Introduction and Objectives

The Tobacco Heating System (THS) 2.2 was developed to reduce or eliminate the formation of harmful and potentially harmful smoke constituents (HPH Cs) in the aerosol through heating and not burning tobacco, while preserving as much as possible the taste, sensory experience, nicotine delivery profile and ritual characteristics of combustible cigarettes (CC).

This study included endpoints to investigate the acceptability of THS 2.2 as a substitute to CC through assessment of subjective effects (questionnaire of smoking urges; modified cigarette evaluation questionnaire [mCEQ]).

Methods

- Open-label, randomized, controlled, 3-arm parallel groups, confinement study.
- 160 healthy smokers aged between 23 and 65 years.
- Subjects smoked CC during 2 baseline days prior to being randomized for 5 days to the following arms: a) ad libitum CC use; b) ad libitum THS 2.2 use; or smoking abstinence (SA).
- The Bofscp were selected based on a variety of criteria:
  - specificity to the source of exposure with other sources being minor or non-existent;
  - detectability using validated methods;
  - reflecting a specific toxic exposure;
  - representing assessment of both gas and particulate phase of the THS 2.2 aerosol;
  - covering a broad variety of chemical and organ toxicity classes (carcinogenic, cardiovascular toxicant, respiratory toxicant, reproductive and development toxicant, addiction potential).
- Urinary Bofscp 24-hr urine samples were collected daily.
- An analysis of variance (ANOVA), adjusted for log-transformed baseline values, sex and daily CC consumption was applied to the log-transformed Bofscp levels with the study arm as a factor.
- The study was conducted in Japan in 2013 according to ICH GCP, approved by an international Review Board, and registered at ClinicalTrials.gov (NCT01970982).

Results

Daily Product Use and Nicotine Exposure

- The average daily product (mean; 95% CI) use between baseline and the end of exposure remained in the same range and was similar in the THS 2.2 and CC arms.
- The total nicotine exposure [mean; 95% CI] measured as nicotine equivalents was similar in both arms throughout the exposure period (THS 2.2/CC ratio >99% [95% CI: 83 to 119%]).

Subjective Effects

- The reductions in Bofscp levels were observed within 24 hours of initiating THS 2.2 use.
- After the 5-day exposure period, the levels of Bofscp were significantly reduced by 56% to 98% in the THS 2.2 arm as compared to CC and approaching levels seen in the SA arm. Exposure to toluidine via the measurement of S-8MA is not presented, as the levels were similar in all study arms.

Conclusions

- The study demonstrated that switching from CC smoking to THS 2.2 use resulted in substantial reductions in exposure to 14 selected HPHCs. The kinetics and the magnitude of decrease of the Bofscp levels observed in the THS 2.2 arm were approaching the levels observed in the SA arm.
- The exposure to nicotine was similar between the THS 2.2 and CC arms indicating that users adapted quickly to the new product and achieve their individual nicotine levels.
- No serious or severe adverse events (AEs) were reported during this study. A total of 11 AEs were reported in 10 study subjects in the safety population. All of the AEs were of mild severity. The incidence and frequency of AEs were comparable in the THS 2.2, CC and SA arms.