Nicotine delivery from e-cigarettes: data and learnings from clinical pharmacokinetic studies

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INTRODUCTION

Nicotine pharmacokinetic studies are important in developing our understanding of nicotine delivery into the body from e-cigarettes and other nicotine-delivery products. Furthermore, data from such studies may potentially be required in a regulatory package, particularly as part of an abuse liability assessment of a novel product.

The objectives of the current studies were to:

- Compare nicotine delivery in e-cigarette naïve smokers and in vapers when they smoked a cigarette with that attained when they use a closed system modular e-cigarette.
- Examine differences in nicotine delivery in studies which required subjects to either take a defined number of puffs or to puff *ad libitum*.

METHODS

- Blood nicotine levels during acute (5-minute) clinical use periods were measured in subjects smoking cigarettes and using e-cigarettes (Table 1).
- Study 1 (ISRCTN74070762; Belfast, U.K.) compared blood nicotine levels in 24 smokers using closed-system modular e-cigarettes according to a defined puffing schedule, with those seen when subjects smoked a market-typical cigarette.
- Study 2 (NCT02474849; Los Angeles, USA) examined blood nicotine in 18 vapers who were occasional smokers using the same modular e-cigarettes *ad libitum* and compared these levels to when subjects smoked a single, market-typical cigarette.
- Both studies were approved by local, independent research ethics committees and were run in accordance with GCP.
- Subjects provided written informed consent prior to study participation and were deemed healthy following medical examination and clinical laboratory screening. Smoking status was verified by exhaled CO measurements.
- Before each study visit subjects abstained overnight from any tobacco or nicotine product use, also verified by exhaled CO.

Study	Product number	Form	Product & manufacturer	Nicotine yield/content	Other ingredients
1	1.1	Combustible tobacco cigarette	John Player Special Blue	1.0 mg/cig†	N/A
	1.2	Closed modular system e-cigarette	Vype vPro ePen¥	1.86% w/w#	Water, glycerol, propylene glycol, 0.3MeQ organic acid, tobacco flavour
2	2.1	Combustible tobacco cigarette	Marlboro Ultralight	0.5 mg/cig†	N/A
	2.2	Closed modular system e-cigarette	Vype vPro ePen¥	1.86% w/w#	Water, glycerol, propylene glycol, 0.3MeQ organic acid, tobacco flavour
	2.3	First-generation e-cigarette	Nicolites	1.33% w/w#	Water, glycerol, propylene glycol, flavourings

Table 1. Study products. †ISO nicotine yield; #nicotine content of liquid solution; ¥ePen power setting of 4.55W (voltage 3.6V, resistance 2.85 Ohms) in Study 1 and 5.6W in Study 2 (voltage 4.0V, resistance 2.85 Ohms). N/A, not applicable.

RESULTS – STUDY 1 (BELFAST)

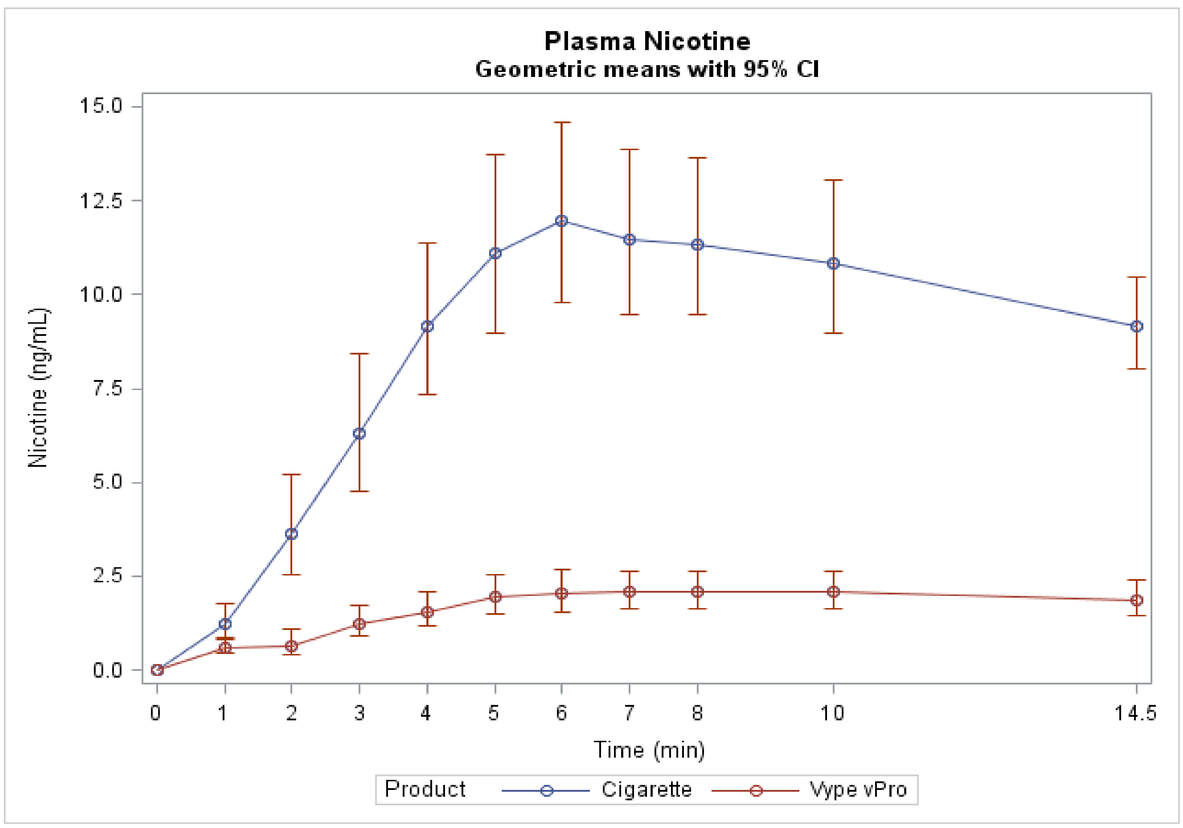

Figure 1. Plasma nicotine levels in smokers smoking a cigarette or using an e-cigarette in Study 1. Subjects smoked a combustible cigarette or used the Vype vPro ePen e-cigarette under defined conditions (10 puffs, each separated by 30 seconds). Blood was drawn at the indicated timepoints and sampled for plasma nicotine levels. Data are geometric means ± 95% confidence intervals for between 23 and 24 subjects in each case.

RESULTS – STUDY 2 (BURBANK)

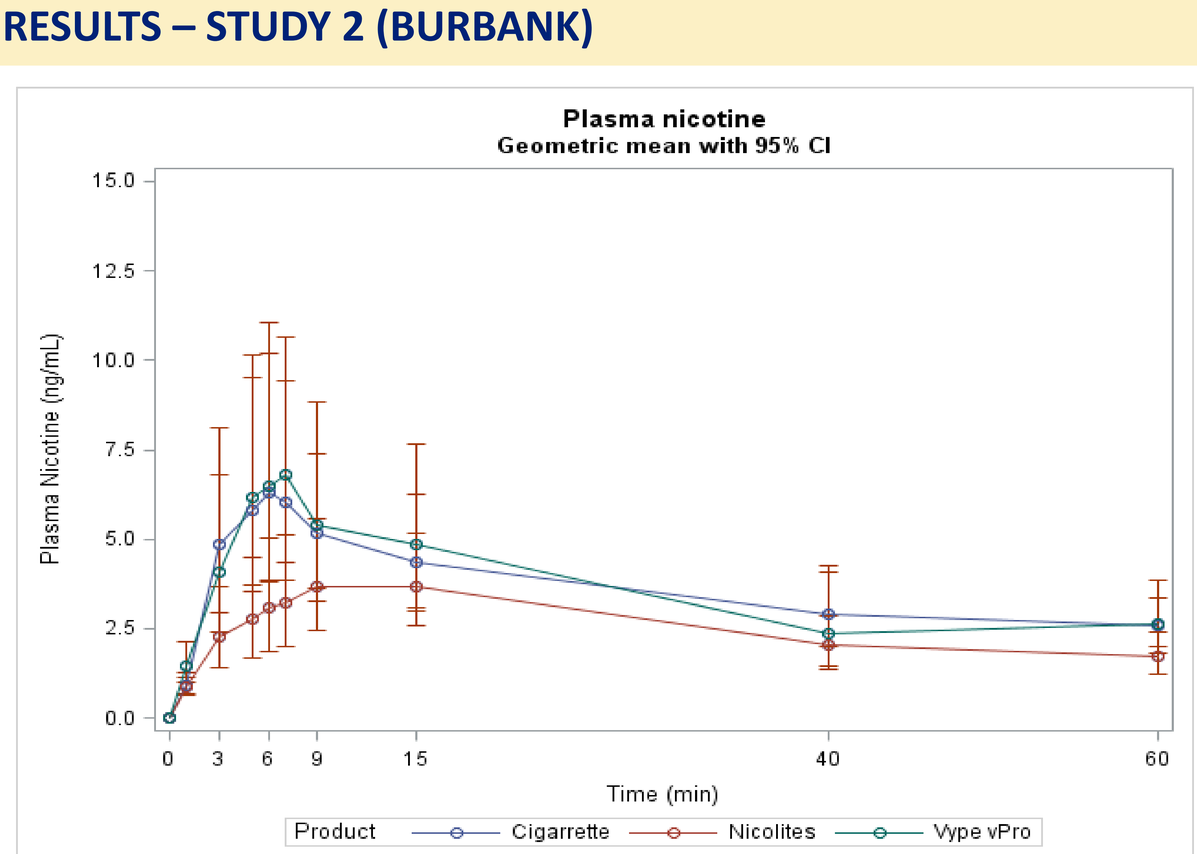

Figure 2. Plasma nicotine levels in e-cigarette users smoking a cigarette or using one of two different e-cigarettes in Study 2. Subjects smoked a combustible cigarette or used their assigned e-cigarette (Vype vPro ePen or Nicolites) by taking ad libitum puffs over a period of 5 minutes. Blood was drawn at the indicated timepoints and sampled for plasma nicotine levels. Data are geometric means ± 95% confidence intervals for 18 subjects in each case.

CONCLUSIONS

- A high level of variability was seen when subjects from different populations and with different smoking histories used similar products. Puffing schedule (defined vs ad libitum) may have contributed to this variability.
- While this may support a need for standardisation of protocols for e-cigarette clinical research, to facilitate comparisons between products in different studies, study design needs to take into account study objectives and cohort, real-world usage patterns and which comparisons need to be made between one product and another.

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