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**Title:** Efficient deposition and sustained lung concentrations of NVA237 after inhalation via the Breezhaler® device in man

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**Body:** Introduction This study in healthy volunteers (HVs) was designed to investigate the bioavailability of inhaled NVA237 (glycopyrronium bromide-GP) delivered via the Breezhaler® device and to investigate the contributions of pulmonary and gastrointestinal (GI) absorption to systemic exposure. GI absorption was blocked with oral activated charcoal (AC) to study the pharmacokinetics (PK) of the NVA237 absorption via the lung. Methods In Part 1, NVA237 400 µg was administered orally to 10 HVs with and without concomitant administration of AC to demonstrate that GI absorption of NVA237 can be blocked. In Part 2 (n=20 HVs) the PK of 200 µg inhaled NVA237 with and without AC were compared to those of an i.v. infusion of 120 µg GP. Plasma PK data were analyzed by non-compartmental and compartmental methods. Results Result of Part 1 showed that oral AC was effective in blocking the oral absorption of NVA237. Absolute bioavailability of orally administered NVA237 (without AC) was estimated to be about 5%. In Part 2 the absolute bioavailability of inhaled NVA237 was about 40%. About 90% of systemic exposure was due to pulmonary absorption, 10% to GI absorption. About 36% of the inhaled dose was deposited and absorbed in the lungs. The mean terminal half-life of NVA237 was 52.5 h and 57.2 h in the inhalation treatments, 6.2 h after the i.v. dose and 2.8 h after the oral dose. Conclusion NVA237 inhaled via the Breezhaler® device is efficiently deposited and absorbed in the lungs. The terminal half life of NVA237 is much longer after inhalation than after i.v. or oral dosing which points to sustained lung concentrations of NVA237 following inhalation.