Evaluation of biological and functional changes in healthy smokers after switching from cigarettes to Tobacco Heating System (THS) 2.2 for 6 months

Introduction

The most effective way for cigarette smokers to reduce their risk of smoking-related diseases, resulting from long-term exposure to harmful and potentially harmful constituents (HPHCs) in cigarette smoke, is to quit smoking. Tobacco harm reduction, replacing cigarettes (CC) with less harmful tobacco products, is a complementary approach for smokers who would otherwise continue smoking. THS 2.2 is a novel tobacco product that electrically heats tobacco at temperatures lower than cigarettes, producing substantially lower HPHC levels, while providing a taste, sensory experience, nicotine delivery that parallels smoking.

Previous clinical studies demonstrated reduced exposure to HPHCs (approaching levels of smoking abstinence) for smokers who switched to THS 2.2 for up to 3 months. This study was designed to further substantiate the harm reduction potential in smokers switching to THS, confirming similar changes in biological and physiological health effects (clinical risk endpoints — CREs) to those observed in smokers who stop smoking.

Methods

This was a randomized, controlled, two-arm parallel group, multicenter US study in healthy adult smokers, not willing to quit smoking, who switched from CC to THS 2.2 relative to continuing to smoke CC over 6 month (Figure 1). The primary objective was to demonstrate statistically significant favorable changes (comparable to smoking cessation) in predominant THS 2.2 switchers (THS use category), for at least 5 out of the 8 CREs tested, with THS-use vs CC-use effect evaluated for each CRE, and with all of the CREs moving into the direction of smoking cessation.

The analysis was performed using a 1-sided test with the Halden-Rüger adjusted type I error (a=1.5625%). These CREs are linked to smoking-related diseases, representative of multiple pathomechanistic pathways that are sensitive to smoking and reversible within 1 year of smoking cessation in the literature.

Results

The population (FAS EX) used for analysis of CREs was analyzed according to three product use categories:

1. THS-use: >70% use and more than 50% of days THS use
2. Dual-use: <70% use or less than 50% of days
3. CC-use: < 1% THS use

Other-use: E-cigarette, quitters, other products

The overall tobacco use in the THS-use category was similar to the reported Baseline CC use, with mean of approximately 16.5 THS/day and 20CC/day in the Dual-use and CC-use categories, the overall tobacco use during the randomized period was lower relative to the baseline CC use.

Exposure to nicotine, as measured by urinary nicotine equivalents; nicotine and cotinine in plasma, was comparable between THS-use and CC-use categories.

Conclusions

This study demonstrated that switching to THS 2.2 results in favorable changes in CREs representative of pathomechanistic pathways underlying the development of smoking-related diseases. These results indicate a lower risk profile in smokers switching from CC to THS 2.2, an alternative candidate modified risk tobacco product.