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Title: Pharmacokinetics (PK) of mometasone furoate and indacaterol in Japanese and Caucasian healthy subjects after once daily inhalation of QMF149

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Body: Background: QMF149 is an inhaled fixed-dose combination of the long-acting β_2 -agonist indacaterol acetate (IND-A) and the corticosteroid mometasone furoate (MF) being developed for the treatment for asthma and COPD. IND maleate is approved for treatment of COPD (Onbrez® Breezhaler® inhalation powder). MF is approved for treatment of asthma (Asmanex® Twisthaler®). As per the Japanese (J) Package Insert for Asmanex® Twisthaler®, the C_{max} and AUC of MF are ~2 and 3-fold higher for J vs. Caucasian (C) subjects, respectively. Objective: To compare steady state PK of IND and MF between J and C healthy subjects after QMF149 inhalation via the Breezhaler® device. Methods: 24 J and 24 C healthy subjects were enrolled in a single-centre, 2-treatment crossover study with 21 days washout period. Subjects received QMF149 150/80µg (IND-A/MF) or 150/320µg o.d. for 14 days in each period. PK was characterised up to 24h on Days 1 and 14. Results: Mean body weight was 14% higher for C vs. J subjects. The maximum geometric mean ratios (90% CI) for C_{max} for IND and MF (J/C) were 1.23 (1.11-1.38) and 1.24 (1.11-1.38), respectively. Those for AUC for IND and MF were 1.22 (1.09-1.36) and 1.30 (1.18-1.44), respectively. No serious adverse events or discontinuations related to study medication occurred. Conclusion: Mean exposure for IND and MF was higher by 23% and 30%, respectively, in J compared with C subjects, while multiple daily doses of QMF149 were safe and well-tolerated in both ethnic groups. Body weight was considered a contributory factor for the observed difference. These results suggest no dose adjustment for QMF149 is required in Asian populations.