A Multi-Center, Multi-Regional, Study on Functional and Biological Changes in Healthy Adult Smokers during One Year of Continuous Smoking Abstinence

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Introduction and Objectives

Background
The frame from smoking mainly results from long-term exposure to harmful and Potentially Harmful Constituents (PHCs) contained in cigarette smoke generated by the combustion of tobacco. Smoking Cessation (SC) is the most effective way to reduce the harm and risk of smoking-related diseases to a minimum risk level which may approach, even near, that of never-smokers. In recent years, the need for SC studies has been increased by the accelerated phasing out of the SC treatment being tested. However, and in contrast, information on long-term functional/biological changes following SC is available in the literature.

Main Objectives
The overall aim of this study was to assess over a one-year period of continuous smoking cessation the reversibility of the harm related to smoking by assessing changes of Biomarkers of Exposure (BIOs) to PHCs and Clinical Endpoint (CE) which are linked to pathophysiologic pathways of smoking-related diseases. These BIOs and CE were selected according to scientific evidence that these endpoints are associated with smoking-related diseases, and the expectation that these effects are reversely smoking cessation over a period of time within the study duration.

Methods

Design
This was a multi-center, multi-visit (K 3 visits), exploratory study conducted in the US, UK, Poland, Germany, and Japan, in healthy adult smokers who were willing to quit smoking and were asked to continuously abstain from smoking during a 52-week period in an ambulatory setting followed by a 28-day Safety Follow-Up period.

To support the subjects to stop smoking, Nicorette Replacement Therapy (NRT) was provided at subjects’ request and used as per country label for up to 3 months. Additionally, smoking cessation support, including counseling and behavioral support, was provided throughout the study and upon subjects’ request.

Participants
Subjects underwent the Information provided for the study and signed the Informed Consent Form. Subjects were aged ≥18 years and declared healthy by the investigator.
Subjects had no disorders or other conditions that would have precluded the subject’s safety or affect the validity of the study results as judged by the investigator.
Subjects were not ≥70 years and declared smoking at least 10 mg cigarette/day for two to 12 months and had been smoking for 10 years.
Subjects had no history of alcohol or drug use.
Female subjects were not pregnant or breastfeeding and those not using any contraceptives.

Smokers were willing to quit smoking in the study by smoking ≤5 cigarettes/day at the end of the study and ≤2 cigarettes/day after week 52.

Results

Demographics
A total of 3,305 smokers willing to quit smoking were enrolled, and 458 successfully completed the study after one year of smoking cessation.

Indicators Data Extraction (6 months)
Flow data were extracted from a subset of 348 subjects, of which 272 were continuously smoking and underwent baseline with Month 6 data as the following: smoking and exposure; on or off tobacco. Nicotine containing products, CO (mg/100 mL) < 10 ppm, cotinine < 100 ng/mL as an active (Month 6, 6 months) Nicotine concentration < 0.5 mg/L at 48 hour-cutoff of Month 6.

Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
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<tbody>
<tr>
<td>Male (%)</td>
<td>522 (48.8)</td>
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<tr>
<td>Female (%)</td>
<td>600 (51.2)</td>
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</tbody>
</table>

Conclusions
The 6-month interim study results indicate that continuously stopping smoking leads to a substantial reduction in exposure to PHCs, subsequently resulting in favorable changes in CE, reflecting multiple mechanisms and biological effects including those mechanisms, inflammatory or oxidative stress, all of which changes are likely to be contributing to the reduction of the risk developing smoking-related diseases.

References

[Please provide references if available.]