Biomarkers Assessment in Healthy Adult Smokers Who Switched from Conventional Cigarettes to Two Types of Non-Combustible Tobacco Products: A Randomized, Controlled Study

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INTRODUCTION

Smoking is a cause of serious diseases including lung cancer, coronary heart disease, emphysema and chronic bronchitis. It is reported that the cause of such diseases is long-term exposure to substances emitted in the smoke generated by burning tobacco leaves for a long-term period.

The study aimed to investigate biomarkers of exposure to selected harmful and potentially harmful constituents (HPHCs) and potential harm [1,2] in subjects who switched to two types of non-combustible tobacco products (a cig-a-like e-cigarette [eDNC1.0a] and a novel heated tobacco product [IT2.0b]) for 60-days.

MATERIALS AND METHODS

This was a randomized, parallel-group study conducted at multiple centers.

A total of 487 healthy male and female regular smokers of greater than five commercially available cigarettes per day (CPD) were randomized into one of the following cohorts on the morning of Day 1 and continued participation through to the end of the study on Day 60:

Cig-a-like e-cigarettes (Logic Power; 72 subjects/cohort)

- Cohort A: eDNC1.0a, tobacco flavor: *ad libitum*
- Cohort B: eDNC1.0a, cherry flavor: *ad libitum*
- Cohort C: eDNC1.0a, menthol flavor: *ad libitum*

Fig. 1: Test product

Novel heated tobacco products (Logic Vapeleaf; 72 subjects/cohort)

- Cohort D: IT2.0b, regular flavor: *ad libitum*
- Cohort E: IT2.0b, menthol green flavor: *ad libitum*
- Cohort F: IT2.0b, menthol purple flavor: *ad libitum*

Fig. 2: Test product

Comparator/reference (36 subjects/cohort)

- Cohort G: Usual brand of combustible cigarette: *ad libitum*
- Cohort H: Tobacco product cessation

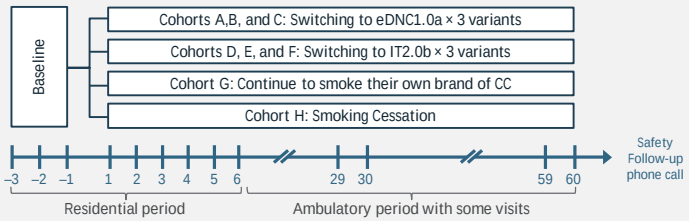

Fig. 3: Study design

RESULTS

Population and characteristics

	Cohort A: eDNC1.0a, tobacco flavor (n = 68)	Cohort B: eDNC1.0a, cherry flavor (n = 71)	Cohort C: eDNC1.0a, menthol flavor (n = 70)	Cohort D: IT2.0b, regular flavor (n = 69)	Cohort E: IT2.0b, menthol green flavor (n = 70)	Cohort F: IT2.0b, menthol purple flavor (n = 68)	Cohort G: Combustible cigarette (n = 35)	Cohort H: Tobacco product cessation (n = 34)	Overall (n = 485)
Completed Study – *n (%)*	47 (69.1%)	53 (74.6%)	56 (73.9%)	51 (73.9%)	52 (74.3%)	57 (83.8%)	27 (77.1%)	18 (52.9%)	361 (74.4%)
Age (year) – *Mean (SD)*	39 (10.7)	40 (11.2)	39 (11.1)	39 (11.0)	39 (11.0)	39 (11.3)	40 (12.1)	41 (10.7)	39 (11.0)
Sex, Male – *n (%)*	39 (57.4%)	38 (53.5%)	38 (54.3%)	38 (55.1%)	38 (54.3%)	36 (52.9%)	19 (54.3%)	20 (58.8%)	266 (54.8%)
Race, Caucasian – *n (%)*	40 (58.8%)	38 (53.5%)	40 (57.1%)	40 (58.0%)	37 (52.9%)	32 (47.1%)	21 (60.0%)	15 (44.1%)	263 (54.2%)
BMI (kg/m^2) – Mean (SD)	27.0 (4.17)	26.6 (4.17)	27.5 (4.00)	27.0 (4.75)	28.1 (4.46)	26.6 (4.08)	27.9 (4.22)	27.4 (3.56)	27.2 (4.23)
FTCD – *Mean (SD)*	5 (1.8)	5 (2.1)	5 (1.9)	5 (2.0)	5 (1.9)	5 (2.2)	5 (1.8)	5 (1.9)	5 (2.0)
CPD – *Mean (SD)*	16 (7.0)	15 (6.3)	14 (6.0)	16 (6.9)	14 (7.2)	15 (6.5)	15 (5.5)	15 (4.5)	15 (6.4)
Regular flavor, Non-menthol – *n (%)*	20 (29.4%)	26 (36.6%)	24 (34.3%)	24 (34.8%)	17 (24.3%)	21 (30.9%)	9 (25.7%)	9 (26.5%)	150 (30.9%)

Product-use and nicotine uptake

Subjects in the eDNC1.0a cohorts self-reported using approx. 0.8–1.2 cartridge per day, and in the IT2.0a cohorts self-reported using approx. 2.0–3.0 capsules per day.

During the ambulatory period, subjects in the test product cohorts self-reported smoking 0.6-2.3 CPD, although the CPD was markedly decreased from screening.

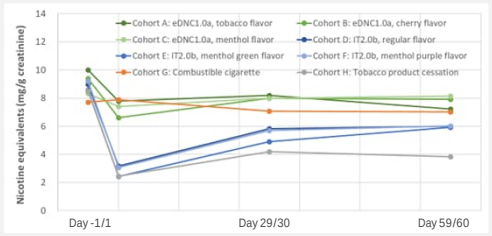

Fig. 4: Nicotine uptake during the study period

Biomarkers of Exposure to HPHCs

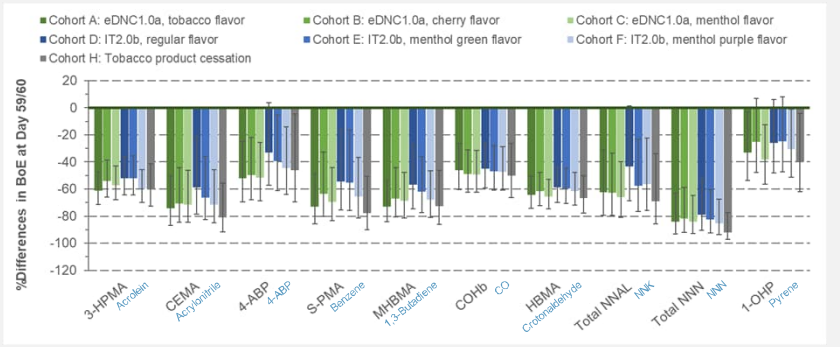

Fig. 5: %Differences in BoE at Day 59/60 related to Cohort G (CC) - Mean ± 99.3%CI

Percent difference values are geometric least squares mean ratio (%) and 99.3% (α = 0.05 / 7) confidence intervals from ANCOVA model conducted on ln-transformed Day 59/60 values with ln-transformed baseline value, study cohort, site, age, sex as fixed effect factors on Day 59/60.

Biomarkers of Potential Harm

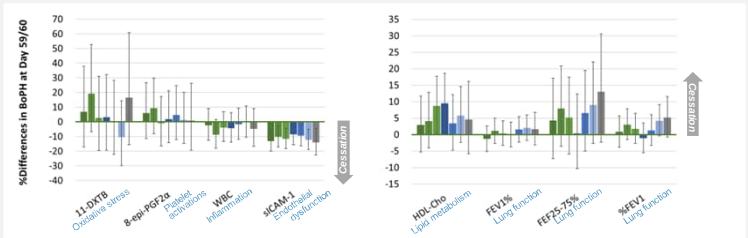

Fig. 6: %Differences in BoPH at Day 59/60 related to Cohort G (CC) - Mean ± 95%CI

Percent difference values are geometric least squares mean ratio (%) and 95% confidence intervals from ANCOVA model conducted on ln-transformed Day 59/60 values with ln-transformed baseline value, study cohort, site, age, sex as fixed effect factors on Day 59/60.

CONCLUSION

- Study data provide evidence of a substantial reduction in exposure to most selected HPHCs when using three flavor variants of cig-a-like e-cigarette (eDNC1.0a) and three flavor variants of novel heated tobacco product (IT2.0b) compared to cigarettes.
- Study data provide early insight of a potentially reduced health risks associated with smoking when using three flavor variants of cig-a-like e-cigarette (eDNC1.0a) and three flavor variants of novel heated tobacco product (IT2.0b) compared to cigarettes.

Reference

[1] Guidance for Industry – Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke under section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act – Draft Guidance (2012)

[2] Institute of Medicine (US) Committee on Qualification of Biomarkers and Surrogate Endpoints in Chronic Disease. Evaluation of Biomarkers and Surrogate Endpoints in Chronic Disease. In: J. MCB, ed. Washington, DC: National Academies Press; 2010

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* The present study was approved by the IRB responsible for review and approval and adhered to the ethical standards of the Declaration of Helsinki, applicable sections of the U.S. Code of Federal Regulations, and ICH E6 GCP.

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