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Title: The GOLDEN-1 study: Safety and bronchodilatory effects of nebulized glycopyrrolate (EP-101) using high efficiency nebulizer in patients with COPD

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Body: Introduction: EP-101 is a long-acting muscarinic antagonist bronchodilator for nebulization using a high efficiency nebulizer for the treatment of COPD. The safety and efficacy of once daily nebulized EP-101 was assessed in this Phase 2b study after 7 days of dosing in patients with COPD. Methods: This was a multicenter, randomized, double-blind, placebo-controlled, 4-period cross-over, incomplete block design study. A total of 140 patients with moderate-to-severe COPD were randomized to receive 4 of 7 treatments: EP-101 (placebo, 25, 50, 100, and 200 µg) once daily via high efficiency nebulizer, open-label tiotropium 18 µg once daily, and open-label ipratropium 500 µg three times daily via jet nebulizer. There was a 7-day washout period between treatments. Results: All doses of EP-101 were well tolerated with similar AE rates between placebo and EP-101 (31.2%, 29.7%, 26.9%, 35.5% and 30.7% for placebo, 25, 50, 100 and 200 µg, respectively). There was no apparent dose-response relationship for incidence and severity of AEs. Mean changes in vital signs and ECG parameters from baseline on Day 7 were comparable between the treatment groups. All doses of EP-101 demonstrated dose-related and significant improvements in FEV_1 AUC (0-24hr) on Day 7 compared with placebo, with estimated differences between EP-101 doses and placebo ranging between 110-169 mL. Conclusion: Once daily dosing with nebulized EP-101 was well tolerated over a 7-day treatment period and provided rapid onset of bronchodilation with clinically meaningful and sustained improvement in lung function over 24 hours in patients with COPD. Funded by Elevation Pharmaceuticals Inc.