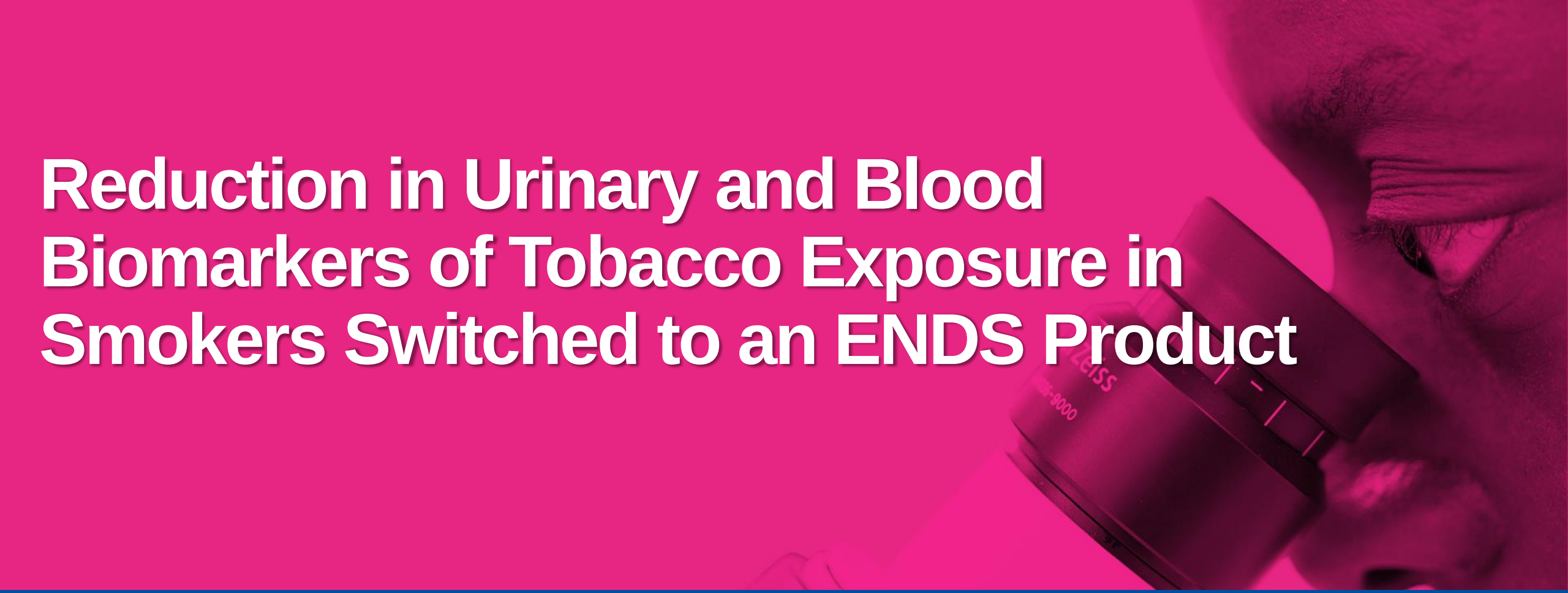
Reduction in Urinary and Blood Biomarkers of Tobacco Exposure in Smokers Switched to an ENDS Product



CORESTA

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Background

Biomarkers of exposure (BoE) can help evaluate exposure to combustion-related, tobacco-specific toxicants after smokers switch from cigarettes to potentially less-harmful products like ENDS.

Three Vuse ENDS products were evaluated in this study:

Vuse Solo, Vuse Vibe and Vuse Ciro, all in Original (tobacco) flavor.

All evaluated products received Marketing Granted Orders by FDA Center for Tobacco Products in October 2021 (Vuse Solo) and Vuse Ciro and Vuse Vibe (May 2022).

Clinical Study Objectives

Assess changes in:

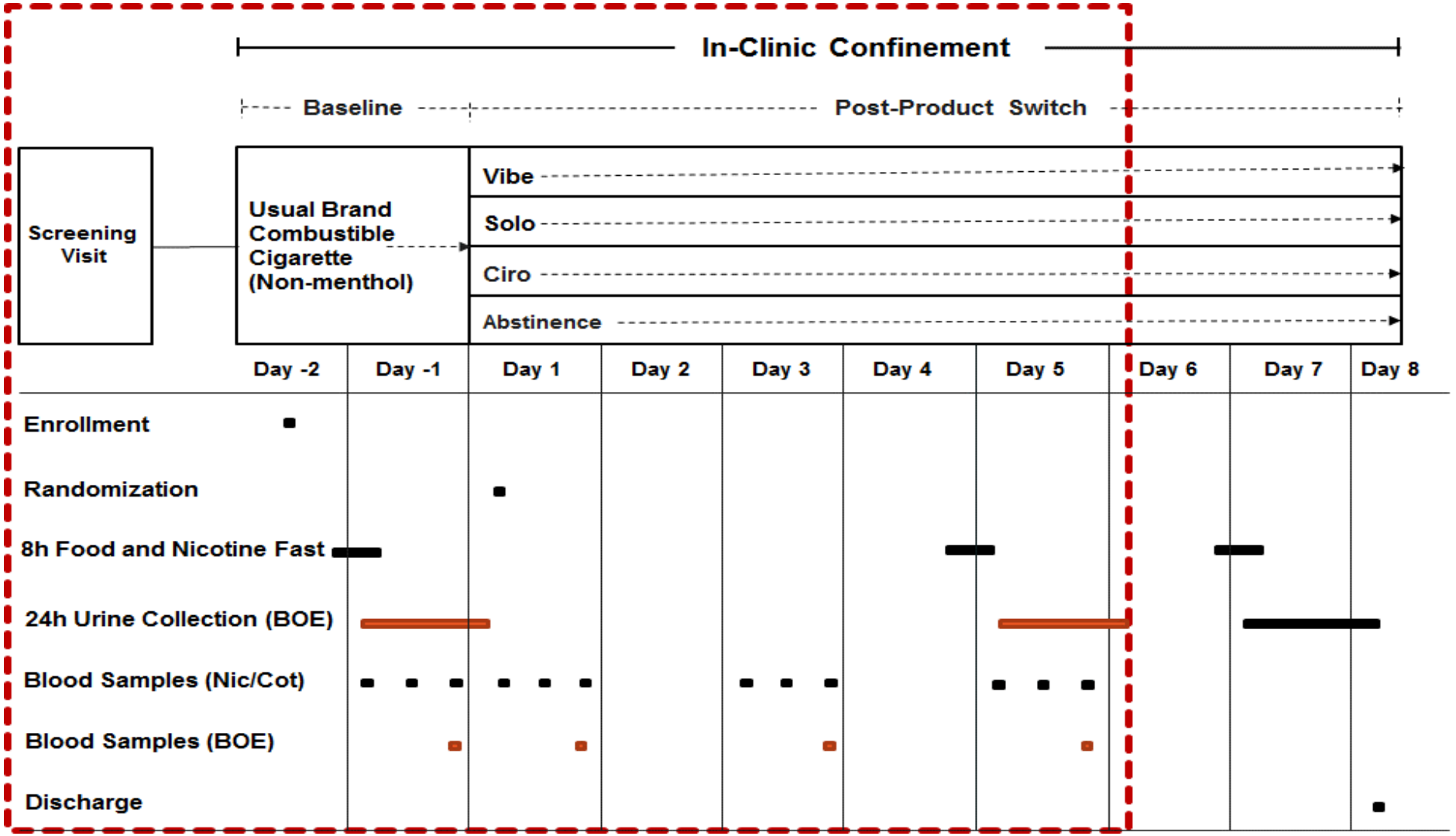
- **BoE in urine and blood**
- **Total nicotine equivalents**
- **Daily product use amounts**

BoE Endpoints

Biomarker	Associated Toxicant	Chemical Classification
Urinary BoE		
• 1-AN • 2-AN • 4-ABP • o-Tol	• 1-aminonaphthalene[1] • 2-aminonaphthalene[1] • 4-aminobiphenyl[1] • o-toluidine[2]	Aromatic Amines
• CEMA • HMPMA • HPMA • MHBMA • SPMA	• Acrylonitrile[1] • Crotonaldehyde[1] • Acrolein[1] • 1,3-butadiene[1] • Benzene[1]	Semi-volatile Organics (Mercapturic Acids)
• 3-OH-B[a]P)	B[a]P[1]	Polycyclic Aromatic Hydrocarbon
• NNAL • NNN	• NNK[1] • NNN[1]	Tobacco-specific Nitrosamines
• Unconjugated nicotine	Nicotine+5 metabolites	Total Nicotine Equivalents
Blood BoE		
• Carboxyhemoglobin	Carbon monoxide[2]	

[1]Constituent included in FDA HPHC list (Federal Register, 2012) and the PMTA ENDS Draft/Final Guidance (FDA, 2016/2019).
[2]Constituent included in FDA list of HPHCs in Tobacco Products and Tobacco Smoke (Federal Register, 2012).

Clinical Study Design



Subject Randomization to ENDS Products

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Smokers of non-menthol cigarettes		
Cohort	**Randomized**	**Completed**
Vibe	37	33
Solo	35	35
Ciro	37	35
Abstinence	16	11
Total	**125**	**114**

Study Results

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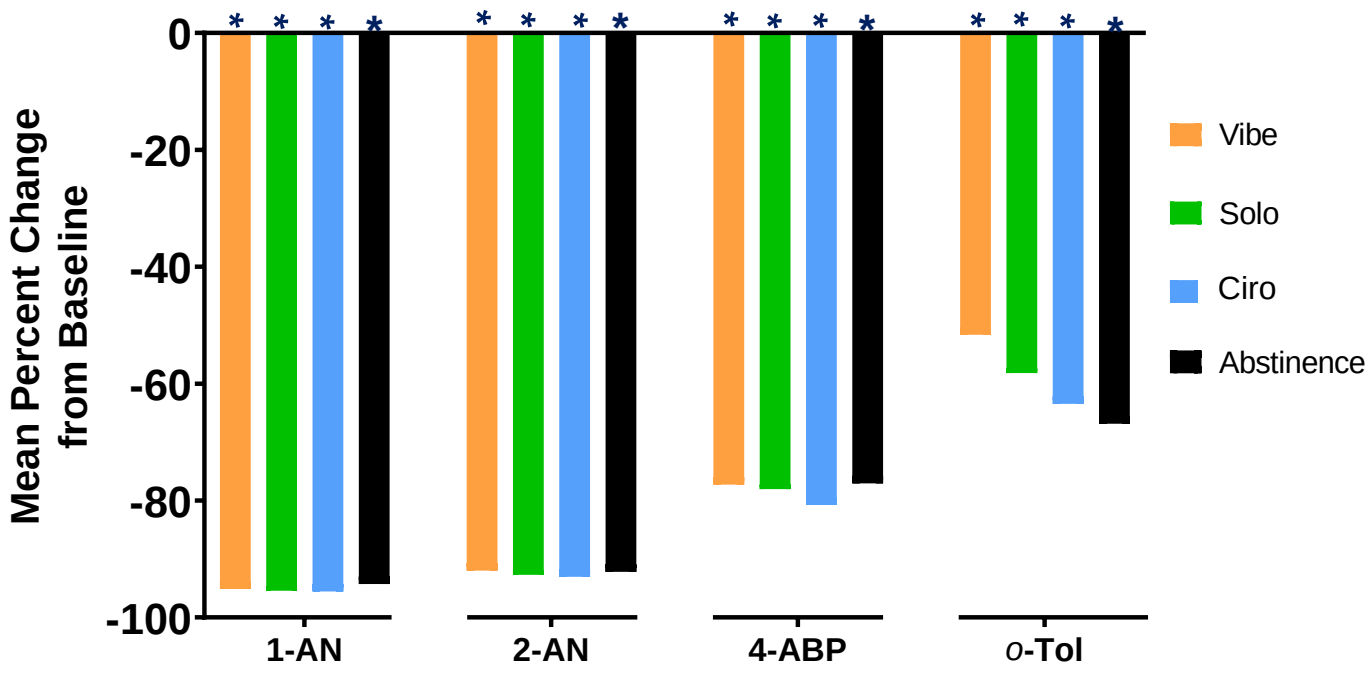
Subject Demographics

Characteristic	Demographics
Avg. age (years)	40 (22-59)
Race (%)	72.4 Caucasian 19.7 African American 7.9 Other
Gender (%)	63 Male 37 Female
Avg. years smoked	25.3 (1-51)
Avg. no. cigarettes smoked/day	17.1 (10-40)

Urinary BoE: Aromatic Amines



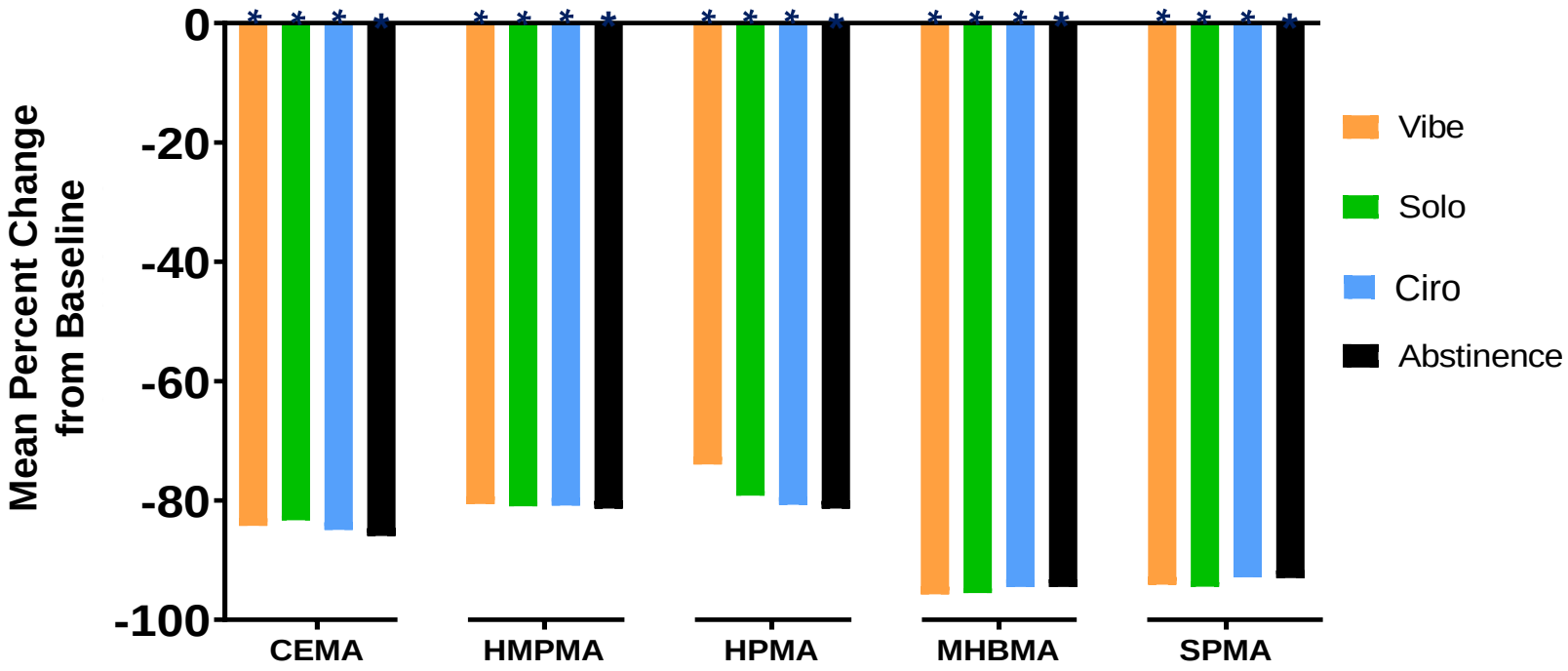
*p<0.05 Bonferroni-adjusted

RESULTS:

All BoE to aromatic amines were significantly reduced post-product switch compared to baseline.

Percent reductions in product-switch cohorts were similar to those observed in the Abstinence cohort.

Urinary BoE: Mercapturic Acids



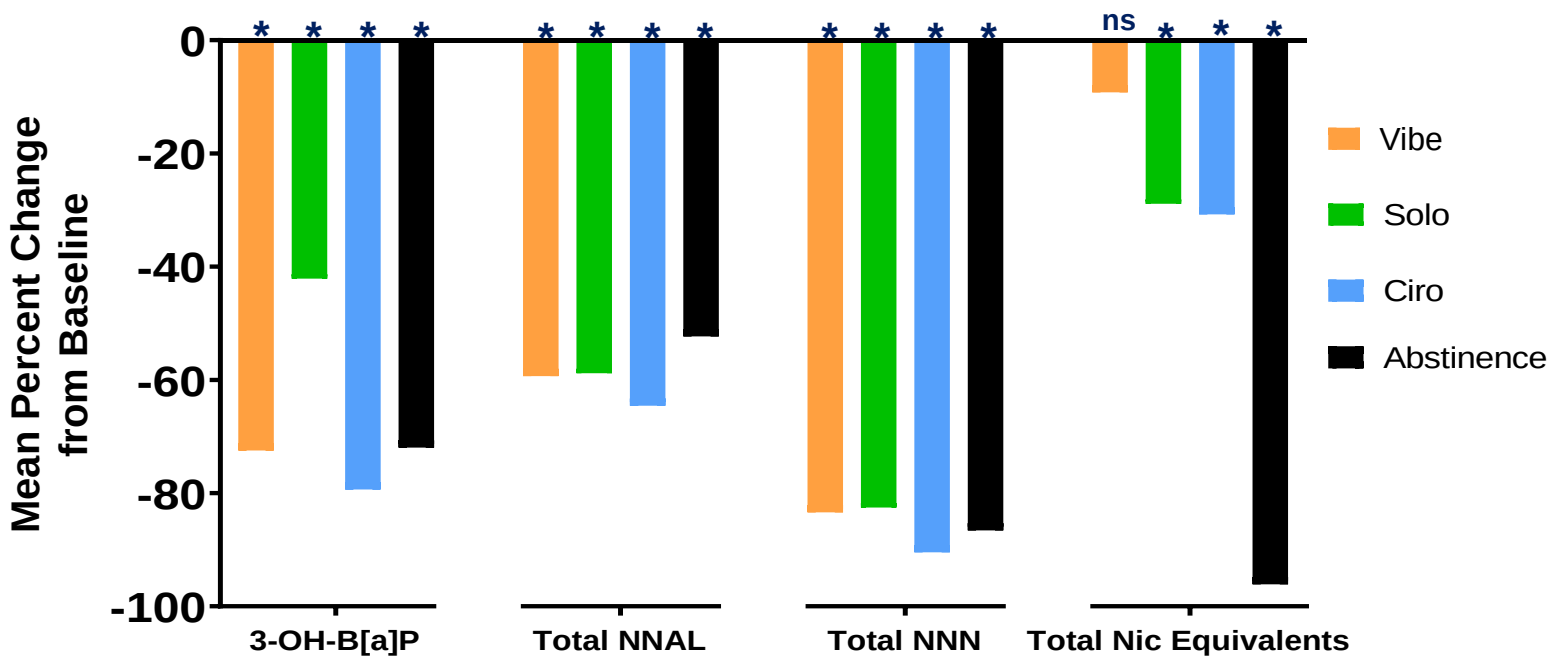
*p<0.05 Bonferroni-adjusted

RESULTS:

BoE to mercapturic acids were significantly reduced in all product-switch cohorts.

Similar reductions were observed in the Abstinence cohort.

Urinary BoE: 3-OH-B[a]P, TSNAs and Total Nicotine Equivalents



*p<0.05 Bonferroni-adjusted; ns = not significant

RESULTS:

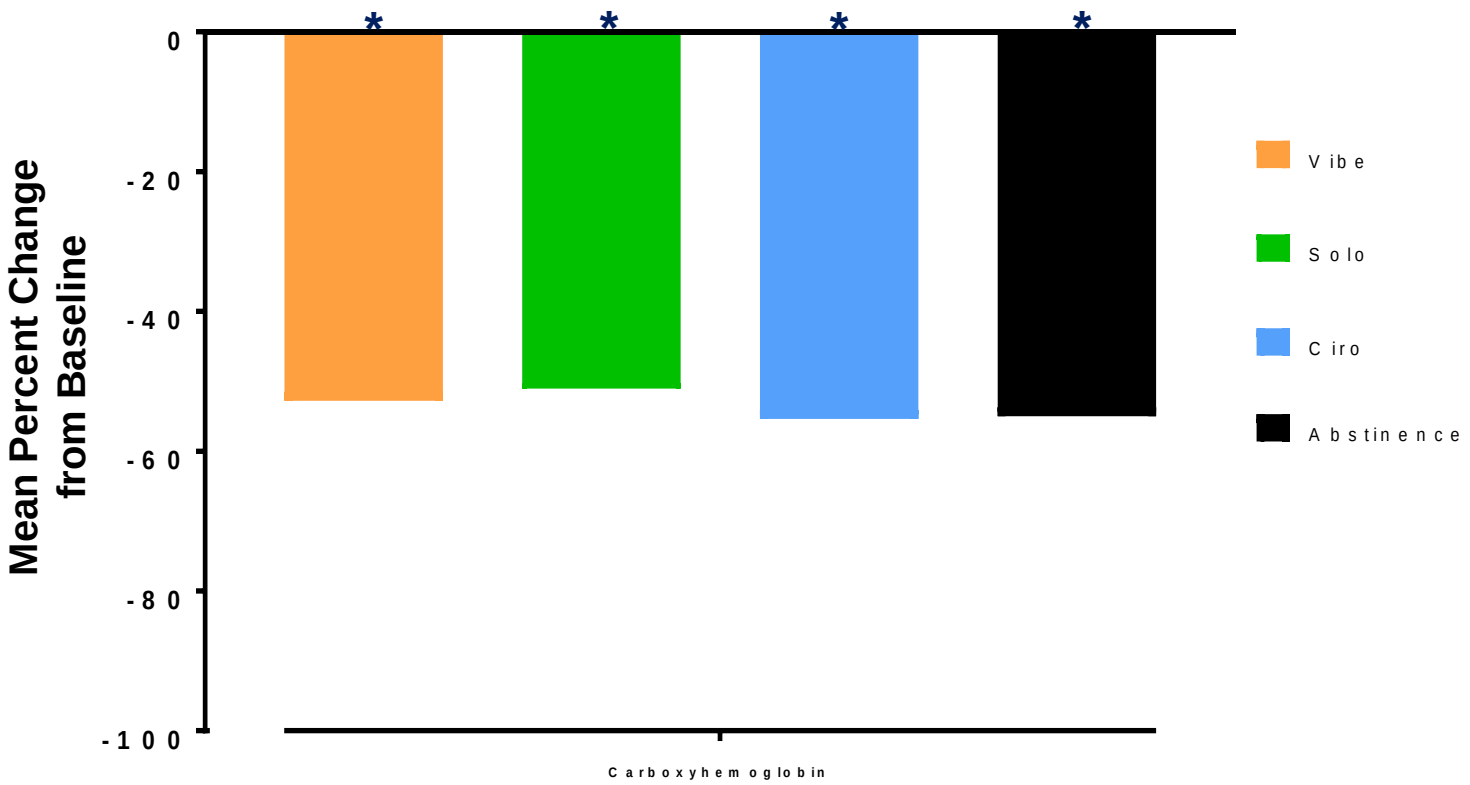
BoE to B[a]P, NNK, and NNN were significantly reduced in all product-switch cohorts.

Significant reductions in TNEq. were observed for subjects in Vuse Solo and Vuse Ciro Cohorts.

Reductions in product-switch cohorts were similar to those observed in Abstinence.

One subject in Abstinence cohort with an extreme data value at baseline was excluded from Total NNN analysis.

Blood BoE: Carboxyhemoglobin

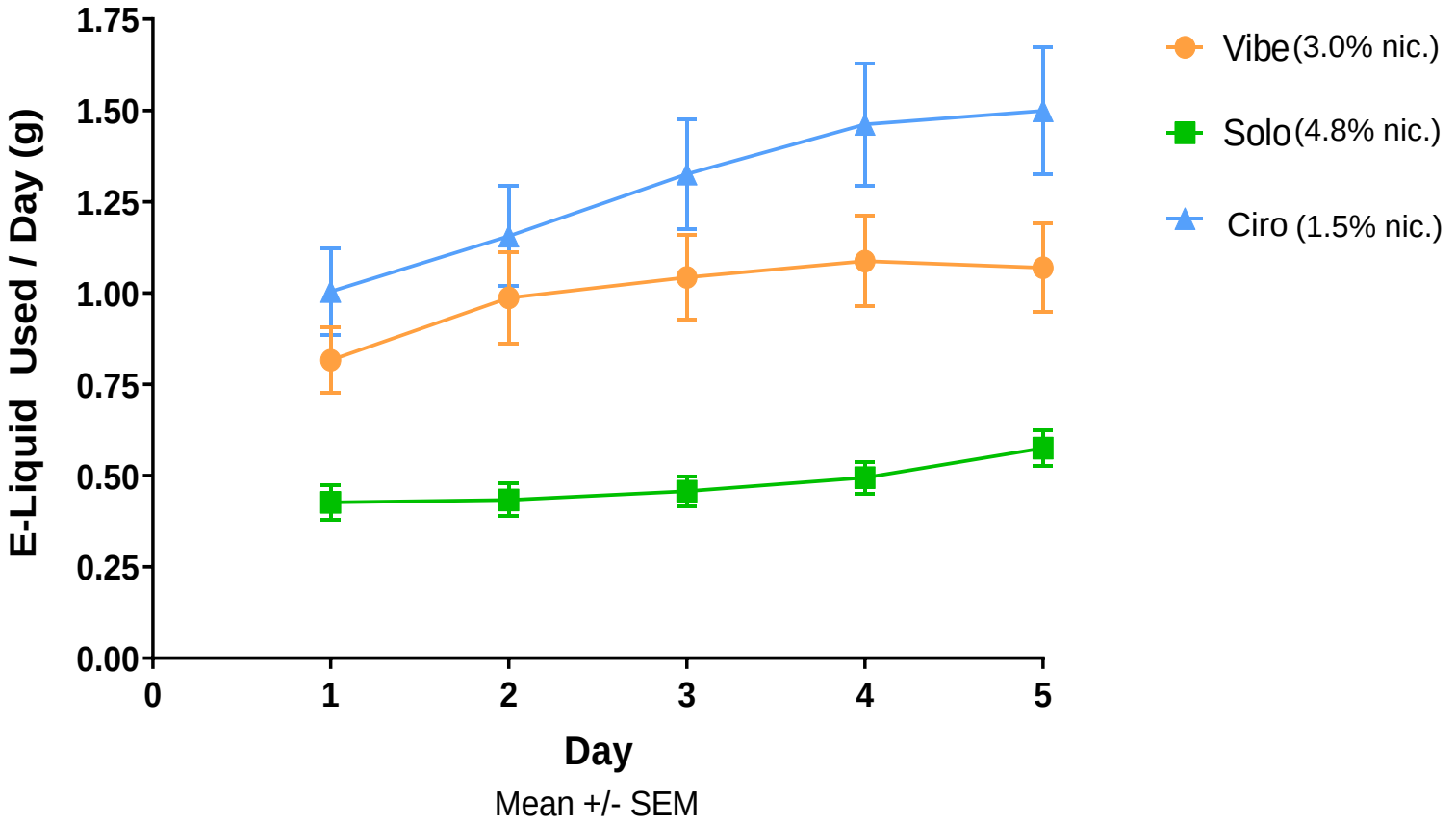


*p<0.05 Bonferroni-adjusted

RESULTS:

BoE to carbon monoxide were significantly reduced post-product switch in all Vuse ENDS and Abstinence Cohorts.

Daily ENDS Product Use



RESULTS:

Generally, the average daily amount of e-liquid used in each cohort increased slightly from Day 1 through Day 4 (Vuse Vibe and Vuse Ciro), & through Day 5 (Vuse Solo).

The amount of ENDS e-liquid used appears to trend with the nicotine level of the product.

Summary

1. Overall, large and statistically significant reductions in BoE (urine and blood) were observed across all three Vuse ENDS product cohorts.

2. Reductions in BoE in all three Vuse ENDS product cohorts were to a similar extent as those seen in Abstinence cohort (except for Total Nicotine Equivalents).

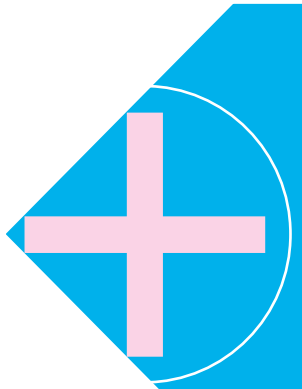
3. Smaller reductions in urinary total nicotine equivalents were observed across the three Vuse ENDS product cohorts compared to reductions observed in other urinary BoEs.

4. Over the 5 days of Vuse ENDS product use, mean daily e-liquid used generally increased for all ENDS product cohorts.

5. No serious adverse events or death were reported in this study.
All adverse events were reported as mild or moderate.

   None led to the discontinuation of Vuse ENDS product use.

Overall Conclusions



For Vuse ENDS users, the exposure to tobacco smoke toxicants was significantly reduced to comparable magnitudes as abstinence from smoking.

The data collected in this study add to the body of evidence supporting that ENDS pose less individual risk to tobacco product consumers than combustible cigarettes.

Acknowledgements

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- **RAIS Colleagues**

  Clinical Study Division

  Submissions

Thank You!

Questions?

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