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Title: Effect of severe renal impairment (SRI) on umeclidinium (UMEC) and vilanterol (VI) pharmacokinetics (PK)

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Body: Introduction: The long-acting muscarinic antagonist UMEC (GSK573719) alone and combined with the long-acting β_2 agonist VI is in development as a once-daily inhaled maintenance bronchodilator treatment for COPD. In healthy subjects, UMEC and VI are predominantly eliminated by the liver with minimal contribution by the kidney. Objectives: As COPD patients are predominantly elderly and renal function decreases with age, the PK, safety and tolerability of UMEC and VI were investigated in subjects with SRI. Methods: Single-blind, non-randomised study of 9 subjects with SRI (CLCr <30mL/min) and 9 healthy controls (HC). Subjects took a single dose of UMEC 125mcg and, after 7–14-days' washout, a single dose of UMEC/VI 125/25mcg. Primary endpoints: UMEC and VI plasma PK parameters. Secondary endpoints: UMEC urine PK, safety, tolerability. Results: All 18 enrolled subjects completed the study. See Table for UMEC and VI plasma exposure data. Urinary recovery of unchanged UMEC (0–24h) was on average lower in SRI vs HC subjects following UMEC (88% lower [90% CI: 81–93]) or UMEC/VI (89% lower [90% CI: 81–93]). UMEC and UMEC/VI were well tolerated.

Conclusions: Administration of UMEC 125mcg or UMEC/VI 125/25mcg to subjects with SRI did not result in clinically significant increases in UMEC or VI exposure vs HC. No dose adjustment for UMEC or UMEC/VI is warranted in patients with SRI. Funded by GSK (DB2114636, NCT01571999).