REDUCED EXPOSURE TO HARMFUL AND POTENTIALLY HARMFUL CONSTITUENTS AFTER FIVE DAYS OF USE OF TOBACCO HEATING SYSTEM 2.2: A COMPARISON WITH CONTINUED COMBUSTIBLE CIGARETTE USE OR SMOKING ABSTINENCE [JAPAN]

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The Tobacco Heating System (THS) 2.2 was developed to reduce or eliminate the formation of harmful and potentially harmful smoke constituents (PHYCs) 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).

The study reported here is part of a global clinical program for THS 2.2 and was designed to demonstrate exposure reduction to selected PHYCs when switching from CC to THS 2.2 in a controlled setting for 5 days, compared to those continuing to smoke CC. Smokers who abstained from smoking were used as a benchmark. The Biobay measured in this study represented 14 PHYCs, considered to provide a representative assessment of human uptake of a variety of toxicants and carcinogens in tobacco-products. This study also included endpoints to investigate the acceptance of THS 2.2 as a substitute to CC through assessment of subjective effects (questionnaire of smoking urges-Brief [QS-Brief]; modified cigarette evaluation questionnaires [MEQ]).

Methods

- Open-label, randomized, controlled, 3-arm parallel groups, confinement study.
- 160 healthy Japanese 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: ad: abstinence CC use; ad: abstinence THS 2.2 use; or smoking abstinence (SA).
- The Biobay 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 (carcinogens, cardiovascular toxicant, respiratory toxicant, reproductive and development toxicant, addiction potential).
- Urinary Biobay 24-hour 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 Biobay 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 (NCT01970882).

Results

Demographics

| Variable | Statistic | THS 2.2 | CC | SA | OVA
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<tr>
<td>Age (years)</td>
<td>Mean (SD)</td>
<td>37.2 (7.4)</td>
<td>37.9 (7.0)</td>
<td>35.4 (8.6)</td>
<td>37.1 (7.1)</td>
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Sex (Male) | n (%) | 40 (50.0) | 20 (50.0) | 20 (50.0) | 80 (50.0)

Daily CC consumption at screening 10-19 light/day | n (%) | 36 (45.0) | 38 (46.0) | 18 (45.0) | 72 (45.0)

Biomarkers of Exposure

<table>
<thead>
<tr>
<th>COHb</th>
<th>1-NA</th>
<th>2-NA</th>
<th>Total NNAL</th>
<th>Total NNK</th>
<th>O-Toluidine</th>
<th>Total NNK</th>
</tr>
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<tbody>
<tr>
<td>Carbon monoxide</td>
<td>Acetone</td>
<td>Acetone</td>
<td>N NNK</td>
<td>N NNK</td>
<td>O-Toluidine</td>
<td>O-Toluidine</td>
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CEMA Acrylonitrile | 1-ChIP Pyrene | 4-AEP 4-amino-phenyl | HRMPMA Crotonaldehyde | HEPE Ethylene oxide

Conclusions

- The study demonstrated that switching from CC smoking to THS 2.2 use resulted in substantial reductions in exposure to 14 selected PHYCs. The kinetics and magnitude of decrease of the Biobay 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.
- These results indicate that THS 2.2 may offer urge to smoke reduction comparable to CC, and could be an acceptable substitute for CC.

Abbreviations

- CL: Clearance; I: Inhalation; LOQ: Limit of quantification; LOD: Limit of detection; S: Smoking; SA: Smoking abstinence; THS: Tobacco heating system; NS: Not significant; *P < 0.05; **P < 0.01; ***P < 0.001.

Competing financial interests

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