Changes in Biomarkers of Exposure and Potential Harm Among Adults Who Switch from Cigarettes to the Ploom® Heated Tobacco System

Jason KS. Hong, MD

Senior Principal Scientist, Altria Client Services

Altria

Horizon Innovations LLC is a joint venture between Philip Morris USA Inc. and JTI (US) Holding Inc. for the commercialization of Ploom® in the U.S. market.

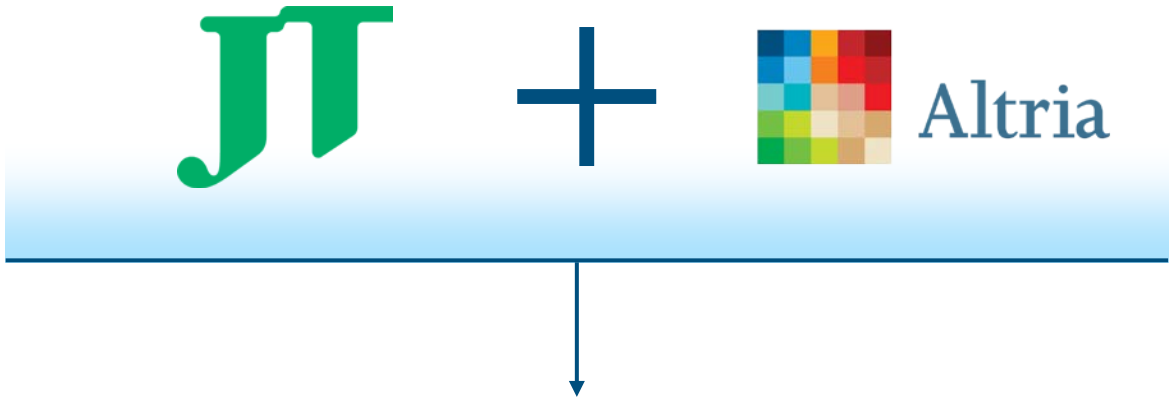
Agenda

- Background
- Overview of Study Design
- Study Results
- Discussion

PARTNERSHIP

Between JT Group and Altria

to Bring Ploom System to U.S. Adults (Age 21+) Who Smoke



Portfolio Approach to Tobacco Harm Reduction Supports Greater Choice

Smokeless Tobacco Products

Modern Oral Tobacco Products

Heated Tobacco Products (HTP)

E-Vapor Products

*PLOOM® is currently unavailable for sale in the United States.

The Ploom® System

Ploom® Device

Heated Tobacco Sticks (HTS)

Generates aerosol without burning of tobacco

Designed to provide satisfying user experiences

Menthol-Flavored Variant

Tobacco-Flavored Variant

Study Overview

STUDY DESIGN

A Multi-site, randomized, parallel-group study including:

HTP ARMS

2 HTS with no combustion

Menthol Variant

Tobacco Variant

COMPARATOR ARMS

Continue to Smoke

Smoking Abstinence

KEY OUTCOMES

Comparison of urinary and blood BOEs between HTP arms and the corresponding Continue Smoking arm following 5 days of *ad libitum* use of HTPs or cigarettes in a confinement setting.

- ✓ Biomarkers of Exposure (BOE)
- ✓ Daily Product Use
- ✓ Biomarkers of Potential Harm (BOPH)
- ✓ Modified Cigarette Evaluations Questionnaire (mCEQ; modified for HTP)

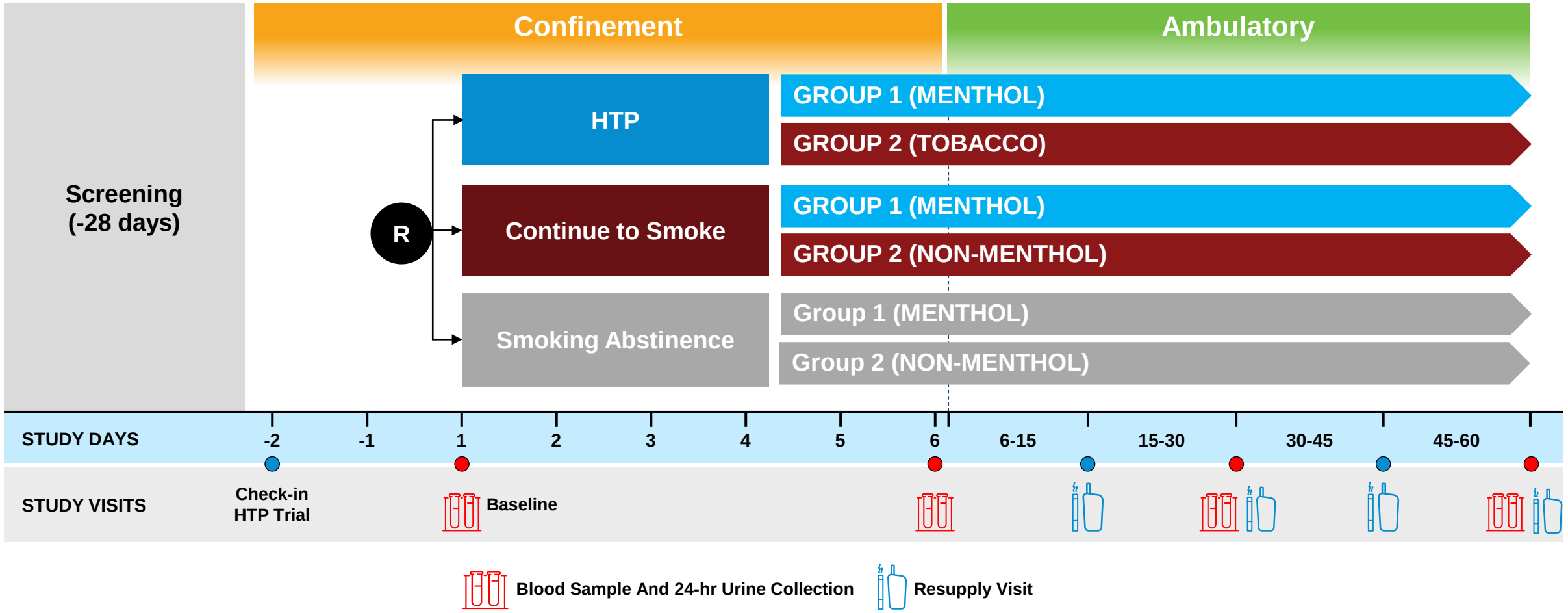
PARTICIPANTS

n=296

Adult Smokers of Combustible Cigarettes

- 10 – 30 cigarettes per day during last 12 months
- No plan to quit smoking in next 3 months

Study Overview



Biomarkers of Exposure Endpoints

Biomarkers	Associated HPHC	Abbreviation	Classification
3-hydroxypropyl mercapturic acid	Acrolein	3-HPMA	RT, CT
2-cyanoethyl mercapturic acid	Acrylonitrile	CEMA	CA, RT
1-amino-naphthalene	1 amino-naphthalene	1-AN	CA
2-amino-naphthalene	2 amino-naphthalene	2-AN	CA
4-aminobiphenyl	4-aminobiphenyl	4-ABP	CA
S-phenyl mercapturic acid	Benzene	S-PMA (SPMA)	CA, CT, RDT
3-hydroxybenzo[a]pyrene	Benzo-a-pyrene	3-OH-B[a]P	CA
2-hydroxybutenyl mercapturic acid	1,3 butadiene	2-MHBMA	CA, RT, RDT
Carboxyhemoglobin	Carbon monoxide	COHb	RDT
3-hydroxy-1-methylpropyl mercapturic acid	Crotonaldehyde	HMPMA	CA
2 hydroxyethyl mercapturic acid	Ethylene oxide	HEMA	CA, RT, RDT
Total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol	4-(methylnitrosoamino)-1-(3-pyridinyl)-1-butanone	NNAL	CA
Total N'-Nitrosonornicotine	N'-Nitrosonornicotine	NNN	CA
Nicotine equivalents* (nicotine, cotinine, 3-hydroxycotinine and their glucuronide conjugates)	Nicotine	NE	RDT, AD

Note: * Total Nicotine Equivalents (NE) was not one of the primary endpoints, AD: Addictive; CA: Carcinogen; RDT: Reproductive and Developmental Toxicant; RT: Respiratory Toxicant.

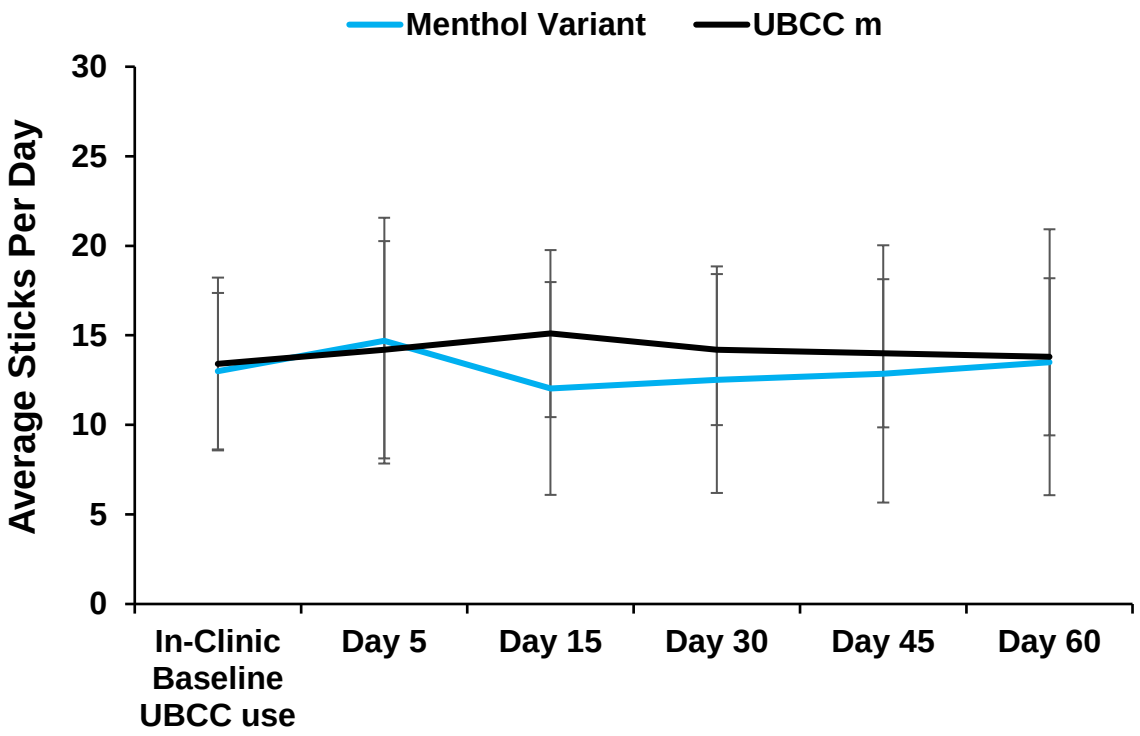
Study Population and Smoking History Summary

Data Category			Menthol Group (n=149)	Tobacco (Non-menthol) Group (n=147)	Total (n=296)
Mean Age (SD)			**37.5 (8.78)**	**39.3 (10.33)**	**38.4 (9.61)**
Body Mass Index (kg/m^2) (SD)			**28.8 (5.6)**	**29.1 (5.7)**	**28.9 (5.6)**
Race (%)		White	**52 (35%)**	**122 (83%)**	**174 (59%)**
		Black or African American	**93 (62%)**	**19 (13%)**	**112 (38%)**
		Other	**4 (3%)**	**6 (4%)**	**10 (3%)**
Sex (%)		Male	**86 (58%)**	**90 (61%)**	**176 (59%)**
		Female	**63 (42%)**	**57 (39%)**	**120 (41%)**
Cigarette per Day (SD)			**15.5 (4.75)**	**16.9 (5.07)**	**16.2 (4.95)**
Years of Cigarette use (SD)			**17.9 (9.30)**	**20.9 (11.14)**	**19.4 (10.34)**

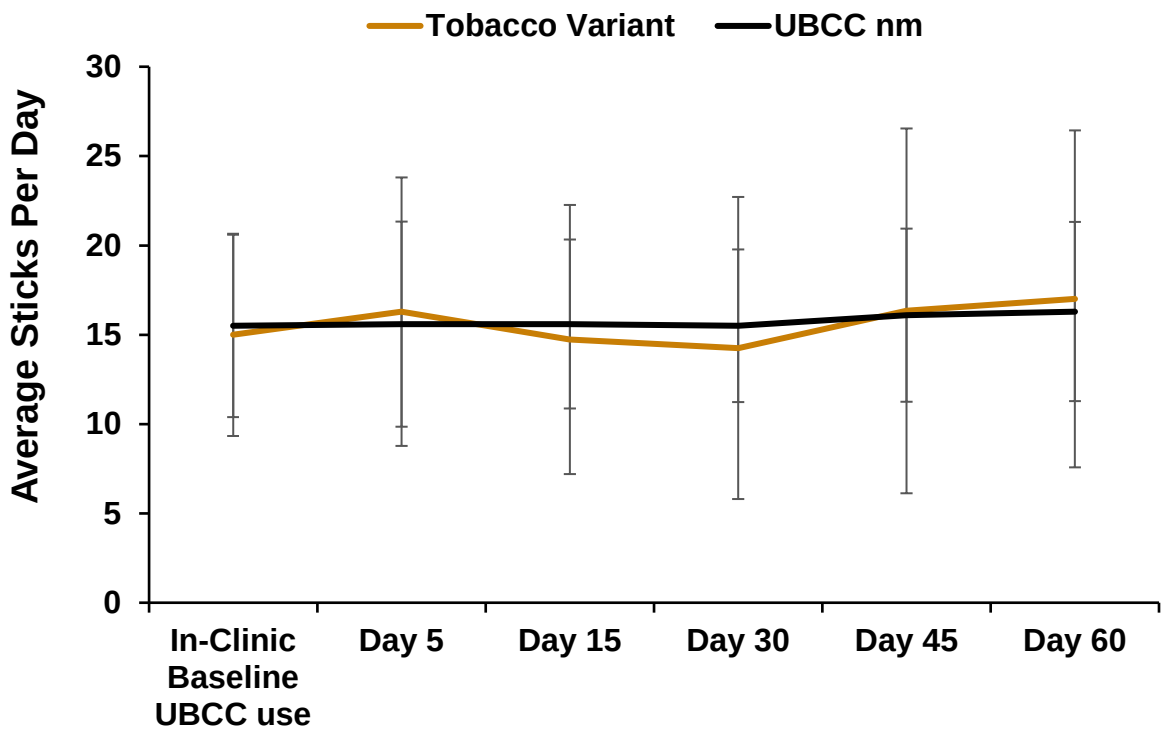
Note: Participants in each flavor group were randomized to one of 3 study arms: HTP arm, Continue to Smoke arm, and Smoking Abstinence arm based on 2:2:1 ratio.

Ploom Use were Comparable to Baseline Cigarette Use

Menthol HTS Versus Menthol Cigarette Use

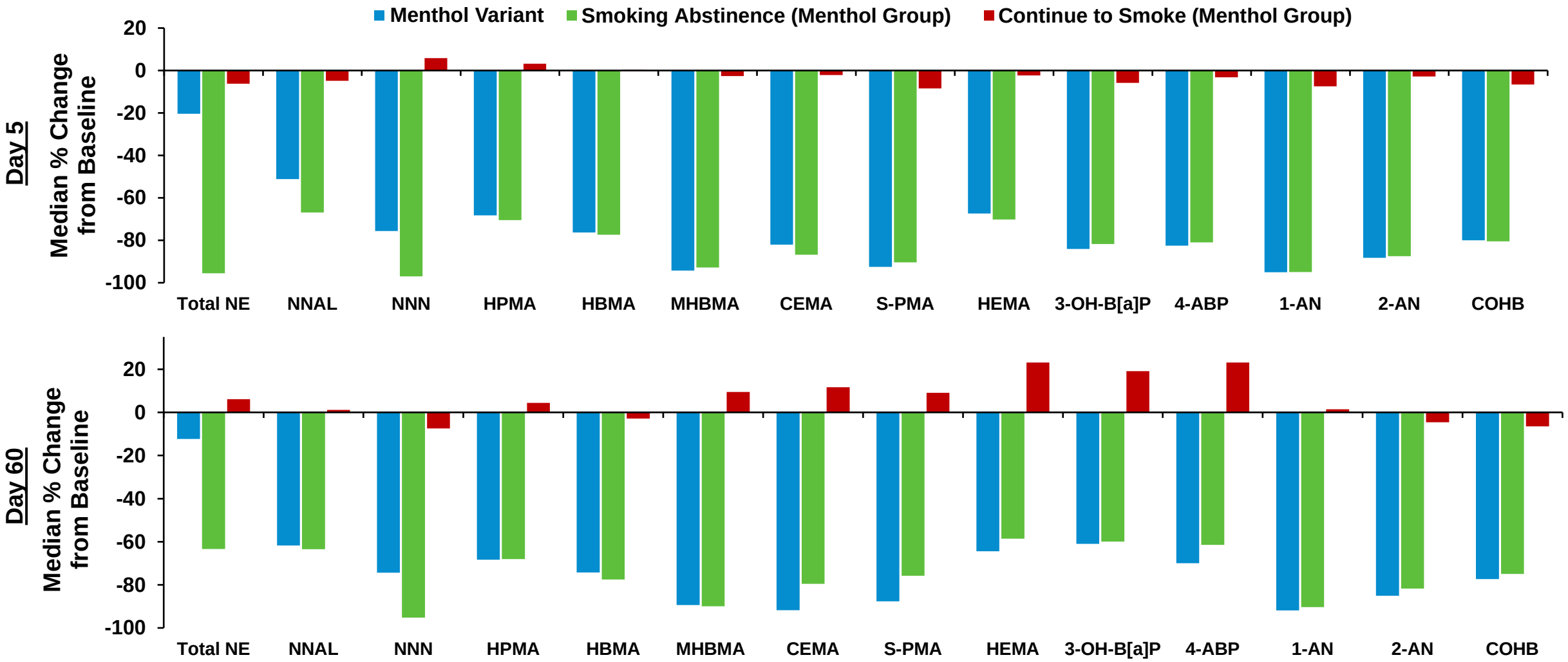


Tobacco HTS Versus Non-Menthol Cigarette Use

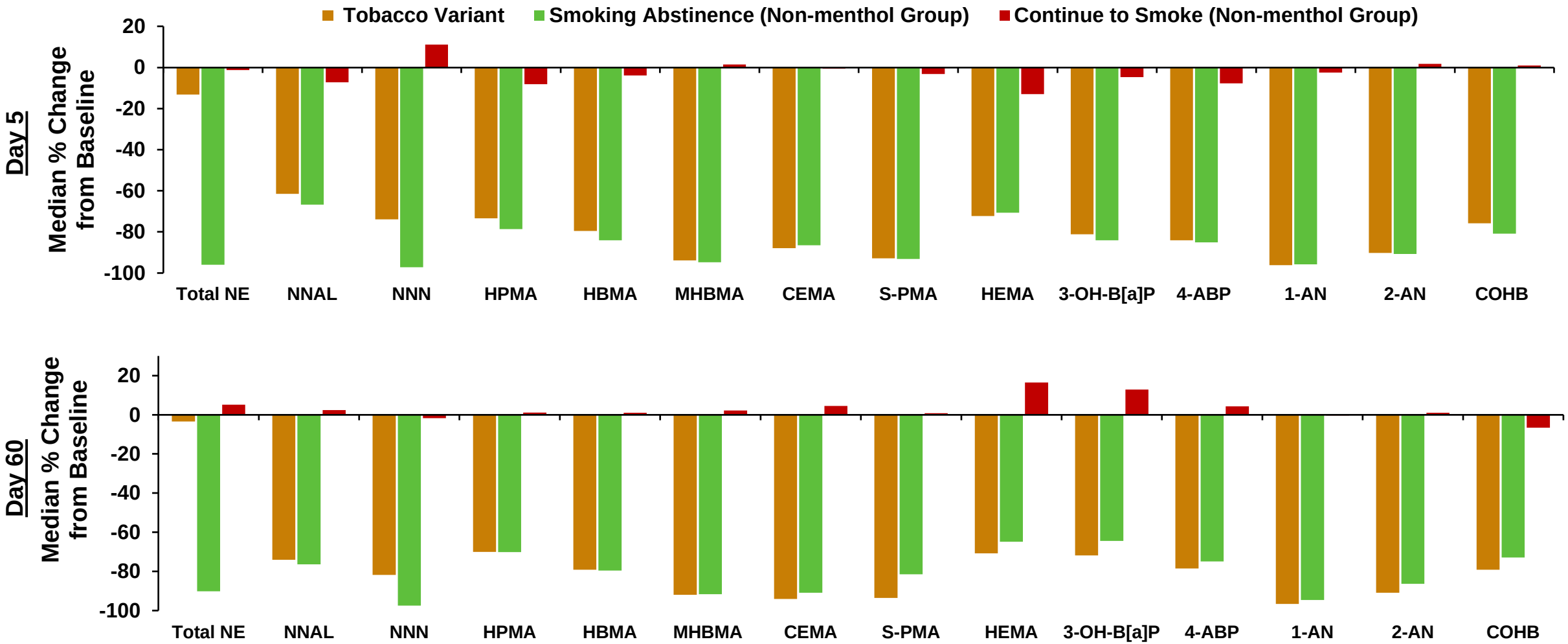


Note: Average sticks used per day shown with SD; Average HTS use were calculated at each follow-up visits (number of packs dispensed – number of packs used and residual HTS); Average number of cigarettes used per day were based on self report from participants in continue to smoke arms (menthol and non-menthol): UBCC m: Menthol Usual Brand Combustible Cigarettes; UBCC nm: Non-menthol Usual Brand Combustible Cigarettes.

Ploom Users Experienced Substantial Reductions in non-nicotine BoEs Similar to Smoking Abstinence



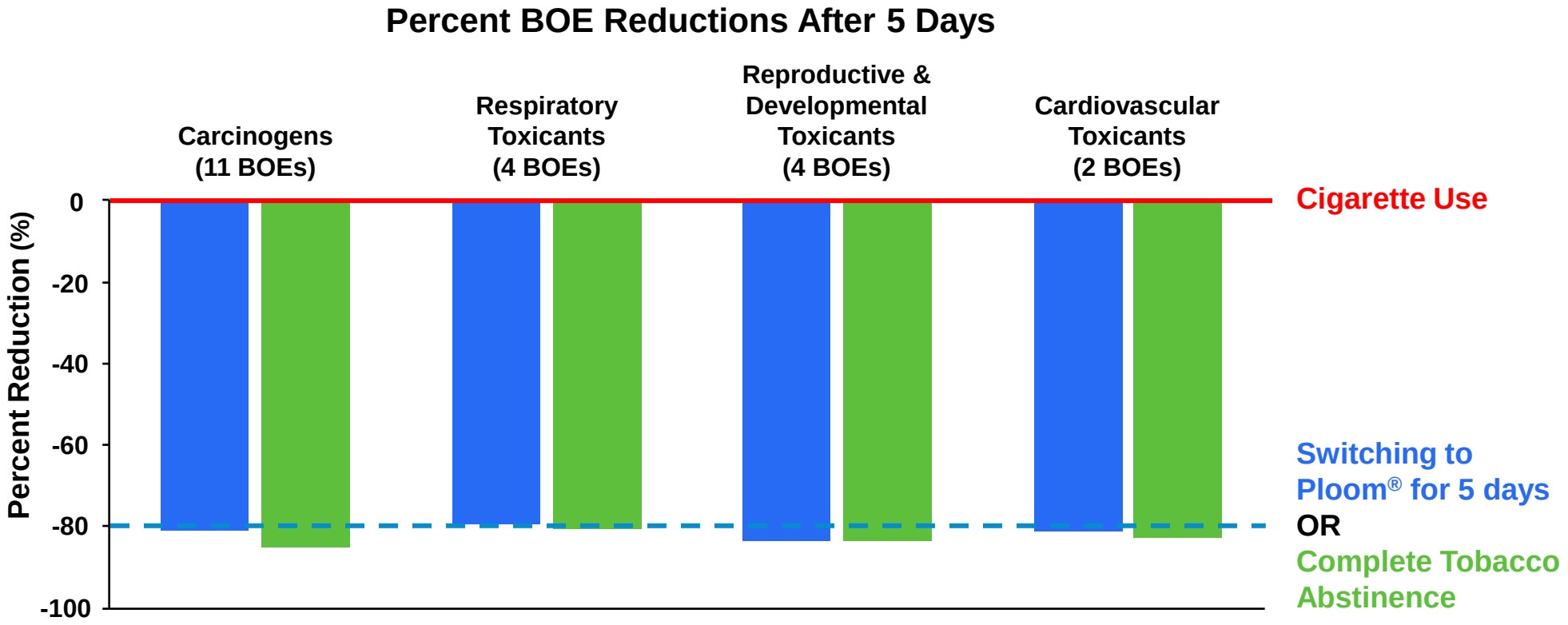
Ploom Users Experienced Substantial Reductions in non-nicotine BoEs Similar to Smoking Abstinence



Overall >80% Reduction in Exposure to Carcinogens and other Harmful Toxicants After Only 5 Days

>80%

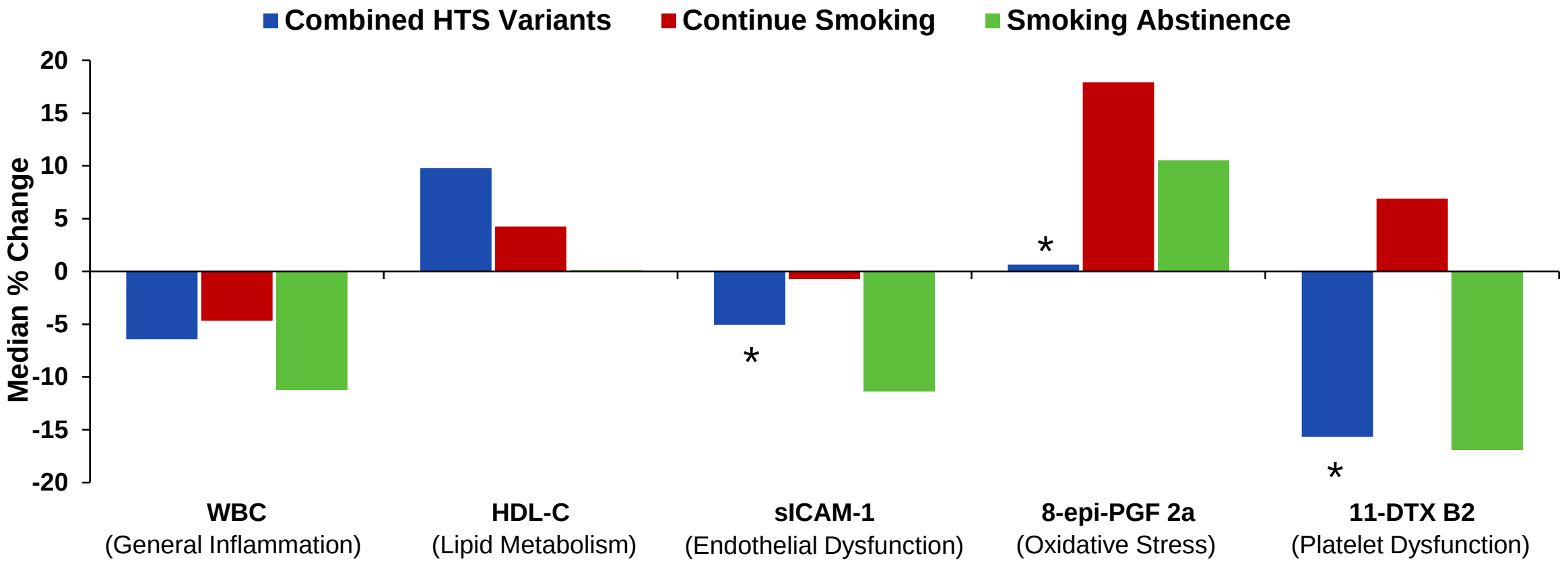
Overall average reduction



Percent reductions in BOEs among adult smokers who completely switched to Ploom® were comparable to complete tobacco abstinence, excluding nicotine

Source: ALCS Clinical Study Report ALCS-REG-23-07-HT. Blue Bars represent median percent reductions in measured BOEs when adult smokers completely switched to Ploom for 5 days in our clinical study. Green Bars represent median percent reductions in measured BOEs when adult smokers abstained from all tobacco for 5 days in our clinical study. Some BOEs have more than one classification and are included for each of their classifications. Nicotine BOE is not included. BOE=Biomarkers of Exposure.

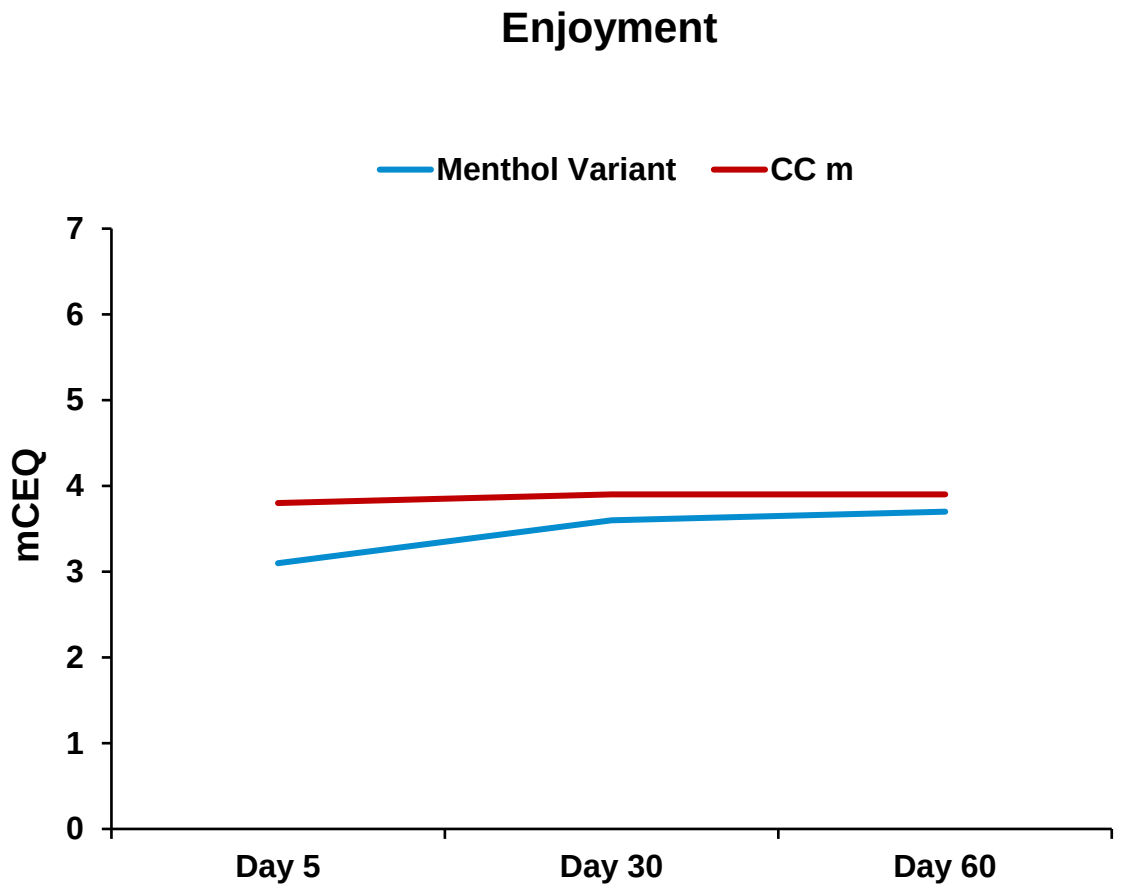
Reductions in BoE led to Favorable Changes in BOPH Associated with Smoking-related Diseases

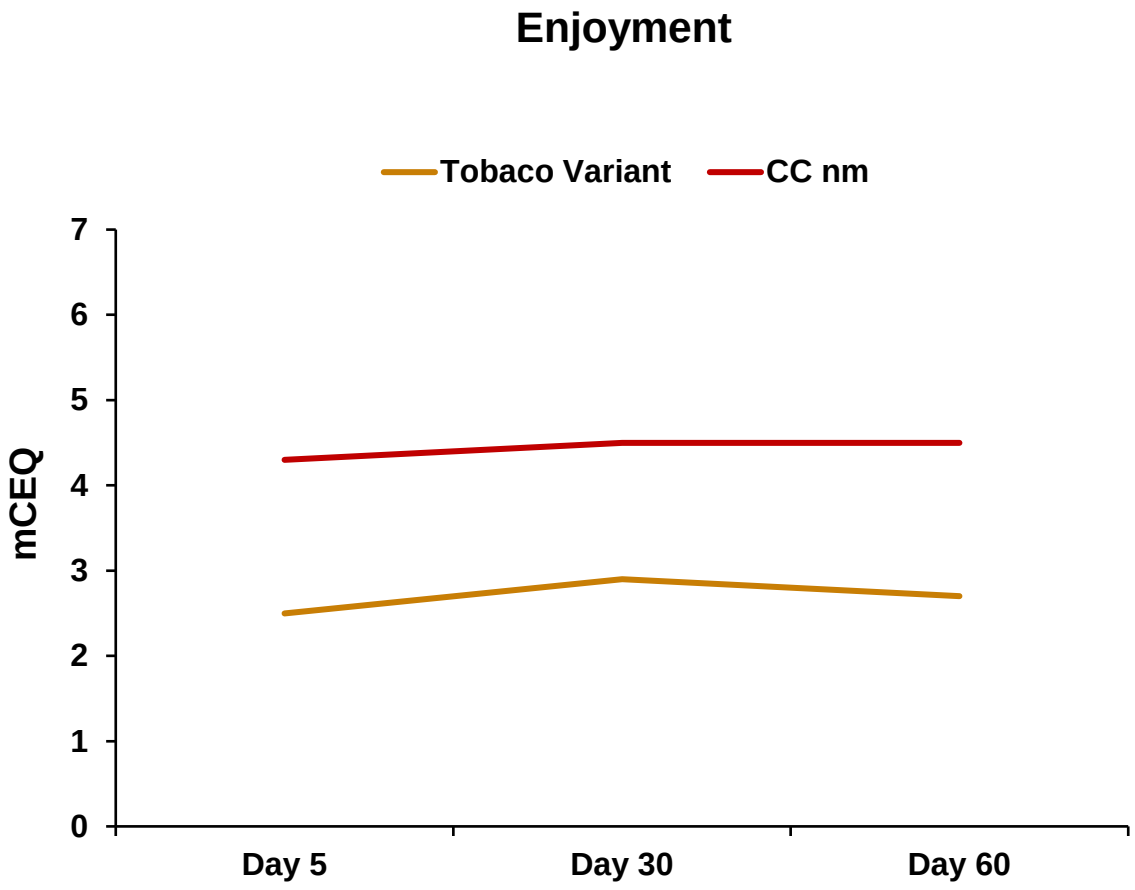


Note: HTS: Heated Tobacco Stick; CS: Continue Smoking; SA: Smoking Abstinence; sICAM-1: Soluble Intercellular adhesion molecule-1; WBC: White blood cell count; HDL-C: High density lipoprotein cholesterol; 11-DTX-B2: 11-Dehydrothromboxane B2; 8-epi-PGF2a: 8-epi-prostaglandin F2 alpha; * Statistically significant difference compared to Continued Smoking arm with significance level at $p<0.05$.

HTS: Heated Tobacco Stick; CS: Continue Smoking; SA: Smoking Abstinence; sICAM-1: Soluble Intercellular adhesion molecule-1; WBC: White blood cell count; HDL-C: High density lipoprotein cholesterol; 11-DTX-B2: 11-Dehydrothromboxane B2; 8-epi-PGF2a: 8-epi-prostaglandin F2 alpha; * Statistically significant difference compared to Continued Smoking arm with significance level at p<0.05.

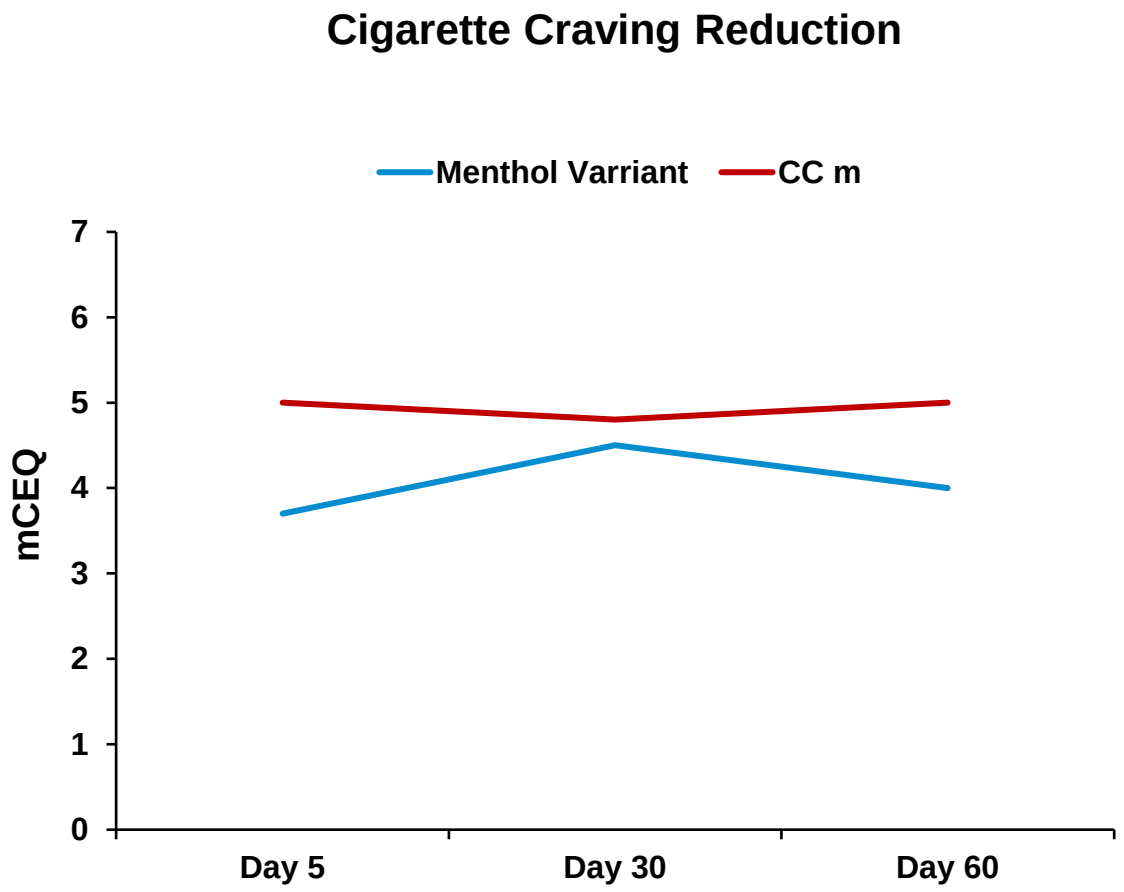
Users Reported Ploom to be an Enjoyable Experience

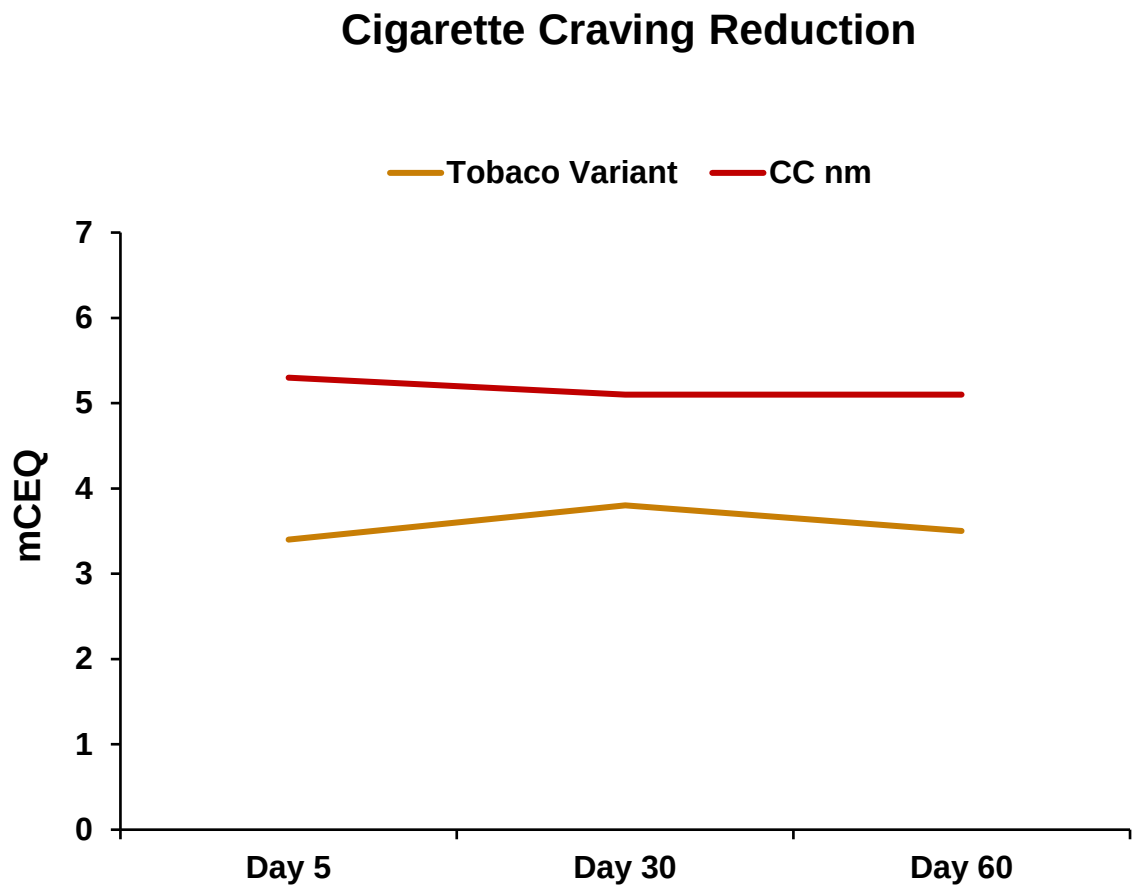




mCEQ: Modified Cigarette Evaluations Questionnaire

Users Reported Ploom Reduced Cigarette Cravings





mCEQ: Modified Cigarette Evaluations Questionnaire

Summary and Conclusion

After 5 days of completely switching to the Ploom® System, adults 21+ who smoke experienced:

- A SUBSTANTIAL REDUCTION in BOEs to HPHCs
  - ~80% **AVERAGE REDUCTION** of non-nicotine BOE across a range of toxicant classes, with reductions comparable to smoking abstinence
- A SIMILAR EXPOSURE TO NICOTINE AS CIGARETTES

Reductions in exposure to HPHCs led to **favorable changes in BOPH associated with smoking-related diseases after 60 days**

Overall, this study demonstrates that:

Switching completely to the Ploom® system from combustible cigarettes substantially reduces exposure to harmful chemicals AFTER 5 DAYS **and may reduce the risk of smoking-related diseases in adults 21+ who smoke and choose to switch completely.**

Acknowledgments

Statistical Lead:	Jingzhu Wang
SAS Programmer:	Raj Maddipatla
Medical Lead:	Jianmin Liu
Bioanalytical Lead:	Mohammad H. Bazargan
Data Management:	Keith Nobles
Senior Director of Clinical Research:	Jeffery Edmiston
JTI Regulatory Science Clinical Director:	Brian K. Nordskog

Any Questions?