

# Abuse Liability Assessments of Vuse Alto Golden Tobacco in Adult Smokers

Kyung soo (Jason) Hong, Sarah A. Baxter-Wright, John Darnell, Elaine Round and Eckhardt Schmidt

# Background and study design

## Regulatory Requirement & Guidance:

- United States Food and Drug Administration (FDA) Center for Tobacco Products' PMTA Guidance for Electronic Nicotine Delivery Systems (ENDS) (2019)
- FDA's Center for Drug Evaluations and Research (CDER) Guidance on Assessment of Abuse Potential of Drugs (2017)

## Study Design:

- A Randomized, Open-Label, Crossover Study to Assess Elements of Abuse Liability for Two Vuse Alto Golden Tobacco 2.4% and 5.0% Electronic Nicotine Delivery Systems in ENDS naïve subjects
- A 9-day confinement study with four test sessions preceded by product acclimation periods and 12-hr tobacco/nicotine abstinence periods

# Study overview

## Two nicotine levels of Vuse Alto Golden Tobacco

- 2.4% and 5.0% nicotine concentrations by weight

## Comparator products

- High Abuse Liability (AL) comparator: Usual brand cigarette (UB CC)
- Low Abuse Liability (AL) comparator: Nicotine gum (NRT)

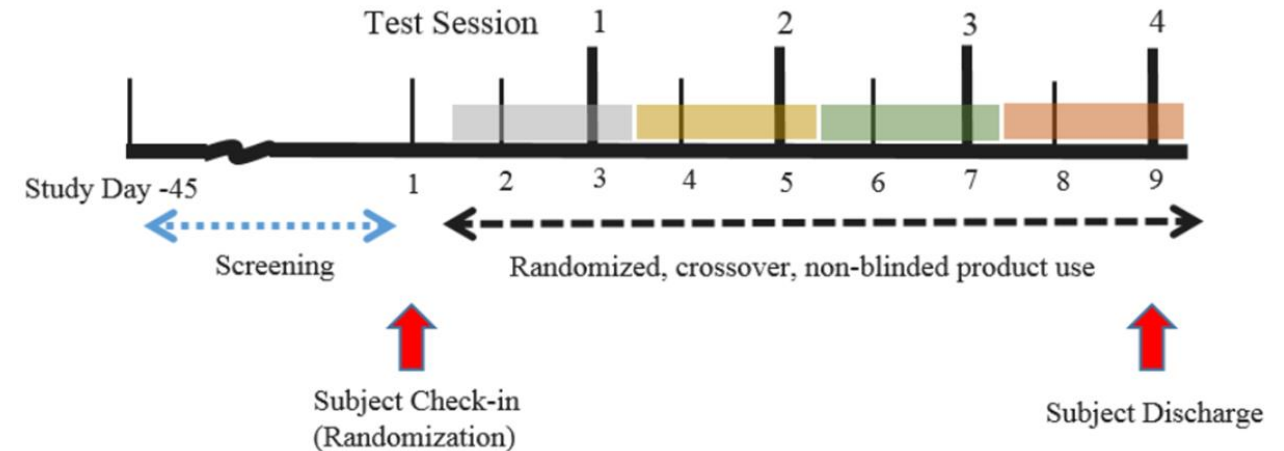
## Test Session Product use and observation duration

- 10 minutes of *ad libitum* use for ENDS and UB Cigarette
- 30 minutes of *ad libitum* use for nicotine gum
- Observed duration of 240 minutes



# Study overview

- 9-day confinement period
- Randomized 4-way cross-over study design
- IP familiarization over 1.5 days prior to Test Sessions:
  - At least 4 IP uses for both ENDS and NRT
- 4 Test Sessions (2 Study IP and 2 comparators) over 9 days
- 4-hour Test Sessions with PK/PD assessments (Days 3 through 9)



IP=Investigational Product; PD=Pharmacodynamic; PK=Pharmacokinetic; ENDS=Electronic Nicotine Delivery System; NRT=Nicotine Replacement Therapy.

# Objectives

## Subjective assessments:

- Product Liking (PL)\*
- Overall Intent to Use Again (OIUA)\*
- Product Effects (PE)
- Urge to Smoke (UTS)
- Overall Product Liking (OPL)

## Pharmacokinetic assessments:

- Plasma nicotine uptake over the first 15 minutes and over 4 hours

## Physiological measures:

- Mean maximum heart rate and blood pressure

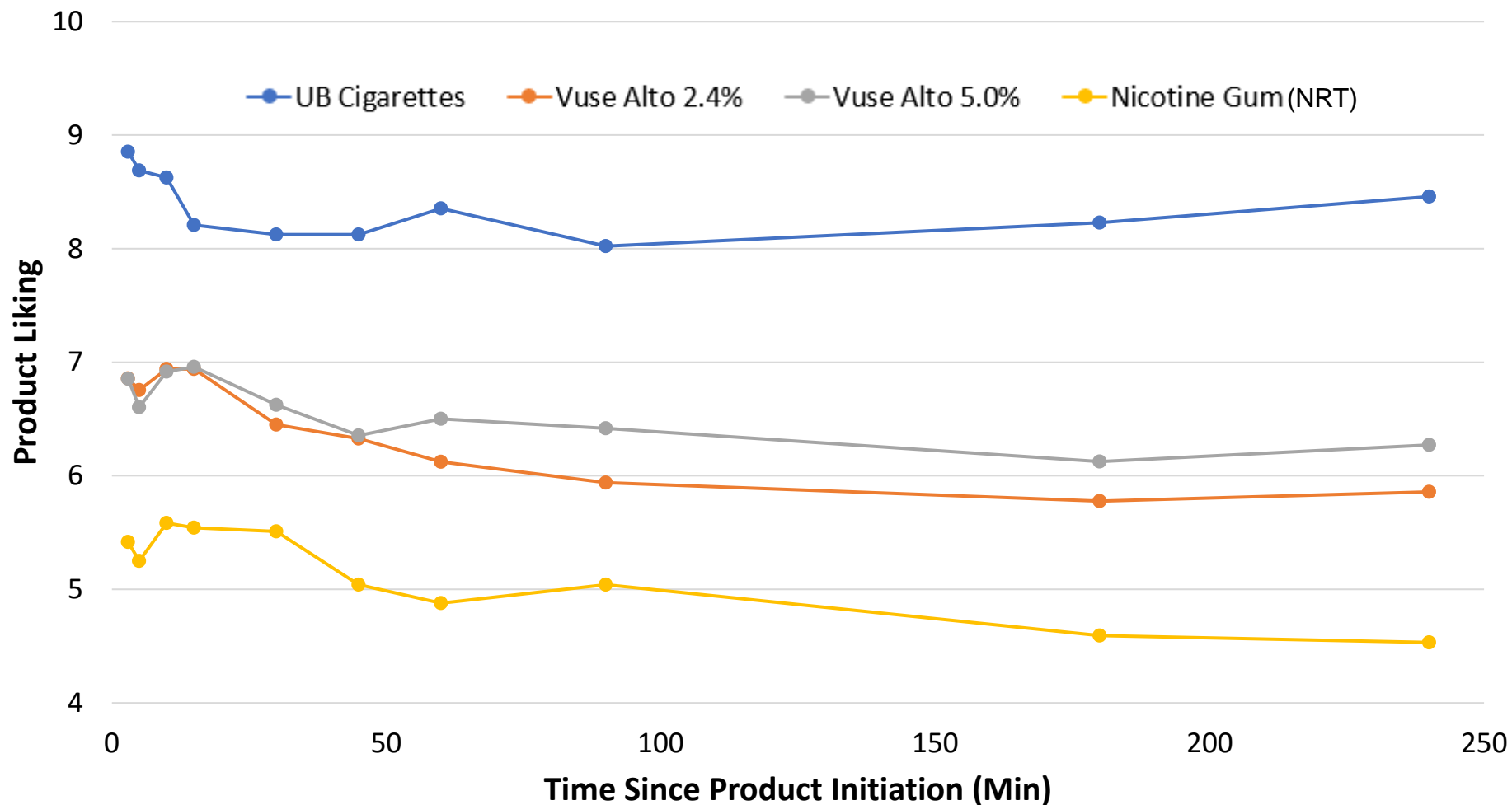
\* Primary outcome measures

# Study population

	Product Sequence				Total
	ABCD	BDAC	CADB	DCBA	
Number of Subjects [Enrolled (Completers)]	12 (11)	12 (11)	13 (13)	13 (13)	<b>50 (48)</b>
Average Age (yrs)	38.3	43.3	44.1	35.8	<b>40.4</b>
Sex (M/F)	5 / 7	9 / 3	7 / 6	6 / 7	<b>27 / 23</b>
Ethnicity [n (%)]	Non-Hispanic 10 (83.3)	Non-Hispanic 12 (100)	Non-Hispanic 10 (76.9)	Non-Hispanic 12 (92.3)	<b>Non-Hispanic 44 (88.0)</b>
Race [n (%)]	White 10 (83.3)	White 9 (75.0)	White 11 (84.6)	White 10 (76.9)	<b>White 40 (80.0)</b>
Average BMI (kg/m <sup>2</sup> )	32.6	29.0	31.0	28.9	<b>30.4</b>
Average Years Smoked	25	23	27	20	<b>24</b>
Average Cigarettes consumed per day	21	19	15	15	<b>17</b>

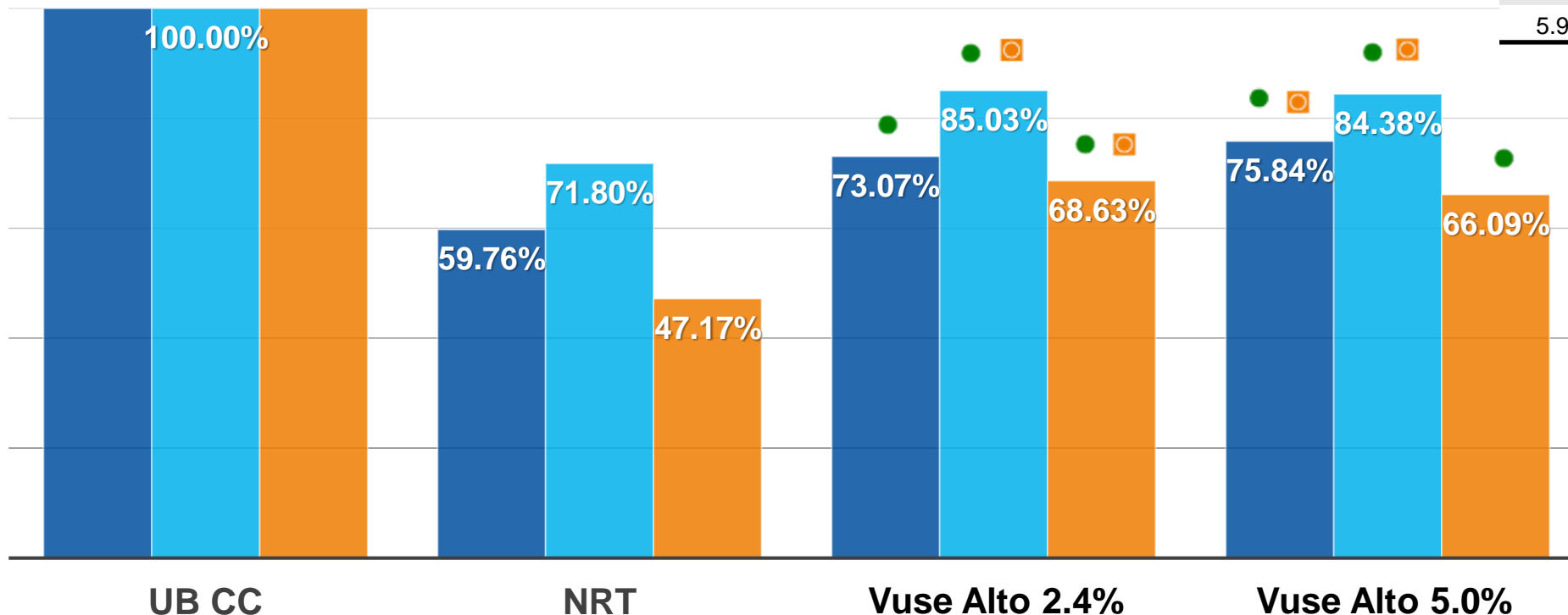
**Product A:** UB filtered, combustible cigarette; **Product B:** Vuse Alto Golden Tobacco, 2.4% nicotine;  
**Product C:** Vuse Alto Golden Tobacco, 5.0% nicotine; **Product D:** 4 mg nicotine polacrilex gum

# Vuse Alto use resulted in higher product liking and overall intent to use again vs. NRT



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■ AUEC (PL 3-240) ■ E (max PL) ■ E (overall IUA)

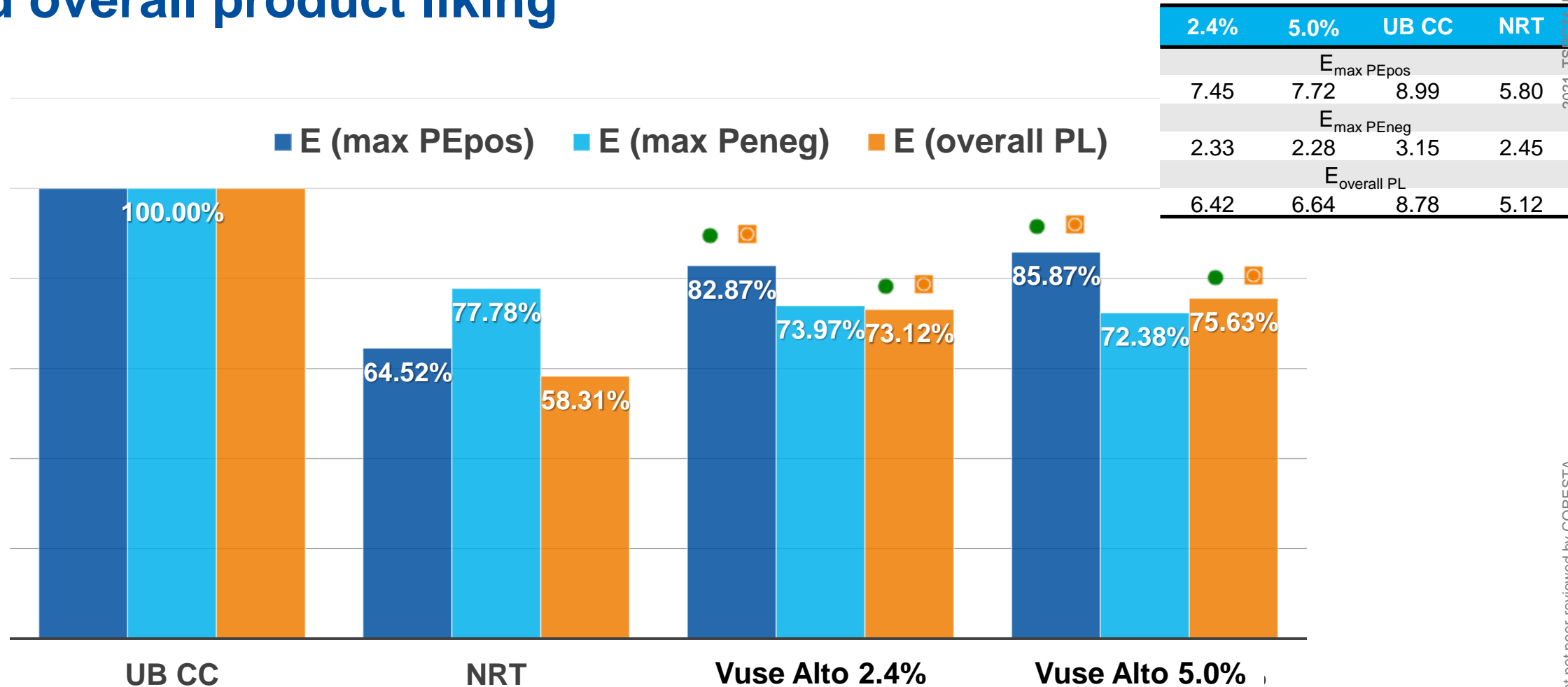


2.4%	5.0%	UB CC	NRT
AUEC <sub>PL 3-240</sub>			
1419.02	1472.84	1941.93	1160.58
E <sub>max PL</sub>			
7.84	7.78	9.22	6.62
E <sub>overall IUA</sub>			
5.95	5.73	8.67	4.09

●: Statistically significantly different from UB CC; ◻: Statistically significantly different from NRT.  
For primary endpoints,  $p \leq 0.0042$  is considered significant following Bonferroni adjustment.

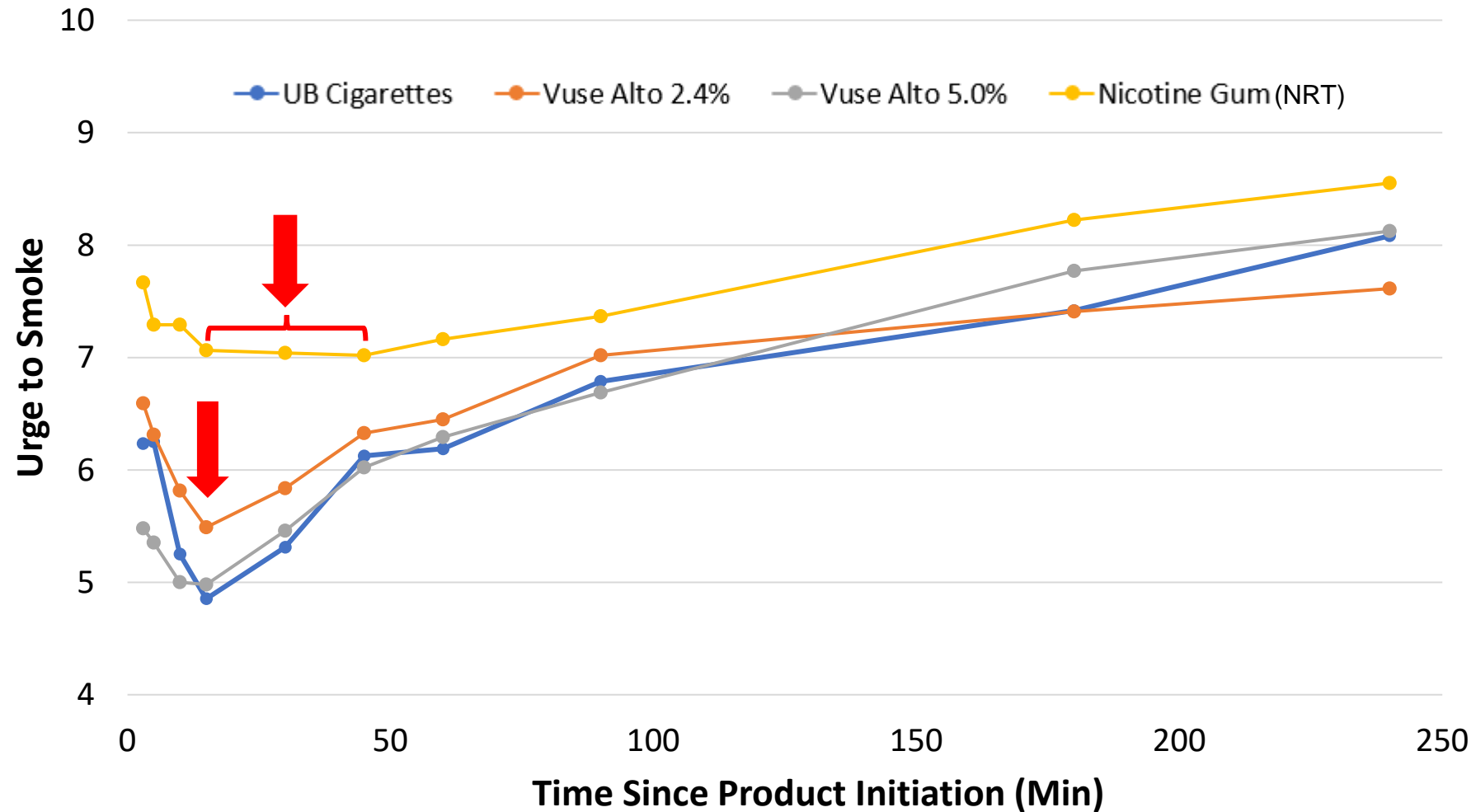


# Vuse Alto use resulted in positive product effects and overall product liking

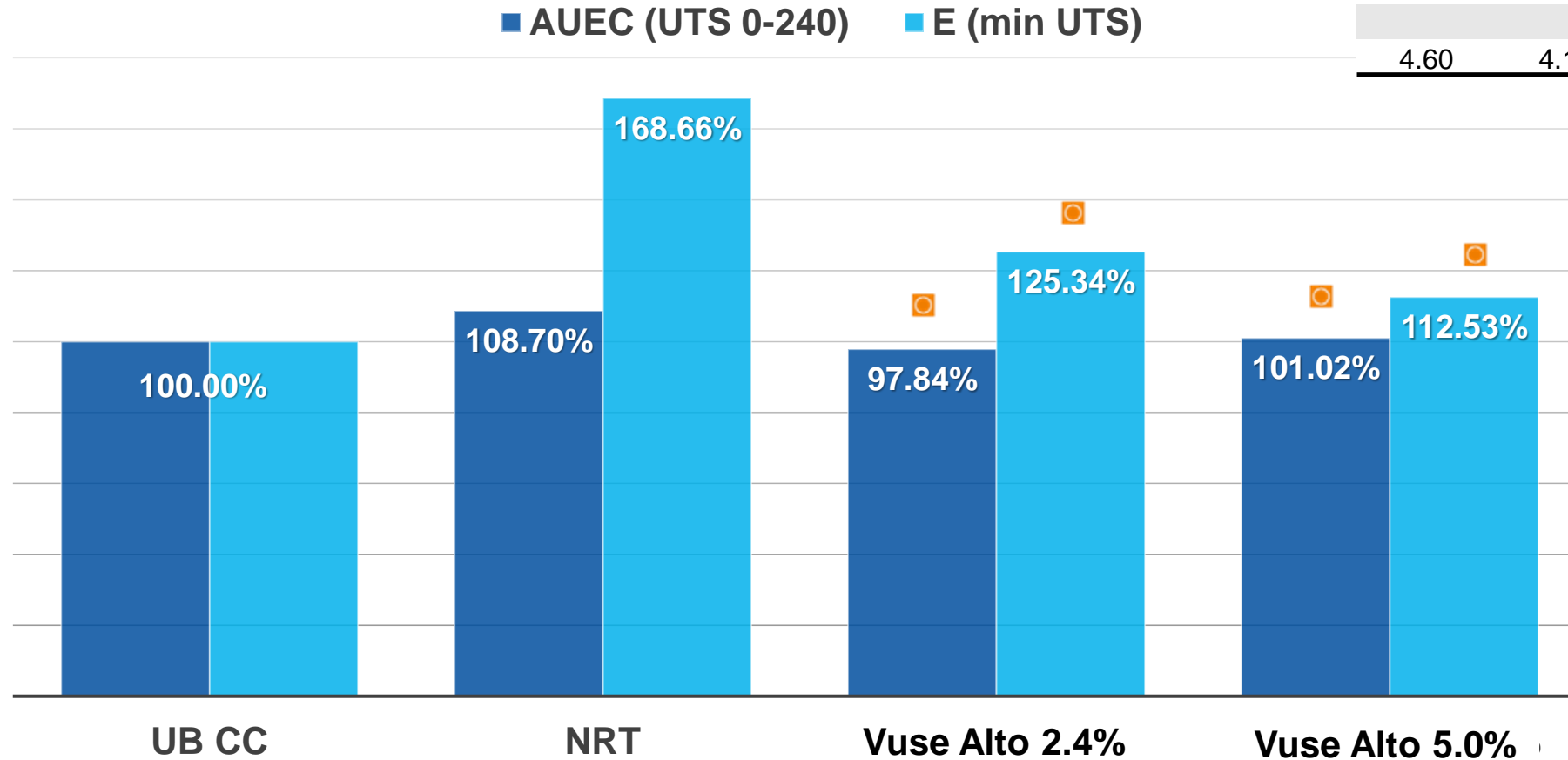


●: Statistically significantly different from UB CC; ◻: Statistically significantly different from NRT.  
For secondary endpoints,  $p \leq 0.05$  is considered significant.

# Vuse Alto use reduced the urge to smoke



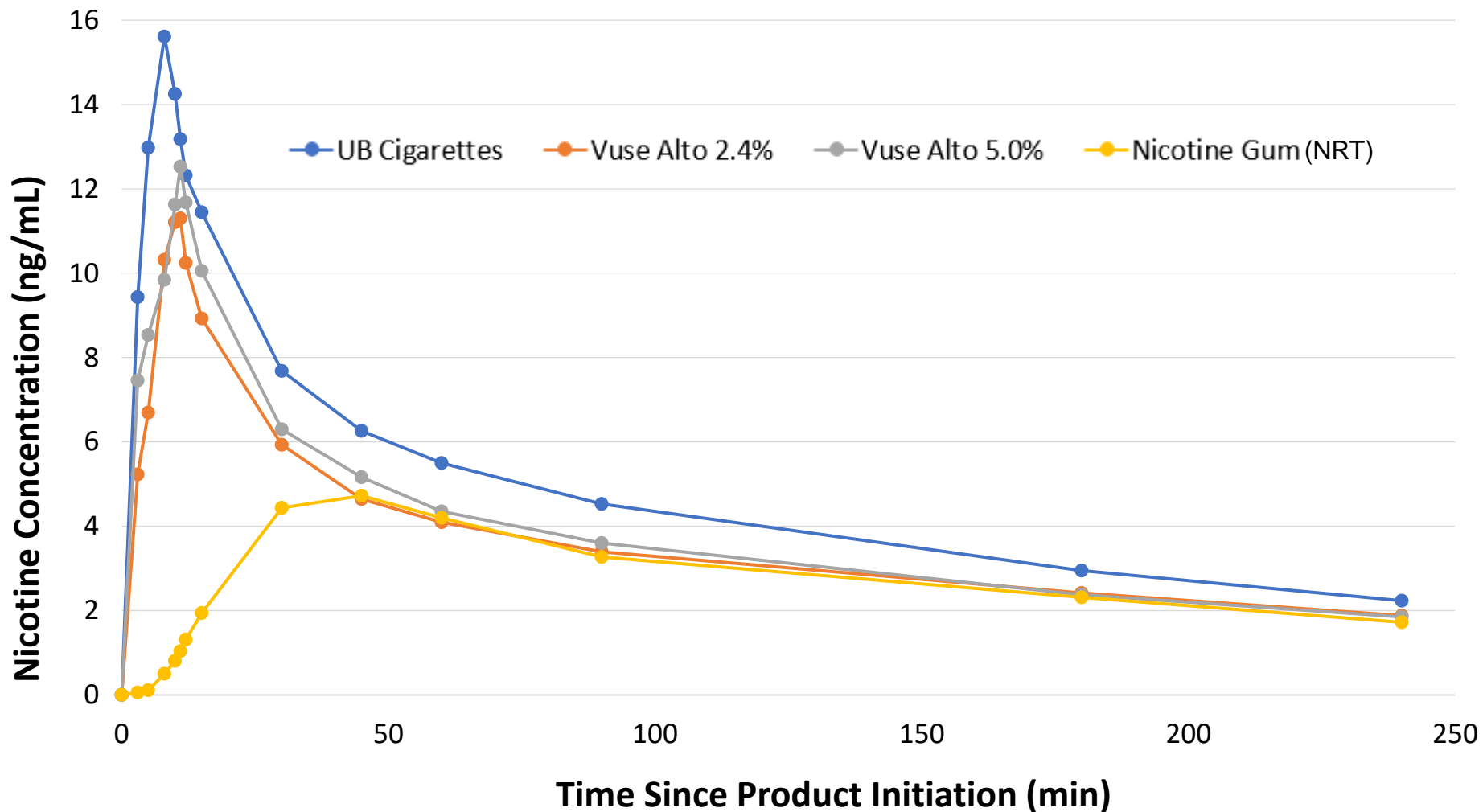
# Vuse Alto use reduced the urge to smoke



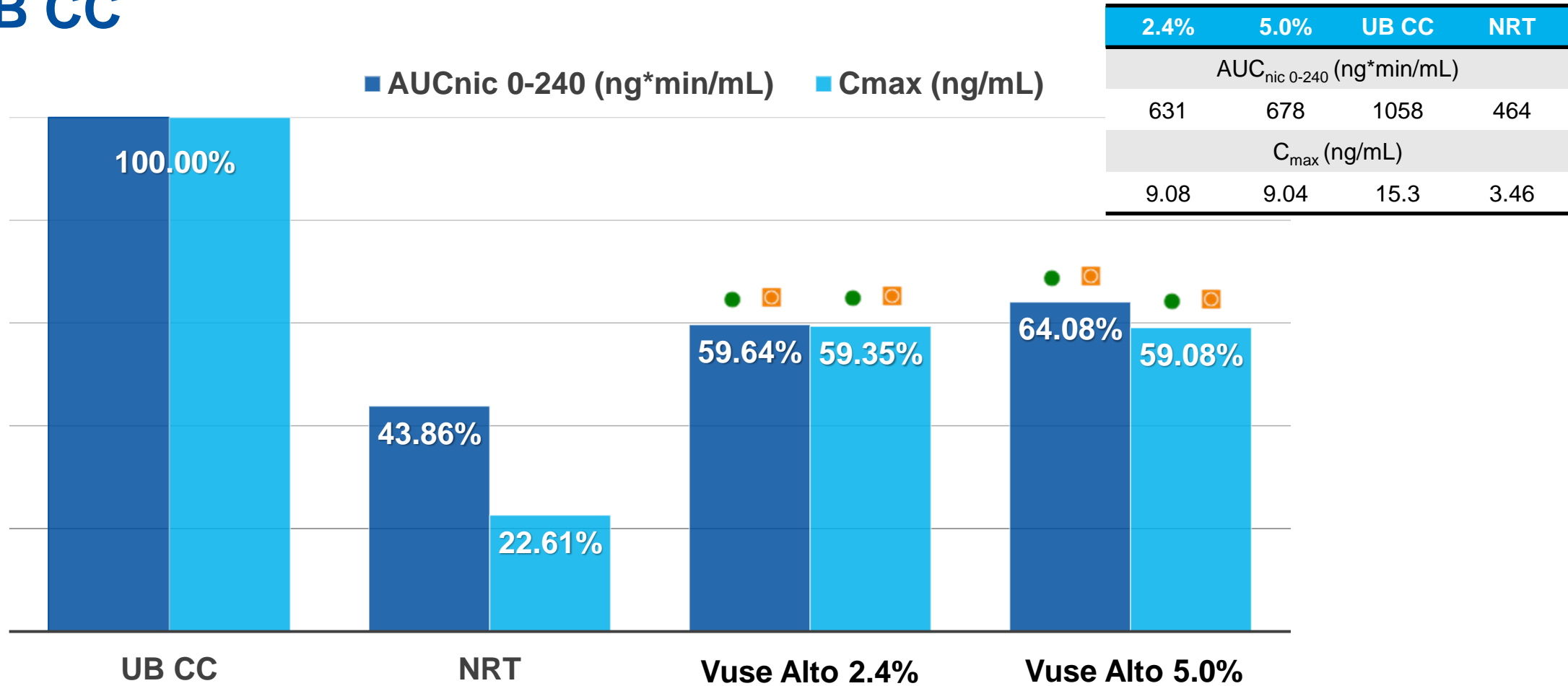
2.4%	5.0%	UB CC	NRT
AUEC (UTS 0-240)			
1630	1683	1666	1811
E <sub>min</sub> UTS			
4.60	4.13	3.67	6.19

●: Statistically significantly different from UB CC; ◻: Statistically significantly different from NRT.  
For secondary endpoints,  $p \leq 0.05$  is considered significant.

# Baseline-adjusted plasma nicotine concentrations over time

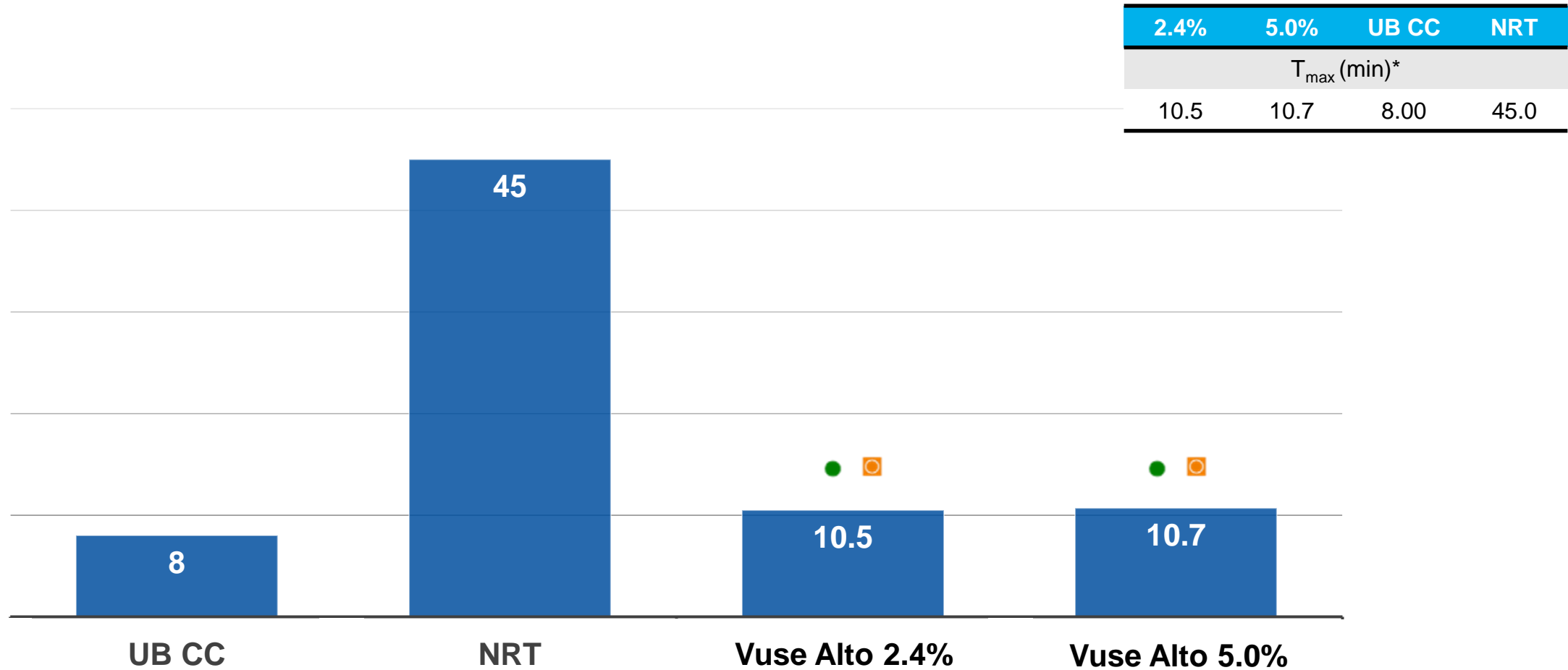


# Vuse Alto use resulted in lower nicotine exposure vs. UB CC



●: Statistically significantly different from UB CC; ◻: Statistically significantly different from NRT. For secondary endpoints,  $p \leq 0.05$  is considered significant.

# T<sub>max</sub>\* (minutes)



\*: Median value presented. ●: Statistically significantly different from UB CC; ◻: Statistically significantly different from NRT. For secondary endpoints, p ≤ 0.05 is considered significant.

# Physiological responses were transient and similar to comparator products

	Vuse Alto 2.4%	Vuse Alto 5.0%	UB CC <sup>1</sup>	NRT <sup>2</sup>
Max. increase in Systolic Blood Pressure (mmHg)	10.8	11.7 <sup>1</sup>	7.61	12.3
Max. increase in Diastolic Blood Pressure (mmHg)	8.45 <sup>1</sup>	7.70 <sup>1</sup>	5.13	8.55
Max. increase in Heart Rate (bpm)	13.2 <sup>2</sup>	14.2 <sup>2</sup>	14.1	8.52

Values presented are mean maximum change from baseline. For secondary endpoints,  $p \leq 0.05$  is considered significant

# Adverse events were mild

Investigational Products (IP)	Alto Golden Tobacco (2.4% & 5%)
Subjects in safety population	49
Total number of AE (Subjects reporting AE)	22 (13)
Most Common AE(s) for All IPs (% of subjects)	Headache 10 (14.3%) Presyncope 3 (6.1%) Others 1 (<1%)
AE per IP	5 / Vuse Alto 2.4%, 6 / Vuse Alto 5.0% 7 / UB CC 3 / NRT 1/ Pre-IP Administration



# Summary

- Product liking scores were higher for Vuse Alto as compared to NRT
- Positive product effects for Vuse Alto were higher than NRT
- All IPs showed similar negative product effects indices
- Vuse Alto resulted in reductions in UTS that were not statistically different from UB CC
- Nicotine PK measures fell between UB CC and NRT
- Physiological responses were transient and consistent with the comparators

# Conclusions

- Subjective effects and PK data for Vuse Alto fell between UB CC and NRT
- Data supports that the Abuse Liability of Vuse Alto lies between UB CC and NRT
- Vuse Alto reduces UTS similar to UB CC
- AEs were mild in severity and no AE caused discontinuation of ENDS IP use or subject discontinuation from the study

# Vuse Alto Abuse Liability Study Team

## Clinical Project Lead

- John Darnell

## Outsourcing Bioanalytical Lead

- Eckhardt Schmidt

## Statistician

- Chao Wei

## Data Manager

- Angela Hicks

## Regulatory

- Jeff Coffield

## CSD Senior Director

- Sarah Baxter-Wright

## CSD Senior Manager

- Patrudu Makena

## CSL Team

Christine Campbell, Gary Dull, Bobbette Jones, and Jeff Smith

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