Supplementary Table 1. Primary Endpoints.

Primary Endpoint	Measurement	Matrix / Function	Timeframe of Reversibility upon Smoking Cessation	Method
High density lipoprotein Cholesterol (HDL-C)[1]	Lipid Metabolism	Serum	Within 3 months	The cholesterol concentration of HDL-c was determined by enzymatic colorimetric assay in serum on a Roche Modular Cobas Testing Platform. This assay has been approved by the U.S. Food Drug Administration for "in vitro" diagnostic use.
Soluble intercellular adhesion molecule-1 (sICAM-1)[2,3,4]	Endothelial Dysfunction	Serum	Within 4 weeks	sICAM-1 was measured in human serum using Enzyme Immunoassay (EIA) performed on Bio-Tek ELx800.
White blood cell (WBC) count (total count)[5,6,7,8]	Inflammation	Blood	Within 6-12 months	The WBC count was determined in whole blood on a Siemens Advia 2120i Hematology Analyser. This assay has been approved by the U.S. Food Drug Administration for "in vitro" diagnostic use.
Carboxyhemoglobin (COHb)[9,10]	Transport of oxygen by hemoglobin	Blood	Within 1-7 days	The determination of COHb in blood was carried out over a calibration range of 0.2% to 50.0% by spectrophotometry on a Radiometer Instrument.
11-dehydrothromboxane B2 (11-DTX-B_2)[11,12,13]	Platelet activation	Urine	Within 2-4 weeks	The determination of 11-dehydrothromboxane B2 was carried out over a calibration range of 25.0 pg/mL to 2500 pg/mL in an aliquot from 24-hour urine collection. Urine containing the analyte and internal standard was extracted using a solid phase extraction procedure and analyzed by Ultra Performance Liquid Chromatography equipped with an AB SCIEX QTRAP® 5500 or an AB SCIEX Triple Quad™ 6500 triple quadrupole mass spectrometer using an Atmospheric Pressure Chemical Ionization source. Negative ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis ($1/concentration^2$) of peak area ratios of the analyte and internal standard.

8-epi-prostaglandin F2 alpha (8-epi-$PGF_{2\alpha}$)[14,15]	Oxidative stress	Urine	Within 1-2 weeks	The determination of 8-iso-Prostaglandin-F2α (Type III) was carried out over a calibration range of 25.0 pg/mL to 1500 pg/mL in an aliquot from 24-hour urine collection. Urine containing the analyte and internal standard was extracted using a 96 well-based solid phase extraction procedure. The extracted samples were analyzed by high pressure liquid chromatography equipped with an AB SCIEX API 4000™ or QTRAP® 5500 triple quadrupole mass spectrometer using an Atmospheric Pressure Chemical Ionization source. Negative ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis (1/concentration) of peak area ratios of the analyte and internal standard.
Forced expiratory volume in one second (FEV_1)[16,17,18,19]	Lung Function	Lung function	Within 6-12 months	The spirometry test was performed in accordance with the 2005 guideline of the American Thoracic Society (ATS)/European Respiratory Society (ERS) Joint Task Force on the standardization of spirometry.[21] The determination of FEV1 in subjects were performed with spirometry using the multi breath (closed-circuit) method technique throughout the course of this study. Spirometry predicted values were standardized to the Third National Health and Nutrition Examination Survey (NHANES III) predicted set. All post-bronchodilator spirometry testing was performed 15-30 minutes post administration of around 400 μg of salbutamol (usually equivalent to 4 puffs assuming 100 g/puff) (TBC). A qualified Pulmonary Physiologist provided technical QA reviews of PFTs for all sessions for central-reading across sites.
Total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol) (Total NNAL)[20]	Exposure to carcinogenic HPHC (NNK)	Urine	Within 3 months	The determination of total NNAL was carried out over a calibration range of 5.00 pg/mL to 1000 pg/mL (NNAL) in an aliquot from 24-hour urine collection. Urine containing the analyte and internal standard was extracted using a solid phase extraction procedure. The extracted samples were analyzed by an HPLC equipped with an AB SCIEX API 4000™ and AB SCIEX Triple Quad™ 6500 triple quadrupole mass spectrometer using an Electrospray ionization source. Positive ions were monitored in the multiple reaction monitoring (MRM) mode. Quantitation was determined using a weighted linear regression analysis (1/concentration^2) of peak area ratios of the analyte and internal standard.

Descriptions of the bioanalytical methods used to measure creatinine and BoExp tested as secondary objectives were published in 2016.[22]

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