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A study to investigate the delivery of nicotine in the blood stream from two variants of e-cigarette devices and a conventional cigarette

Submission date
02/11/2018

Recruitment status
No longer recruiting

Registration date
08/11/2018

Overall study status
Completed

Last Edited
17/08/2022

Condition category
Other

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
It has become increasingly important to reduce the health burden associated with the use of tobacco, with a number of initiatives currently in place to persuade individuals to quit smoking. Despite these efforts, smoking rates in adult populations worldwide remain relatively high, and the World Health Organisation (WHO) predicts there will be around 1.5 billion tobacco smokers worldwide by 2050.
Due to this, it is important to develop products which aim to reduce or prevent harm for those who wish to continue to smoke. One of these products in development and use worldwide are electronic-cigarettes (e-cigarettes). E-cigarettes also contain nicotine; however, they are considered a lower risk alternative to conventional cigarettes as they do not use tobacco as a means of delivering nicotine. E-cigarettes deliver a vapour which contains a significantly lower number of chemical toxicants compared to cigarette smoke.
In this study, we will investigate the delivery and levels of nicotine in the bloodstream from 2 variants of e-cigarettes developed by British American Tobacco, and a conventional cigarette. The 2 types of e-cigarettes will contain different e-liquid formulations. Nicotine delivery of the e-cigarettes will be compared to the conventional cigarette in order to determine which e-cigarette product is most similar to the conventional cigarettes.

Who can participate?
Healthy adults aged 19-60 who are current daily users of e-cigarettes and current smokers of conventional factory-made cigarettes for at least one year prior

What does the study involve?
Subjects will attend a screening visit to assess eligibility to participate in the study. Once deemed eligible, subjects will be admitted into the clinic (day 1) within 28 days of the screening visit, in which they will remain in the clinic for 8 days until discharge (day 8). During the subjects stay at the clinic, they will be allowed to familiarise with the study products a day before their assessment. During the assessment period, subjects will use their assigned products for a maximum of 5 minutes. Before, during and up to 2 hours after product use, blood samples will be collected for nicotine analysis. Subjects product satisfaction questionnaire will be completed,

and heart rate will be monitored at predefined intervals during this 2-hour period. The same procedure will be repeated on each study day until all the study products are used.
No later than one week after discharge from clinic, a post-study follow-up will be performed, which will be conducted via a telephone call with the subjects.

What are the possible benefits and risks of participating?
The possible benefit to participants taking part in this study is that the tests involved may help them learn about their general health or discover any unknown medical conditions. As participants already use tobacco products (e-cigarettes and cigarettes), only the standard risks and side effects associated with nicotine and tobacco use apply. Participants are not likely to be exposed to nicotine levels higher than the ones they are usually exposed to when smoking. The possible side effects of e-cigarette use include headache, dizziness, nausea, palpitations, mouth and throat irritation, skin irritation and gastrointestinal disturbances. Subjects will be monitored for any of the listed symptoms.

Where is the study run from?
Simbec Research Limited (UK)

When is the study starting and how long is it expected to run for?
September 2018 to February 2019

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

Who is the main contact?
Dr James K. Ebajemito
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

Integrated Research Application System (IRAS)
254373

Protocol serial number
BAT40118015/RD683-34202

Study information

Scientific Title
A randomised controlled single centre open-label pharmacokinetic study to examine nicotine delivery from different variants of an e-cigarette and a conventional cigarette in healthy subjects

Study objectives
Use of e-cigarette will increase plasma nicotine to levels that are comparable to a combustible cigarette. Nicotine delivery and satisfaction will be modified by the inclusion of different formulations in the e-cigarette liquid.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales Research Ethics Committee 2, 25/10/2018, 18/WA/0353

Primary study design
Interventional

Study design
Interventional single-centre open-label eight-armed randomised crossover study

Study type(s)
Other

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

Interventions
A computer generated randomisation scheme will determine the order in which the subjects will use the study e-cigarettes/cigarette at study days 1-8. Participants will participate in all 8 arms of the study but the order in which they do will be randomly allocated. The study arms are as follows:
Arm A: Combustible cigarette (ad libitum puff)
Arm B: Combustible cigarette (fixed puff)
Arm C: E-cigarette - EPEN2.0BT (ad libitum puff)
Arm D: E-cigarette - EPEN3.0BT18 (ad libitum puff)
Arm E: E-cigarette - EPEN3.0MB18VP (ad libitum puff)
Arm F: E-cigarette - EPEN3.0MB30VP (ad libitum puff)
Arm G: E-cigarette - EPEN3.0MB18VP (fixed puff)
Arm H: E-cigarette - EPEN3.0MB12VP (ad libitum puff)
After a minimum of 12 hours nicotine abstinence, subjects will smoke a combustible cigarette or use e-cigarette ad libitum (with puffs counted) or fixed for 5 minutes.

Intervention Type
Other

Primary outcome(s)
Plasma nicotine levels will be analysed for the following parameters using blood samples 5 minutes before the first puff, and then at 1, 3, 5, 7, 9, 15, 30, 45, 60, 90, 120 minutes following the first puff:
1. Cmax
2. Tmax
3. AUC0-120)

Key secondary outcome(s)
1. Heart rate, assessed using a heart rate monitor 5 minutes before the first puff, and then at 1, 3, 5, 7, 9, 15, 30, 45, 60, 90, 120 minutes following the first puff
2. Product satisfaction scores, assessed using the Subjective Product Satisfaction Questionnaire 5 minutes before the first puff and 15 and 120 minutes following the first puff
3. Product use:
3.1. Device mass loss (DML), assessed using weighing scales before and after product use during familiarisation and during each session
3.2. Puff number, assessed through observation with a click counter throughout each session
3.3. Use count, assessed through observation with a click counter throughout each session

Completion date
28/02/2019

Eligibility

Key inclusion criteria
1. Aged 19-60 (demonstrated by government issued proof of identification)
2. Body mass index (BMI) of 18.5-30.0 kg/m², inclusive
3. Body weight exceeding 52 kg for males or 45 kg for females
4. In good health, as judged by the PI or the appropriately qualified designee based on:
4.1. Medical history (confirmed by volunteer)
4.2. Physical examination
4.3. Vital signs assessment
4.4. 12-lead ECG
4.5. Clinical laboratory evaluations
4.6. Lung function tests
5. Written informed consent to participate in the study and will have agreed to abide by the study restrictions
6. Ability to comprehend the informed consent form (ICF), ability to communicate well with the PI or the appropriately qualified designee, understand and comply with the requirements of the study, and judged suitable for the study in the opinion of the PI or the appropriately qualified designee
7. Willing to refrain from consuming alcohol within 24 hours prior to admission
8. Prior to study start, subjects must be current daily users of e-cigarettes and current smokers of conventional factory-made cigarettes, and must have done so for at least 1 year. Product use status will be confirmed with a urinary cotinine level of ≥200 ng/ml and a product use history questionnaire at screening. Subjects must be smoking a maximum of 21 per week of 6-10 mg ISO tar cigarettes
9. E-Cigarette users e-liquid must contain at least 18 mg/ml nicotine
10. Willing to use the study products (cigarette product or e cigarette) and use only the products provided to them during clinical confinement, and to abstain from product use when instructed

11. Women of non-childbearing potential may be included if they are either surgically sterile (hysterectomy and/or oophorectomy) or postmenopausal for more than 1 year and must have a negative urine pregnancy test result during screening. Women who are surgically sterile must provide documentation of the procedure by an operative report.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
24

Key exclusion criteria
1. Male subjects who do not agree, or whose partners of childbearing potential do not agree, to use a barrier method of contraception (i.e., a condom with spermicide) in addition to a second highly effective method of contraception used by their female partners or to refrain from donating sperm from admission (day -1) until end of follow-up period
2. Female subjects of childbearing potential who do not agree to use a highly effective method of birth control in conjunction with male barrier method contraception (i.e. a condom with spermicide) from the time of signing the ICF until end of follow-up period
3. Female subjects who are pregnant or breastfeeding. This will be confirmed at screening and admission. Any female subject who becomes pregnant during this study will be withdrawn
4. Donated:
4.1 ≥400 ml of blood within 90 days prior to screening
4.2 Plasma in the 7 days prior to screening
4.3 Platelets in the 6 weeks prior to screening
5. Acute illness (e.g. upper respiratory tract infection, viral infection) requiring treatment within 4 weeks prior to screening
6. 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
7. Planning to quit smoking/vaping in the next 12 months, prior to enrolment. All subjects will be informed that they are free to quit smoking/vaping and withdraw from the study at any time
8. Significant history of alcoholism or drug/chemical abuse within 24 months prior to screening, as determined by the PI or the appropriately qualified designee
9. Positive urine drugs of abuse or alcohol screen (confirmed by repeat) at screening or admission
10. Serum hepatitis
11. Carriers of the hepatitis B surface antigen (HBsAg)
12. Carriers of the hepatitis C antibody
13. Positive result for the test for human immunodeficiency virus (HIV) antibodies

14. Used prescription or over-the-counter (OTC) bronchodilator medication (e.g. inhaled or oral β-adrenergic agonists) to treat a chronic condition within the 12 months prior to screening
15. Received any medications or substances (other than tobacco) which are known to be strong inducers or inhibitors of cytochrome P450 (CYP) enzymes within 14 days or 5 half-lives of the drug (whichever is longer) prior to screening
16. Perform strenuous physical activity (exceeding their normal activity levels) within 7 days prior to screening or admission
17. Employees and immediate relatives of the tobacco industry or the clinical site
18. Participation in a new chemical entity clinical study within the previous 3 months or a marketed drug clinical study within the 30 days before first dose of IMP
19. Any clinically relevant abnormal findings on the physical examination, medical history, ECG, lung function tests or clinical laboratory panel, unless deemed not clinically significant by the PI or the appropriately qualified designee
20. No use of a flavoured e-cigarette e-liquid
21. Diagnosed with a significant history of urticaria or asthma (childhood asthmas is acceptable)
22. Have, or who have a history of, any clinically significant neurological, gastrointestinal, renal (including urinary tract infection or nephrolithiasis), hepatic, cardiovascular, psychiatric, respiratory, metabolic, endocrine, haematological or other major disorder that, in the opinion of the PI or the appropriately qualified designee, would jeopardise the safety of the subject or impact on the validity of the study results
23. Acute illness (e.g. upper respiratory tract infection, viral infection, etc.) requiring treatment within 4 weeks prior to screening.
24. Any treatment with smoking cessation medications (e.g. bupropion, varenicline or any NRTs) within 30 days of the planned first product use occasion
25. Previously been diagnosed with any form of malignancy
26. Previously randomised into or withdrawn from this study
27. In the opinion of the PI or the appropriately qualified designee, should not participate in this study

Date of first enrolment
31/10/2018

Date of final enrolment
04/12/2018

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Merthyr Tydfil Industrial Park,
Cardiff Road
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Merthyr Tydfil

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Sponsor information

Organisation
British American Tobacco (Investments) Ltd

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. 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. Requests for data should be made to clinical_info@bat.com and data 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?
Results article	results	01/12/2020	24/11/2020	Yes	No
HRA research summary			28/06/2023	No	No
Protocol (other)			17/08/2022	No	No