Changes in Clinical Risk Endpoints Linked to Cardiovascular and Other Smoking-Related Diseases after Switching from Cigarettes to the Tobacco Heating System (THS) 2.2 for Six Months


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Introduction and Objectives

Background

Tobacco harm reduction, by substituting less harmful tobacco products for cigarettes, is a complementary approach to smoking prevention and cessation and is intended for smokers who would otherwise continue to smoke. The Tobacco Heating System (THS) 2.2 is a novel tobacco product with the potential to prevent or reduce the harm compared with conventional smoking. It heats a tobacco plug in a controlled manner, never allowing the temperature to exceed 350°C, preventing combustion and thereby reducing exposure to selected toxicants.

Main Objectives

• Demonstrate statistically significant changes in four out of eight clinical risk endpoints (CREs) for smokers switching from CC to THS compared with continued smoking for six months.

Methods

Study Design

This was a randomized, controlled, two-arm parallel group, multicenter U.S. study in adult smokers who switched from CCs to THS compared with those who continued to smoke CCs over six months. The primary objective was to demonstrate modification of CREs in THS users (≥ 70%) for at least five out of the eight CREs. 984 subjects were randomized to CC (n = 496) or THS (n = 488). Additional biomarkers of exposure and CREs of inflammation, lipid metabolism, endothelial function, platelet function, oxidative stress, and lung function were evaluated in the study.

Study Conduct

The study was approved by an Institutional Review Board and initiated in March 2015. The study was conducted according to the principles of International Conference on Harmonisation Good Clinical Practice and registered on ClinicalTrials.gov (NCT02294368).

Statistical Analysis

Success Criteria:

To establish that the risk profile of IQOS is modified compared to cigarettes.

1. All 8 CREs must move directionally toward the changes reported upon smoking cessation in the literature.

2. A 5 out of 8 CREs show significantly larger changes in THS compared to continued smoking.

3. A 5% significant CRE endpoint is established.

Results

Changes in Clinical Risk Endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Change from CC Use</th>
<th>Observed Change</th>
<th>LS Mean Difference/Relative Reduction</th>
<th>Holm-Sidak Adjusted P value</th>
<th>1-Sided 96.875% CI</th>
<th>2-Sided Directional Change vs. SA (literature)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL-C</td>
<td>Difference</td>
<td>3.01 mg/dL</td>
<td>1.10, 5.80</td>
<td>0.001*</td>
<td>≥ 0.031</td>
<td>n.s.</td>
</tr>
<tr>
<td>FEV1</td>
<td>Difference</td>
<td>-0.145</td>
<td>-2.42, 0.04</td>
<td>0.030</td>
<td>≥ 0.015</td>
<td>≥ 0.015</td>
</tr>
<tr>
<td>sICAM-1</td>
<td>Difference</td>
<td>-3.09</td>
<td>-7.50, 1.06</td>
<td>0.193</td>
<td>≥ 0.015</td>
<td>≥ 0.015</td>
</tr>
</tbody>
</table>
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Conclusions

The Exposure Response Study was designed to answer important regulatory questions on the effects of THS as it is actually used by adult smokers.

We evaluated biological and functional changes in healthy, adult smokers who switched to THS compared with continued CC smoking. The study demonstrated that all CREs moved in the same direction as the smoking cessation effect observed in the literature. Five out of eight endpoints showed significant favorable changes after switching to THS vs. continued smoking, notwithstanding up to 30% of cigarettes smoking in the primary analysis population.

The results obtained through this study further substantiate the harm reduction potential of THS while providing evidence on product use and acceptance of THS by smokers.

Competing Financial Interest

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