Robustness of YUTREPIA™, a Dry-Powder Inhaled Formulation of Treprostinil, in Patient Misuse Scenarios

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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). A robust and easily used alternative inhaled treprostinil would improve patient compliance and quality of life.

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) with low resistance and high robustness to potential patient misuse.

In vitro aerosol performance results are presented to support the robustness of the dosage form to potential patient misuse scenarios[1].

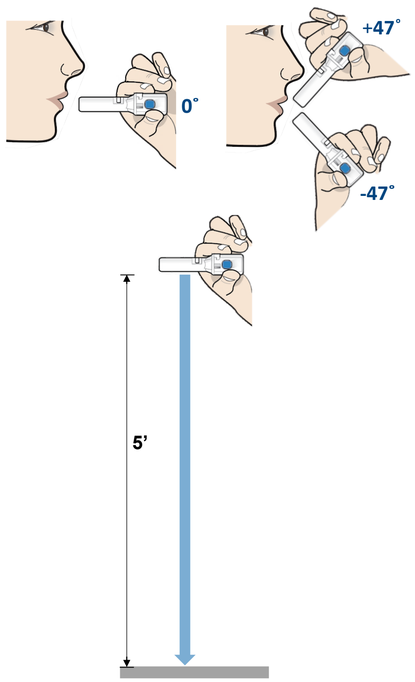
Methods

Liquidia studied the effect of varying DPI orientation on YUTREPIA dosing *in vitro* by measuring aerosol performance at inhaler angles of -47°, 0°, and +47° relative to horizontal after loading and puncturing the capsule within the device.

The effects of patients accidentally dropping the DPI were investigated *in vitro* using a drop height of 5 feet to approximate mouth distance from the ground and simulate two potential patient misuse scenarios. The first scenario investigated the effects of dropping the DPI with the mouthpiece facing down after loading and puncturing the capsule. The second scenario explored the effects of dropping the DPI with the mouthpiece facing up after loading but before puncturing the capsule.

Each study used capsules containing doses of 26.5 mcg and 106 mcg of YUTREPIA. These doses bracket the YUTREPIA capsule strength range as the lowest and highest strengths currently available and results are considered to support all four dosage strengths.

Standard USP <601> *in vitro* methods assessed aerosol performance. Emitted dose (ED) was measured using a Dosage Unit Sampling Apparatus (DUSA); Aerodynamic Particle Size Distribution (APSD) results were collected using a Next Generation Impactor (NGI).

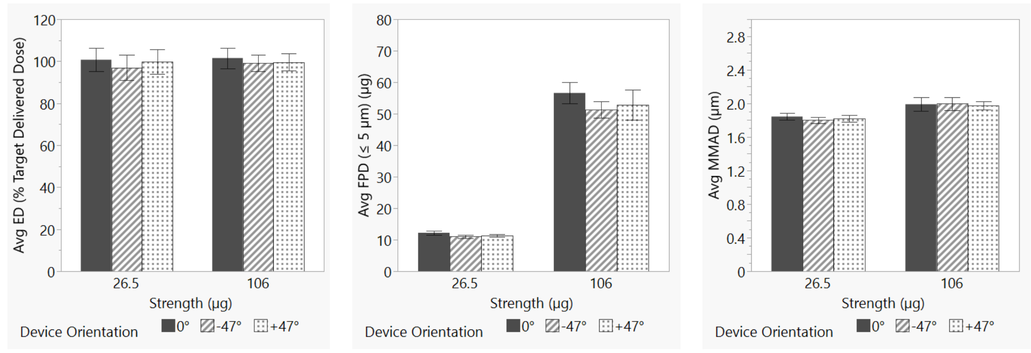


1. Melani AS, Bonavia M, Cilenti V, et al. Inhaler mishandling remains common in real life and is associated with reduced disease control [published correction appears in Respir Med. 2012 May;106(5):757. DelDonno, Mario [corrected to Del Donno, Mario]]. *Respir Med*. 2011;105(6):930-938. doi:10.1016/j.rmed.2011.01.005

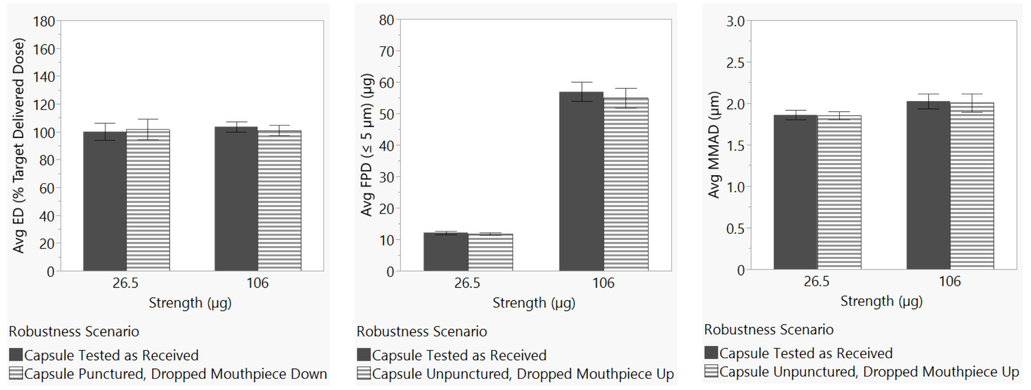
Results

Emitted Dose (ED), Fine Particle Dose (FPD), and Median Mass Aerodynamic Diameter (MMAD) demonstrate consistent *in vitro* exposure while varying device orientation and dropping the inhaler before or after puncturing the capsule.

DUSA and APSD assessments for 26.5 mcg and 106 mcg doses show no significant differences in ED and FPD at -47˚ and +47˚ compared to results at 0˚. APSD results show MMAD is not significantly altered and is ≤2.0 µm for both dosage strengths at all orientations.



DUSA and APSD evaluations for 26.5 mcg and 106 mcg doses show dropping the DPI from 5 feet before or after puncturing the capsule has no significant effect on ED and FPD. APSD results for both doses show dropping the device does not significantly alter the MMAD.



Conclusions

The aerosol performance of YUTREPIA is not affected by real-world patient misuse scenarios such as varying the inhalation orientation or dropping the DPI. The robustness of YUTREPIA results in consistent drug exposure to patients.