Pharmacokinetics of nicotine and subjective effects following the single use of a non-menthol and menthol version of tobacco heating system 2.2 in two studies in Japan: A comparison with single use of a combustible cigarette and nicotine gum

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The study objective was to evaluate the pharmacokinetic (PK) profile of nicotine following single use of THS 2.2 non-menthol or menthol compared to combustible cigarettes (CC) and nicotine gum (NRT). Two open-label, randomized, two-period, four-sequence crossover studies were conducted, each in 62 healthy Japanese smokers. Each period consisted of 2 days, with 1 nicotine wash-out day, and 1 THS 2.2, CC or NRT single use day with every subject exposed to 2 of the 3 products. A total of 16 venous blood samples were collected, including 1 sample prior to product use. Urge-to-smoke was assessed using the Questionnaire of Smoking Urges-brief (QSU-b). The studies were conducted according ICH GCP and registered with ClinicalTrials.gov, number NCT01959607 and NCT01967706. The overall shape of the nicotine concentration-time curves for THS 2.2 non-menthol and menthol were similar to CC with comparable values for AUC(0-last) and C_max in both studies. AUC(0-last) and C_max were higher in THS 2.2 compared to NRT in one study, with a comparable C_max and a lower AUC(0-last) in the other study. The t_max was not different for CC and THS 2.2 and shorter for THS 2.2 compared to the NRT. The reduction of QSU-b total score observed after THS 2.2 and CC use were similar and greater than the reduction following NRT use. THS 2.2 was well tolerated. The PK profile for both THS 2.2 was comparable to CC in both studies. A transient reduction in urge-to-smoke was observed with THS 2.2, comparable to CC and higher than NRT.

Keywords: Pharmacological effects, Modified risk tobacco product.