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A study to assess if nicotine delivered via an e-cigarette can have an effect on appetite in healthy adult smokers

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Registration date 25/02/2021	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 14/02/2023	**Condition category** Other	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims

Reducing the negative health burden of tobacco use is a public health priority and has led to a series of regulatory and educational initiatives to encourage people not to smoke. Despite these efforts, smoking rates in adult populations worldwide remain relatively high and the World Health Organization (WHO) has forecast that there will be around 1.5 billion tobacco smokers worldwide in 2050.

It is therefore important to complement existing initiatives with strategies to attempt to reduce or prevent harm in those who will otherwise continue to smoke. Tobacco harm reduction, the substitution of cigarette smoking with potentially reduced-risk products (PRRPs), is a strategy that, if widely adopted, could offer substantial public health gains. For many years, tobacco researchers and policy experts have embraced the idea that alternative sources of nicotine, that provide sensory, behavioural, and physiological effects similar to smoking, might entice smokers away from combustible cigarettes. This could lead to them either quitting smoking or switching to long-term nicotine use without incurring the harm anticipated from exposure to cigarette smoke.

In the absence of both tobacco and combustion as a means of transferring nicotine, e-cigarettes deliver a vapour that is considered to contain significantly less chemical toxicants compared to cigarette smoke. An independent scientific expert panel was able to demonstrate the potential reduction in the harm of using e-cigarettes compared to combustible cigarettes. This conclusion was recently endorsed by both Public Health England and the U.K. Royal College of Physicians. The use of e-cigarettes to help smokers either reduce or quit smoking has been proposed as having the potential to play a major role in tobacco harm reduction, and this potential is further supported by data from large survey studies in the UK. The cross-sectional data also suggest that e-cigarettes are a more effective aid to smoking cessation than more traditional nicotine replacement therapy products.

Smoking is known to have a range of effects on the body. These effects are not well understood, but, include effects on body weight. Published scientific evidence suggests that smoking and

more specifically nicotine may affect some aspects of body weight maintenance, including but not limited to appetite. The ability of nicotine delivered via PRRPs to affect appetite has not been widely researched and may be an important aspect of the acceptability of these products to existing smokers. Weight gain after quitting smoking has been associated with a 4-5 kg average increase in body weight. It is anticipated that smokers, who would otherwise continue to smoke, can be encouraged to switch to PRRPs if they are shown to have similar effects on the body and appetite.

The aim of this study is to determine if nicotine delivered via an e-cigarette has an effect on appetite (calorie consumption) following a 12 h period of no nicotine in comparison with a conventional cigarette.

Who can participate?
Healthy adults aged 25-45 who smoke at least 10 cigarettes per day and are familiar with e-cigarette products.

What does the study involve?
Screening assessments will be carried out within 28 days prior to the first study session 1. Eligible participants will be asked to return for the testing sessions.

Following the completion of the screening procedures, eligible participants will be invited to attend the first study session (approximately 1.5 days in duration, from the morning prior to the study session until the afternoon of the session day). On admittance to the Clinical Unit, participants will undergo a familiarisation period with the ePro/eCOA solution (this will happen at the first study session only) until they are comfortable with using the system. Following 12 h overnight nicotine abstinence, participants will receive a standardised breakfast. Participants will then be asked to complete a series of baseline questionnaires assessing their sleep quality, caffeine dependence, emotion, motivation to eat, and cigarette craving, as well as receiving a blood test, before using one of the study products (or no study product) for a 5 min period. A subset of the questionnaires and blood samples will then be repeated at scheduled timepoints over the following 60 min period. After 70 min, participants will be provided with a meal according to participant wishes and 500 ml of water and instructed to “eat and drink until they feel comfortably full”. Finally, after consumption of this meal, participants will again complete a subset of questionnaires.

Participants will repeat 5 study sessions, with at least 7 days between each session, until they have used all 5 of the study products. The order in which the study products are used by each participants will be decided randomly.

What are the possible benefits and risks of participating?
There are no direct benefits to participants for taking part. However, the subjects will undergo a medical examination, which may provide them with information on their state of health. Subjects will be able to ask for advice to stop using tobacco/nicotine products and will be provided with a smoking cessation helpline number.

The main risks are the side-effects of using nicotine products (such as headache, dizziness, palpitations, and mouth and throat irritation), which participants should be familiar with as a result of being regular users of these products.

Where is the study run from?
Simbec Orion (UK)

When is the study starting and how long is it expected to run for?
From September 2020 to July 2021 (updated 02/06/2021, previously: June 2021)

Who is funding the study?
British American Tobacco (UK)

Who is the main contact?
Olivia O'Shea, olivia_oshea1@bat.com

Contact information

Type(s)
Public

Contact name
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Additional identifiers

Protocol serial number
BAT4120025

Study information

Scientific Title
An exploratory randomised crossover study to investigate the effect of nicotine on appetite in healthy adult smokers, who use an e-cigarette, after a period of smoking abstinence

Study objectives
That acute nicotine delivery (delivered via an e-cigarette) can influence appetite in regular smokers following a 12-hour period of nicotine abstinence in a similar manner to a combustible cigarette.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/02/2021, Wales Research Ethics Committee 1 (Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)7973 687815; Wales.REC1@wales.nhs.uk), ref: 20/WA/0276

Primary study design
Interventional

Study design
Single-centre interventional randomized partially-blinded 5-period crossover study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cigarette smoking

Interventions
The order of the Investigational Product use will be randomised (using a Williams Latin square design) for this 5-period crossover study. The Investigational Products in this study are as follows:
1. No Treatment (Control 1)
2. Combustible Cigarette (Control 2)
3. EPEN3.0_VGT00 (Placebo 1)
4. EPEN3.0_VGT12 (Intervention 1)
5. EPEN3.0_VGT18 (Intervention 2)

Each participant will use the e-Cigarette or cigarette for a 5 min session of ad-libitum puffing regimen (puffing as participants feel necessary for 5 min). Participant will use one Investigational Product per study session. There will be 5 study sessions for each participant. Participants will abstain from nicotine, caffeine, and alcohol 12 h prior to the start of each study session. There will be at least 7 days between the administrations of each study session.

Intervention Type
Other

Primary outcome(s)
1. Calorie consumption (calorie counting) measured via Ad libitum meal at 70 min during each study session

Key secondary outcome(s)
1. Leptin measure via a blood sample taken at 15 min prior to, and 0, 15, 30, 45, and 60 min after product usage
2. Ghrelin measure via a blood sample taken at 15 min prior to, and 0, 15, 30, 45, and 60 min after product usage
3. Insulin measure via a blood sample taken at 15 min prior to, and 0, 15, 30, 45, and 60 min after product usage
4. Glucose measure via a blood sample taken at 15 min prior to, and 0, 15, 30, 45, and 60 min after product usage
5. Peptide YY (PYY) measure via a blood sample taken at 15 min prior to, and 0, 15, 30, 45, and 60 min after product usage
6. Glucagon-like Peptide-1 (GLP-1) measure via a blood sample taken at 15 min prior to, and 0, 15, 30, 45, and 60 min after product usage
7. Motivation to eat, as measured using the Subjective Appetite Questionnaire (VAS) at 15 min prior to, and 0, 15, 30, 45, 60, and 100 min after product usage

Completion date
20/07/2021

Eligibility

Key inclusion criteria
1. Healthy male or female subject, between 25 and 45 years of age, inclusive;
2. Female subject of childbearing potential willing to use a highly effective method of contraception or 2 effective methods of contraception, if applicable (unless of non-childbearing potential or where abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the subject) from the screening until the end of the follow-up period;
3. Female subject of non-childbearing potential. For the purposes of this study, this is defined as the subject being amenorrhoeic for at least 12 consecutive months or at least 4 months post-surgical sterilisation (including bilateral fallopian tube ligation or bilateral oophorectomy with or without hysterectomy; documentation of the procedure is required);
4. Female subject with a negative pregnancy test at Screening who is not breastfeeding or lactating;
5. Female subject of menopausal status confirmed by demonstrating at Screening that the serum level of the follicle stimulating hormone (FSH) falls within the respective pathology reference range. In the event a subject's menopausal status has been clearly established (for example, the subject indicates she has been amenorrhoeic for 10 years, confirmed by medical history, etc), but serum FSH levels are not consistent with a postmenopausal status, determination of the subject’s eligibility to be included in the study will be at the Investigator’s discretion following consultation with the Sponsor;
6. Subject with a body mass index (BMI) of 18.5-29.9 kg/m2;
BMI = body weight (kg) / [height (m)]2;
7. Subject with a negative urinary drugs of abuse (DOA) screen (including alcohol) test results, determined within 28 days before Study Session 1 (Day 1) (N.B.: A positive test result may be repeated at the Investigator’s discretion);
8. No clinically significant abnormalities in vital signs (blood pressure, pulse rate, respiration rate, oral temperature) determined within 28 days before Study Session 1 (Day 1);
9. Subjects who are current daily users of conventional factory-made cigarettes and/or roll your own cigarettes (minimum of 10 cigarettes per day) and who have done so for at least 3 years. Subjects should also be familiar with using e-cigarettes (i.e. have used e-cigarettes over a period of greater than 1 month within the last 2 years). Product use status will be confirmed with a urinary cotinine level of ≥200 ng/mL and product use history questionnaire at screening;
10. Subjects who are regular breakfast eaters and have no current diagnosis of any eating disorder;
11. Subjects who are willing to consume the study standardised breakfast and ad libitum meal;
12. Subjects who are willing to comply with the study protocol;
13. Subject must be available to complete the study (including all follow up visits);
14. Subject must satisfy an Investigator about his/her fitness to participate in the study;
15. Subject must provide written informed consent to participate in the study;
16. Subjects who are willing to use a tobacco flavoured e-cigarette.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
42

Key exclusion criteria
1. Subjects who have an acute illness (e.g. upper respiratory tract infection, viral infection, etc) requiring treatment within 4 weeks prior to Screening or on admission;
2. Use of any medications or substances (other than tobacco), including vitamins, herbal and dietary supplements which are known to be strong inducers or inhibitors of cytochrome P450 (CYP) enzymes within 14 days or 5 half-lives (whichever is longer) prior to Screening;
3. Subjects who are self-reported non-inhalers (smokers/vapers who draw smoke/aerosol from the cigarette/e-cigarette into the mouth and throat but who do not inhale). Subjects who are observed as non-inhalers at Admission by the clinic staff will be excluded;
4. Subjects who, prior to enrolment, are planning to quit/alter smoking/vaping within the duration of the study (to follow-up telephone call). All subjects will be informed that they are free to quit smoking/vaping and withdraw from the study at any time;
5. Evidence of renal, hepatic, central nervous system, respiratory, cardiovascular or metabolic dysfunction;
6. A clinically significant history of drug or alcohol abuse [defined as the consumption of more than 14 units for male and female subjects) of alcohol a week] within the past two years;
7. Inability to communicate well with the Investigators (i.e., language problem, poor mental development or impaired cerebral function);
8. Vegans, vegetarians or those with other dietary restrictions or food-related allergies (e.g., restrictions for medical, religious or cultural reasons, etc);
9. Subjects with a positive COVID-19 PCR (Antigen) test prior to Day 1.

Date of first enrolment
26/02/2021

Date of final enrolment
25/06/2021

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre

Simbec Orion
Merthyr Tydfil Industrial Park
Merthyr Tydfil
United Kingdom
CF48 4DR

Sponsor information

Organisation
British American Tobacco (United Kingdom)

ROR
https://ror.org/01znsh139

Funder(s)

Funder type
Industry

Funder Name
British American Tobacco

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Deidentified participant level data will be available on request from Olivia O'Shea (olivia_oshea1@bat.com). This includes all data captured using the eCRF, questionnaires and full bioanalytical reports available in SDTM format for at least 5 years. This data will be available immediately following publication. Data will be available to anyone who wishes access to the data and for any purpose upon request. Requestors must sign a data access agreement.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		26/10/2022	14/02/2023	Yes	No
HRA research summary			28/06/2023	No	No