OBJECTIVES

To compare the nicotine pharmacokinetic (PK) profiles and nicotine delivery of six flavors of 4mg on!® nicotine pouches relative to subject’s own brand cigarettes under controlled use conditions.

To compare the subjective effects of six flavors of 4mg on!® nicotine pouches relative to subject’s own brand cigarettes under controlled use conditions.

RESULTS

PRODUCT USE, QUESTIONNAIRE & PK BLOOD DRAW

STUDY DESIGN

Study Title: A Randomized, Controlled, Crossover Clinical Study to Characterize the Nicotine Pharmacokinetics and Subjective Effects of Six 4mg on!® Nicotine Pouch Products Relative to Combustible Cigarettes in Adult Smokers.

Key Inclusion/Exclusion Criteria:
- Inclusion Criteria:
  - Healthy adult males & females 21 to 85 years of age
  - Self-reported adult exclusive smokers of combustible manufactured cigarettes (at least 10 per day, for at least 12 months).
  - Positive urine cotinine (≥500 ng/ml, at screening).
- Exclusion Criteria:
  - Use of any TDN pouch products within the 30 days prior to screening.
  - Attempted to quit smoking in the 3 months prior to Day -1.
  - Self-reported pullers (draw smoke into mouth but don’t inhale).
  - Planning to quit smoking or postponement of quitting smoking.

METHODS

STUDY PRODUCTS

Six Flavors of the 4mg on!® Nicotine Pouches at the 4mg Nicotine Level and Subject-Provided (That Own-Pack) Combustible Cigarettes

<table>
<thead>
<tr>
<th>Flavor</th>
<th>Product Name</th>
<th>Place</th>
<th>Target PK Nicotine</th>
<th>Max Nicotine Per Pouch</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>on!® Original</td>
<td>4mg</td>
<td>4.07</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>on!® Cinnamon</td>
<td>4mg</td>
<td>3.59</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>on!® Original</td>
<td>4mg</td>
<td>3.60</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>on!® Citrus</td>
<td>4mg</td>
<td>3.62</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>on!® Coffee</td>
<td>4mg</td>
<td>3.30</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>on!® Original</td>
<td>4mg</td>
<td>3.30</td>
<td></td>
</tr>
</tbody>
</table>

BACKGROUND & PURPOSE

BACKGROUND

There is overwhelming scientific evidence regarding a risk continuum in the range of tobacco products available currently in the market. According to this body of evidence, combustible tobacco products such as conventional cigarettes are the most risky and non-combustible tobacco products present relatively lower risks. Moreover, cigarettes and smokeless tobacco (ST) users (including dual users of cigarettes and ST products) are seeking alternatives to their current products.

The lead products used in this study were pouch products containing tobacco-derived nicotine and flavors. These nicotine pouch products are intended for adult smokers and ST users (including dual users of cigarettes and ST products) who desire a more convenient alternative to cigarettes and smokeless tobacco products currently commercially available in the US.

The 4mg nicotine pouches are oral tobacco-derived nicotine products. These nicotine pouch products are intended for adult smokers and ST users (including dual users of cigarettes and ST products) who desire a more convenient alternative to cigarettes and smokeless tobacco products currently commercially available in the US.

PURPOSE

The purpose of this study was to develop scientific evidence to address the regulatory guidance set forth by the Food and Drug Administration (FDA) regarding assessment of abuse liability in support of premarket tobacco product applications (PMTAs). This study was designed to investigate the reinforcing effects of oral tobacco-derived nicotine (TDN) pouch products currently marketed as 4mg nicotine pouches, relative to adult subject’s own brand combustible cigarettes, as well as to characterize product use behavior under ad libitum use conditions. The relative reinforcing effects of the 4mg nicotine pouches may provide evidence to assess their abuse potential relative to subject’s own brand combustible cigarettes amongst adult (21 - 65 years) age smokers.

CONCLUSIONS

1. 1. The product "Helped" right now
   2. 2. The product "Warned" right now
   3. 3. The product helped me do "Other" right now
   4. 4. The product helped me "Learn" right now
   5. 5. The product helped me "Focus" right now
   6. 6. The product helped me "Plan" right now

REFERENCES