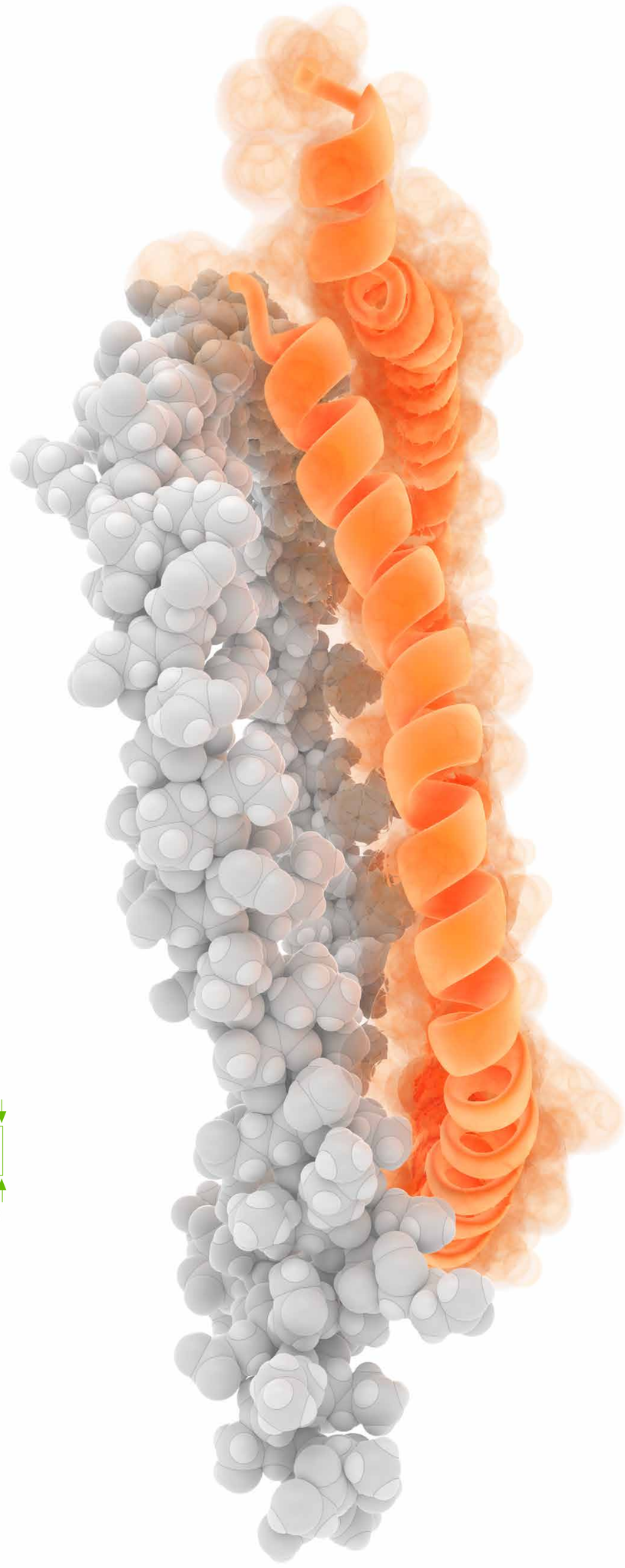
A Multi-Center, Multi-Regional, Study on Biological and Functional Changes

in Healthy Adult Smokers during One Year of Continuous Smoking Abstinence

C. T. Tran, L. Felber Medlin, N. Lama, B. Taranu, E. Pierri, J. Ancerewicz, P. Picavet, G. Baker, C. Haziza, F. Lüdicke —
PMI R&D, Philip Morris Products S. A., Quai Jeanrenaud 5, CH-2000 Neuchâtel, Switzerland (Part of Philip Morris International group of companies)

PMI SCIENCE
PHILIP MORRIS INTERNATIONAL



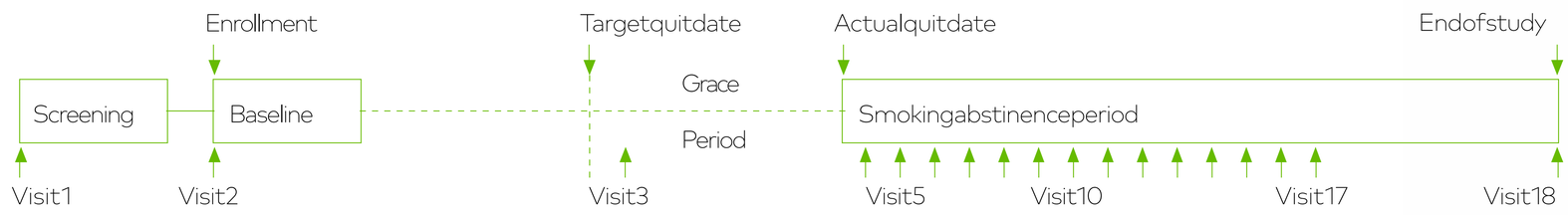
Introduction and Objectives

The harm from smoking mainly results from long-term exposure to Harmful and Potentially Harmful Constituents (HPHCs) 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 relative risk level which may approach, overtime, that of never-smokers. In most SC studies, the main focus is on the successful quitting rate of the SC/approach treatment used. However, only limited information on short- to long-term functional/biological changes following SC is available in the literature.

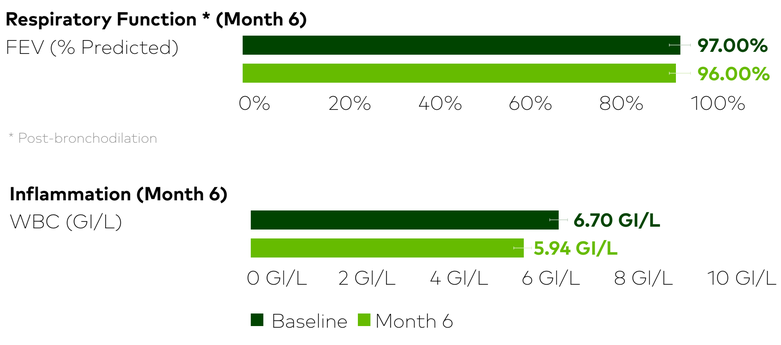
The overall aim of this study was to assess over a one-year period of continuous smoking abstinence the reversibility of the harm related to smoking by assessing changes of Biomarkers of Exposure to HPHCs (BoExp: CO in exhaled breath along with 8 urinary BoExp compounds) and Clinical Risk Endpoints (CREs) which are linked to pathophysiological pathways of smoking-related diseases. Selected CREs were associated with cardiovascular diseases (lipid metabolism, inflammation, platelet function, oxidative stress, endothelial dysfunction, metabolic syndrome, acute cardiovascular effect); respiratory diseases (spirometry); and genotoxicity (total NNAL). These BoExp and CREs were selected according to epidemiological evidence that the endpoints are associated with smoking-related diseases, sensitive to smoking status, and the expectation that these effects are reversed by SC over a period of time within the study duration.

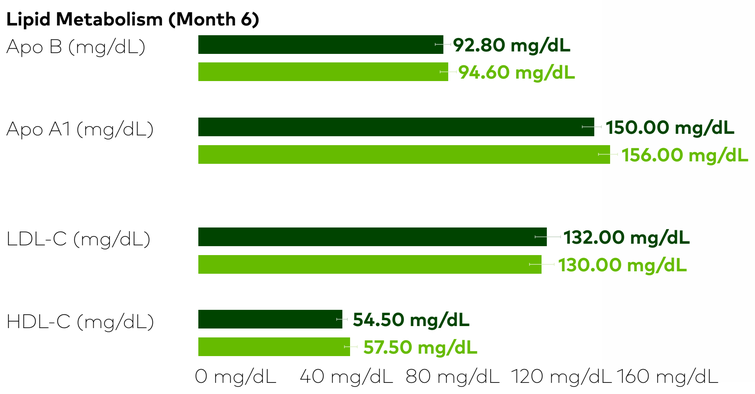
Methods

This was a multi-region, multi-center, ambulatory 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 (1-year) period. To support the subjects to stop smoking, Nicotine Replacement Therapy (NRT) was provided at subjects' request and used as per country label for up to 3 months. Additionally, SC support, including counseling and behavioral support, was provided throughout the study and upon subjects' request. Data analysis of the full study (1 year continuous SC) is ongoing. This poster presents the data of an interim analysis from data extracted from a subset of 348 subjects of which 272 were continuously smoking abstinent until Month 6 based on the following criteria: self-reported use of tobacco/nicotine containing products, CO breath test ≤ 10 ppm, cotinine test < 100 ng/mL in spot urine (Month 5 onwards), free cotinine concentration < 50 ng/mL in 24-hour-urine (at Month 6). For the whole study, a total of 1,185 smokers willing to quit smoking were enrolled, and 436 successfully completed the study after one year (analysis ongoing).



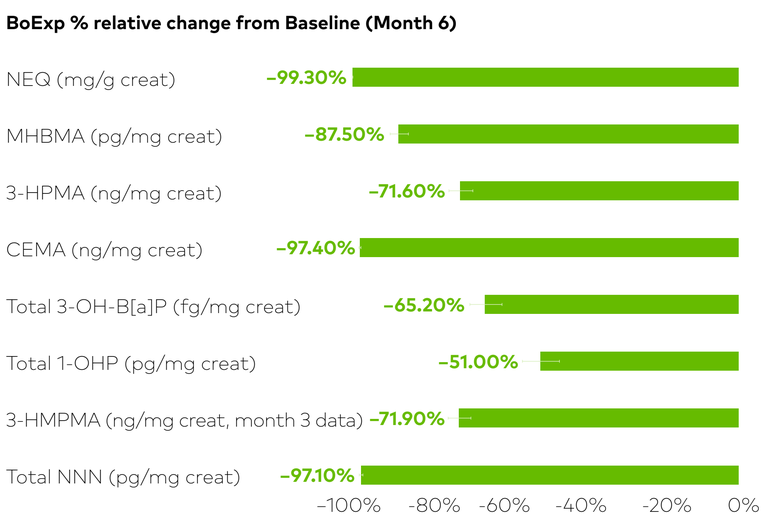
Results





ApoA1 – key component of high density cholesterol particles

Pathway	Endpoint	Relative change from baseline	95% CI
Inflammation	hs-CRP (mg/L)	1.33%	14.5, −10.3
	Homocysteine (µmol/L)	−10.4%	−7.58, −13.1
Platelet function	Platelet count (Gl/L)	5.13%	2.94, 7.36
	Fibrinogen (mg/dL)	−1.55%	0.653, −3.71
	11-DTX-B2 (pg/mg creat)	−26.8%	−20.9, −32.3
Oxidative stress	8-epi-PGF_{2a} (pg/mg creat)	−18.8%	−14.3, −23.1
	Myeloperoxidase (µg/L)	−6.73%	2.17, −14.8
Endothelial Dysfunction	s-ICAM-1 (ng/mL)	−12.3%	−10.0, −14.6
	Albumin urine (mg/g creat)	−0.665%	10.4, −10.6
Acute Cardiovascular Effect	COHb (%)	−74.4%	−71.6, −77.0
Genotoxicity	Total NNAL (pg/mg creat)	−96.5%	−97.0, −95.9



Conclusions

The 6-month interim study results indicate that continuously stopping smoking leads to a substantial reduction in exposure to HPHCs, subsequently resulting in favorable changes in CREs reflecting improvements of multiple mechanisms and biological functions including lipid metabolism, inflammation or oxidative stress. All of these changes are likely to be contributing to the reduction of the risk of developing smoking-related diseases

Global Forum on Nicotine, June 14 – 16, 2018. Warsaw, Poland