE trial involves 2 categories of PAH patients: those who transitioned to YUTREPIA™ after being on a stable dose of nebulized treprostinil for at least 3 months and taking a maximum of 2 oral PAH therapies (Transition group), and prostacyclin-naïve patients who added YUTREPIA™ to a maximum of 2 oral PAH therapies (PCY Naïve group). Patients who successfully completed the INSPIRE trial were eligible for the OLE, which aimed to evaluate the long-term effects of inhaled treprostinil. The analysis focuses on characterizing the exploratory efficacy endpoints of inhaled treprostinil in the INSPIRE OLE at 24 months.

YUTREPIA™ is formulated using PRINT® technology, which ensures particles of uniform size and shape to enhance deep-lung drug deposition. This approach enhances the drug's effectiveness in reaching the target area within the lungs. YUTREPIA™ is administered through a portable, convenient, capsule-based dry powder inhaler (DPI) that delivers treprostinil doses in just 2 breaths per capsule. This user-friendly design offers patients an efficient and accessible method to receive their medication for managing PAH.

YUTREPIA™ PRINT Formulation



Free-Flowing Particles

Methods

The INSPIRE trial (LTI-301) evaluated the long-term safety and tolerability of YUTREPIA™ in PAH WHO Group 1 patients. Adverse events (AEs) and exploratory measures, including 6-minute walk distance (6MWD), WHO FC, and N-terminal pro-B-type natriuretic peptide (NT-proBNP), were evaluated.

A total of 92/121 (76%) patients completing INSPIRE trial transitioned into the OLE study. The OLE patients were evenly divided between Naïve and Transition Groups; 77 (84%) were females, and 65 (71%) were in FC II, with the remaining patients in FC III. Seventy-three percent of patients received dual oral PAH therapies (ERA plus PDE5i or sGC). Data were analyzed with no imputation for missing data.*

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

YUTREPIA™ Inhaler

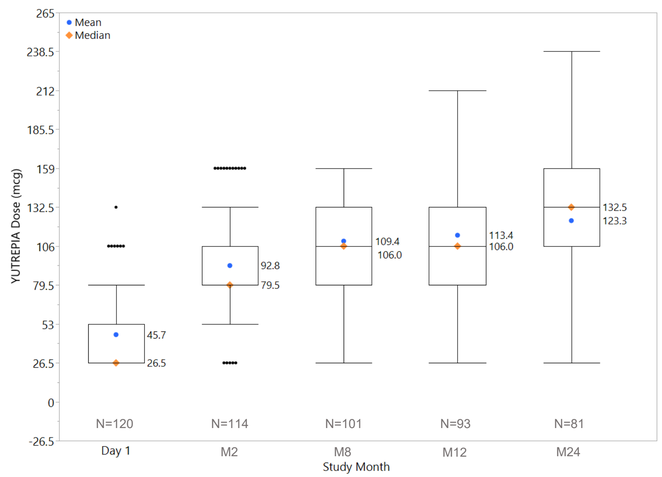
Results

At 24 months, the median dose of YUTREPIA™ was 132.5 mcg, 32.1% of patients achieved a dose ≥159 mcg, and the highest dose was 238.5 mcg (≥27 breaths of nebulized treprostinil) of treprostinil QID. The most common AEs were known effects of inhaled prostanoid therapy. WHO FC was either improved or maintained through 2 years for most patients. The overall 6MWD was relatively stable, with the mean change from baseline of 8.4 meters. No apparent changes from baseline for NT-proBNP were observed.

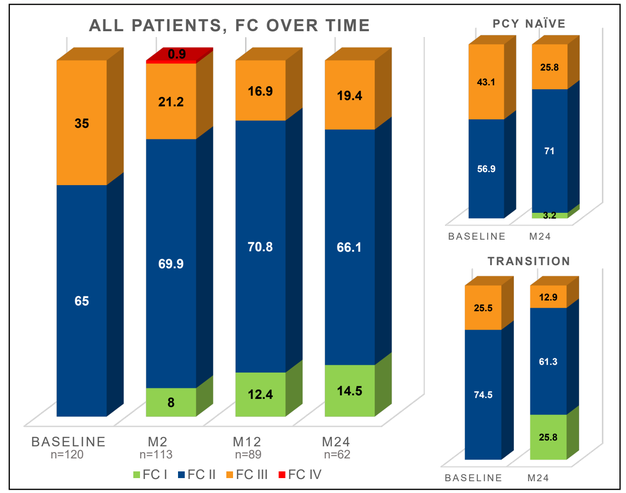
INSPIRE: Patient Demographics & Screening Characteristics Split by Dose at Month 24

		All Patients (n=62)*	< 132.5 mcg (n=33)*	≥ 132.5 mcg (n=29)*
Sex	Female	52 (83.9%)	30 (90.9%)	22 (75.9%)
Age (years)	Mean ± SD	55.5 ± 14.0	53.1 ± 14.8	58.3 ± 12.4
BMI (kg/m²)	Mean ± SD	30.9 ± 7.0	31.1 ± 7.1	30.6 ± 6.9
PAH Duration (years)	Mean ± SD	5.94 ± 4.88	5.86 ± 5.00	6.03 ± 4.73
Change From Baseline in WHO Functional Class at Month 24 Visit*	Improved	18 (29.0%)	8 (24.2%)	10 (34.5%)
	Maintained	40 (64.5%)	22 (66.7%)	19 (62.1%)
	Declined	4 (6.5%)	3 (9.1%)	1 (3.4%)
PAH Therapy	PDE5i alone	14 (22.6%)	6 (9.7%)	8 (12.9%)
	ERA alone	2 (3.2%)	1 (1.6%)	1 (1.6%)
	sGC alone	-	-	-
	ERA + PDE5i	45 (72.6%)	26 (41.9%)	19 (30.6%)
	ERA + sGC	-	-	-
	None†	1 (1.6%)	-	1 (1.6%)

Mean and Median YUTREPIA™ Dose (mcg) Over Time



Mean Functional Class With 24-Month Functional Assessment



Conclusion

Long-term treatment with inhaled treprostinil (YUTREPIA™) was well tolerated and demonstrated persistent benefit for patients with PAH who remained on therapy at 24 months. At 24 months, 18.5% of patients achieved a dose of 132.5 mcg (≥15 breaths of nebulized treprostinil) while 32.1% of patients achieved a dose ≥159 mcg (≥18 breaths of nebulized treprostinil).

SD, standard deviation; BMI, body mass index; ERA, endothelin receptor agonist; PDE5i, phosphodiesterase 5 inhibitor; sGC, soluble guanylate cyclase stimulator.
*Missing data attributed to the COVID-19 pandemic. †One patient transitioned from nebulized treprostinil and did not have any additional PAH specific background medications.

Conflict of Interest Disclosures: C. Burger reports that he contributed to the medical writing of this poster, and is a consultant for Merck, Insmed, Janssen, and Gossamer. **S. Sahay** reports fees for being a speaker for United Therapeutics, Janssen, and Bayer, an advisor for Bayer, Janssen, Gossamer Bio, Liquidia Technologies, and Keros, and a consultant for Liquidia Technologies, Bayer, and Keros, as well as receiving clinical trial support from Janssen, United Therapeutics, Bayer, Gossamer Bio, Liquidia Technologies, Novartis, and Keros, and receiving a research grant from United Therapeutics. Honorarium for speaking engagement is received by Houston Methodist Foundation. **S. Patel** is an employee and shareholder of Liquidia Therapeutics, Inc. **A. L. Galloway** reports she is an employee, patent writer, and shareholder of Liquidia Technologies, Inc. **D. MacLennan** reports he is an employee and shareholder of Liquidia Therapeutics, Inc. **J. M. Elwing** reports being a consultant/advisor for United Therapeutics, Altavant, Aerovate, Bayer, Gossamer Bio, Liquida, Acceleron/Merck, Janssen, Insmed as well as receiving research support/grants from United Therapeutics, Gossamer Bio, Bayer, Acceleron/Merck, Altavant, Aerovate, Tenax, Pharmosa, Actelion/Janssen, Lung LLC

Reference: Hill NS, Feldman JP, Sahay S, et al. INSPIRE: safety and tolerability of inhaled Yutrepia™ (treprostinil) in pulmonary arterial hypertension (PAH). *Pulm Circ* 2022; 12: e12119.