

Reduction in Biomarkers of Exposure Following Short-Term Switching From Cigarettes to Velo Nicotine Pouches in Adult Smokers

Melissa A. Tapia¹, John Darnell¹, Yen Nguyen², Thomas Kerby¹, Claude Cavallo¹, Milly N. Kanobe¹, Filimon Meichanetzidis³, Robert Leverette¹, Nathan Gale², Patrudu Makenna¹, Sarah A. Baxter-Wright¹ and Kristen Jordan¹

¹RAI Services Company, 401 N. Main Street, Winston Salem, NC 27101, USA
²BAT(Investments) Limited, Research and Development, Regents Park Road, Southampton SO15 8TL, UK.
³Former employee of BAT(Investments) Limited

Introduction

Combustible cigarette smoking remains a leading cause of tobacco-related diseases, largely due to exposure to harmful toxicants formed during tobacco combustion. Oral nicotine pouches, which deliver nicotine but do not contain tobacco leaf and are not combusted when used, present a reduced-exposure alternative product for adult smokers.

Changes in biomarkers of exposure (BoE) relevant to tobacco combustion-associated HPHCs in smokers who switched exclusively to Velo Pouch use for five days, were compared to those who continued usual-brand (UB) cigarette smoking or abstained from tobacco/nicotine use.

Methodology

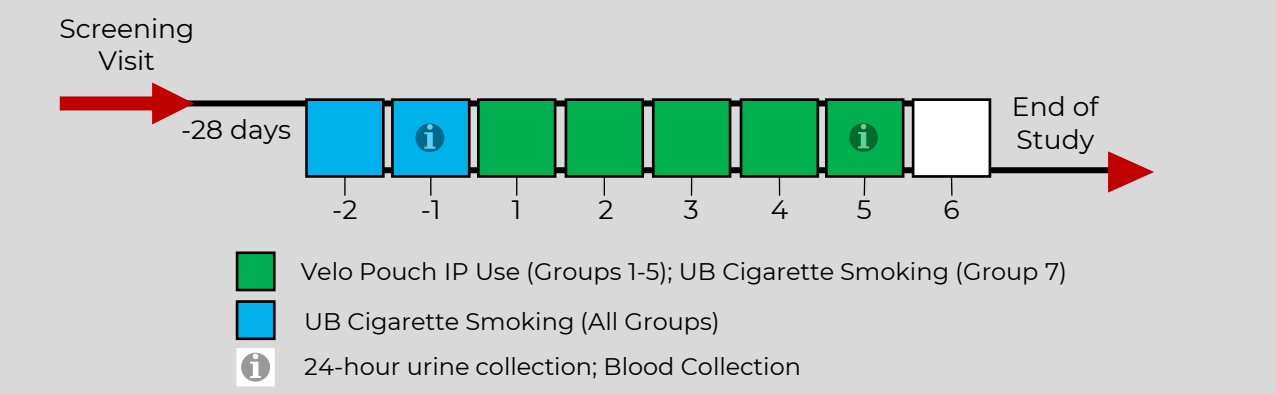


Figure 1. Study Schematic

- Day -2:** subjects trialed three of the Study investigational products (IP)
- Day -1 to 1:** 24-hour urine collection (started at ~7:00 a.m.) + blood collection (~7:00 p.m.)
- Day 1:** Subjects randomized to one of seven product use groups (see Table 1, below)
 - Groups 1-5: *ad libitum* use + three required use periods per day (~11:00 a.m., 3:00 p.m., and 7:00 p.m.)
 - Group 7: *ad libitum* smoking + three required use periods (~11:00 a.m., 3:00 p.m., and 7:00 p.m.)
 - Group 6: did not use any tobacco- or nicotine-containing product
- Day 5 to 6:** 24-hour urine collection (started at ~7:00 a.m.) + blood collection (~7:00 p.m.)

Key Inclusion/Exclusion Criteria:

21-60 years of age, smoke's an average of 10 cigarettes per day for at least 6 months, with no clinically significant diseases;
Females who were pregnant, breastfeeding or intended to become pregnant during the course of the study were excluded

Group	
1	Velo Mini Pouch Cool Mint, 4 mg nicotine
2	Velo Mini Pouch Cool Mint, 8 mg nicotine
3	Velo Mini Pouch Smooth, 8 mg nicotine
4	Velo Slim Pouch Smooth, 10 mg nicotine
5	Velo Slim Pouch Cool Mint, 12 mg nicotine
6	Tobacco and Nicotine Abstinence
7	Continued UB Cigarette Smoking

Table 1. Study Groups

References

Azopardo et al. (2023). "Assessment of biomarkers of exposure and potential harm, and physiological and subjective health measures in exclusive users of nicotine pouches and current, former and never smokers." *Pluym, et al (2022). "Assessment of the exposure to NNN in the plasma of smokeless tobacco users."*
Edmiston et al. (2022). "A Randomized, Controlled Study to Assess Biomarkers of Exposure in Adult Smokers Switching to Oral Nicotine Products." *J Clin Pharmacol.*
Gale et al. (2023). "Changes in Biomarkers of Exposure on Switching From a Conventional Cigarette to the glo Tobacco Heating Product: A Randomized, Controlled Ambulatory Study." *Nicotine Tob Res.*
Hecht et al. (2013). "Tobacco smoke biomarkers and cancer risk among male smokers in the Shanghai cohort study." *Cancer Lett.*
Rensch et al. (2023). "A randomized, controlled study to assess changes in biomarkers of exposures among adults who smoke who switch to oral nicotine pouch products relative to continuing smoking or stopping all tobacco use." *J Clin Pharmacol.*
FDA (2012). Harmful and potentially harmful constituents in tobacco products and tobacco smoke: established list. Fed Regist 77: 20034-20037.

	Biomarkers of Exposure	Abbreviation	Collection Matrix
Primary	Total NNAL (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol [NNAL] + glucuronides)	Total NNAL	Urine (24-hour)
	Total NNN (N'-nitrosonornicotine [NNN] + glucuronides)*	Total NNN	Urine (24-hour)
Secondary	S-phenyl mercapturic acid	S-PMA	Blood
	Monohydroxybutyl mercapturic acid	MHBMA	Urine (24-hour)
	3-hydroxypropyl mercapturic acid	3-HPMA	
	4-aminobiphenyl	4-ABP	
	1-aminonaphthalene	1-AN	
	2-aminonaphthalene	2-AN	
	3-hydroxy-1-methylpropyl-mercapturic acid	HMPMA	
	2-cyanoethyl mercapturic acid	CEMA	
	3-hydroxy-benzo[a]pyrene	3-OH-B[a]P	
	1-hydroxypyrene	1-OHP	
	Total nicotine equivalents (molar sum of nicotine, cotinine, 3-hydroxycotinine and their glucuronides)	T-Neq	
	Carboxyhemoglobin (% saturation of hemoglobin)	COHb	Blood

Table 2. Biomarkers of Exposure and Collection Matrix; *Total NNN in blood represents NNN only; no conjugates were detected.

Results

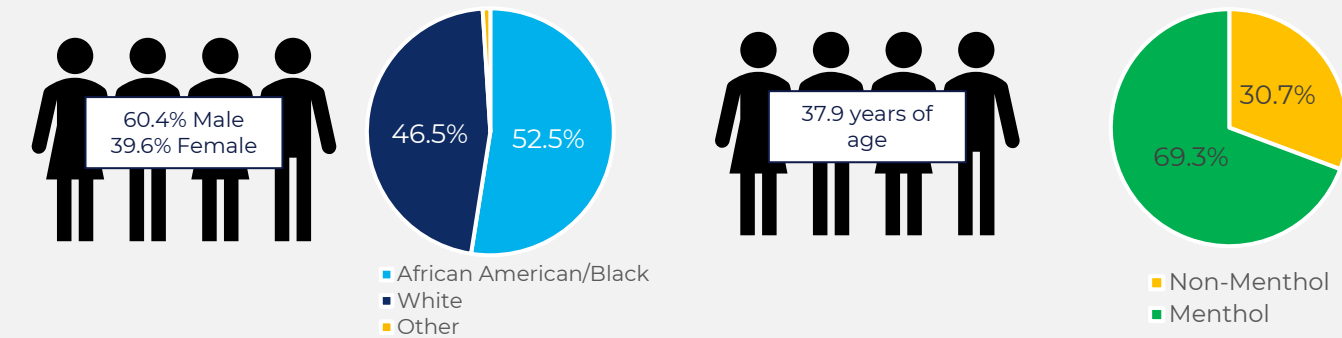


Figure 2. Participant Demographic and Baseline Characteristics

Biomarkers of Exposure Median Percent (%) change

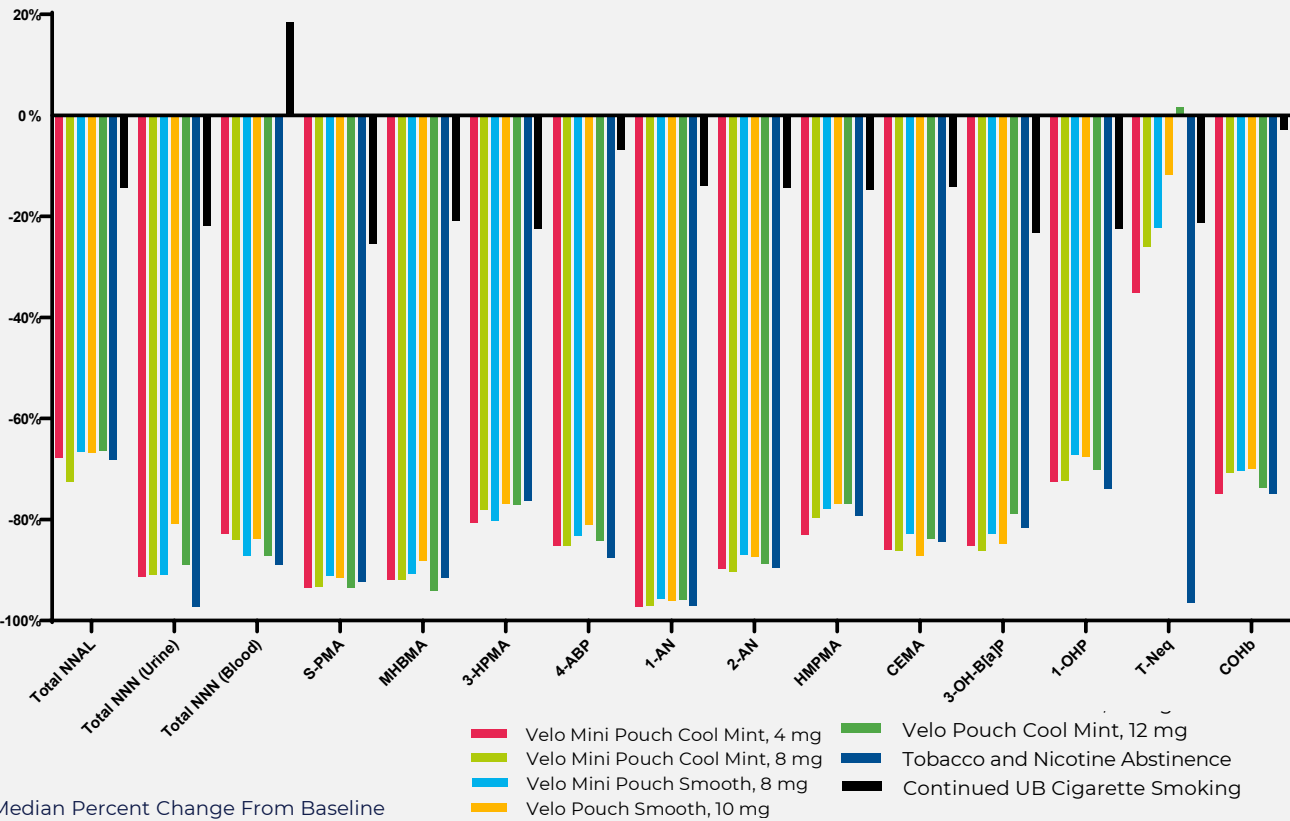


Figure 3. Median Percent Change From Baseline

Acknowledgements

The authors are grateful to Celerion for conducting the study and conducting the bioanalysis of a majority of the BoE examined in the study and ABF for conducting the bioanalysis of Total NNN in blood.

Significance Testing

Biomarker	Velo Mini Pouch Cool Mint, 4 mg nicotine	Velo Mini Pouch Cool Mint, 8 mg nicotine	Velo Mini Pouch Smooth, 8 mg nicotine	Velo Slim Pouch Smooth, 10 mg nicotine	Velo Slim Pouch Cool Mint, 12 mg nicotine
Total NNAL	YES	YES	YES	YES	YES
Total NNN (Blood)	YES	YES	YES	YES	YES
Total NNN (Urine)	NO	NO	YES	NO	NO
S-PMA	YES	YES	YES	YES	YES
MHBMA	YES	YES	YES	YES	YES
3-HPMA	YES	YES	YES	YES	YES
4-ABP	YES	YES	YES	YES	YES
1-AN	YES	YES	YES	YES	YES
2-AN	YES	YES	YES	YES	YES
HMPMA	YES	YES	YES	YES	YES
CEMA	YES	YES	YES	YES	YES
3-OH-B[a]P	YES	YES	YES	YES	YES
1-OHP	YES	YES	YES	YES	YES
T-Neq	NO	NO	NO	NO	NO
COHb	YES	YES	YES	YES	YES

Table 3: Statistically significant change from baseline in the Velo BoE cohort groups compared to continued UB smoking cohort; Data are for the per-protocol population. Statistical significance was defined as p-value < 0.05
*Differences between Total NNN urine and blood results may be due, in part, to the fact that previous studies have shown blood NNN to be a more accurate indicator of exposure.

Investigational Product Use Behavior:

- Across all Velo Pouch IPs, subjects used on average 6-8 pouches per day
- Subjects used Velo Pouch IPs for an average duration of approximately 30-34 minutes

Safety Results:

- A total of 32 subjects (15.8%) reported an adverse event (AE) during the study—10 subjects (5.0%) prior to randomization and 22 subjects (10.9%) after randomization. The most frequently reported AE was headache. Most AEs were mild in severity and resolved by end of study.

Key Findings

- The average reduction in BoE from baseline across all five Velo Pouch IPs varied between 29% and 97% (excluding T-Neq).
- Nicotine exposure (T-Neq) was maintained among subjects who continued smoking, as expected, with no statistically significant differences observed between Velo Pouch groups and the continued UB smoking group.
- The use of the Velo Pouch IPs under study conditions was generally well tolerated by the subjects in this study.

Conclusion

Switching completely from cigarette smoking to Velo Pouch use leads to significant reductions in exposure to biomarkers associated with lung cancer, emphysema, and chronic bronchitis.

Point your phone's camera at the QR code to find our library of publications

Follow us:

www.ReynoldsScience.com

Contacts

M.A Tapia, tapiam@rjrt.com
K.G Jordan, jordank2@rjrt.com

@RAI_News

