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A study to assess nicotine uptake into the blood from and liking of two tobacco heating products compared to cigarettes and a nicotine replacement therapy

Submission date
31/07/2018

Recruitment status
No longer recruiting

Registration date
07/08/2018

Overall study status
Completed

Last Edited
01/09/2022

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Cigarette smoking contributes to numerous illnesses including lung cancer, chronic obstructive lung disease and heart disease. The health risks of cigarette smoking are due to chemical toxicants in cigarette smoke which can lead to changes in the body, causing disease. Nicotine is mainly responsible for the addictive properties of cigarette smoking. The sponsor of this study is British American Tobacco (Investments) Limited, a manufacturer of tobacco products. The sponsor is developing an alternative approach to conventional (normal) cigarettes by developing new products which may reduce some of the risks of tobacco-related diseases. This study is designed for research purposes to collect data on newly developed tobacco heating products (THPs) in adult smokers. The main aim of this study is to assess how nicotine is absorbed into the blood of subjects when they smoke their usual brand cigarette, or use a THP, or use a NRT (Nicorette Inhaler) for 5 min. Product liking, intent to use the study product again, urge to smoke a cigarette and urge to use the study product will also be assessed.

Who can participate?
Healthy adults aged 19 to 60 who smoke at least 10 cigarettes per day and have smoked for at least one year

What does the study involve?
Subjects first attend a screening visit to assess eligibility to participate in the study. Once deemed eligible, subjects attend a randomisation visit where they are assigned the order in which they will use the 4 study products, based on 4 pre-defined sequences (an equal number of subjects will be assigned to each sequence). At the end of this visit, subjects are given the study product assigned for their next visit to take home and use for familiarisation before their next visit (unless their next visit is to assess their own-brand cigarette, which in such case is not provided).
At their next visit, subjects will be admitted to the testing clinic the evening before their assessment and will be required to abstain from nicotine and tobacco use for a minimum of 12

hours prior to the assessment. At the assessment on the following morning, subjects use their assigned study product in a single use session for a maximum of 5 minutes. Before, during and up to 4 hours after this use session blood samples are taken for nicotine analysis and subjects are asked to complete a number of questionnaires. At the end of the session, subjects are given the study product assigned for their next visit to take home and use for familiarisation before their next visit (unless their next visit is to assess their own-brand cigarette, which in such case is not provided).
These visits are repeated until subjects have used all 4 of the study products.

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, only the standard risks of 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 THP use are the same as those of tobacco products, with the most common being dizziness, nausea, mild headache, dry mouth, dry throat, cough and diarrhoea. The most common side effects of using the Nicorette Inhaler are headache, cough, throat irritation, hiccups and nausea, along with hypersensitivity, burning sensations, change in taste, tingling or numbness, abdominal pain, diarrhoea, dry mouth, indigestion, flatulence, increased amount of saliva, inflammation of the mouth/lips, vomiting and fatigue.

Where is the study run from?
Centro Ricerche Cliniche di Verona (Italy)

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

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

Who is the main contact?
Nathan Gale
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Contact information

Type(s)
Public

Contact name
Mr Nathan Gale

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-000701-23

Protocol serial number
BAT3117013

Study information

Scientific Title
An assessment of nicotine kinetics and liking profiles of two tobacco heating products in comparison to combustible cigarettes and a nicotine replacement therapy

Study objectives
Cmax and AUC0-240min for THP are non-inferior compared to NRT
Tmax for THP is earlier than for NRT
Cmax and AUC0-240min for THP are not higher than for subject's usual brand cigarette
Liking of THP is non-inferior compared to NRT
Overall intent to use THP again is non-inferior compared to NRT
Reduction in urge to smoke is superior for THP compared to NRT
Urge to use THP is superior compared to urge to use NRT

Ethics approval required
Old ethics approval format

Ethics approval(s)
Comitato etico per la Sperimentazione Clinica (CESC) delle Province di Verona e Rovigo (Ethics Committee for Clinical Trials of the Provinces of Verona and Rovigo), 20/06/2018, 1778CESC

Primary study design
Interventional

Study design
Single-centre open-label randomised four-period crossover study

Study type(s)
Other

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

Interventions
The following investigational products will be used in the study:
1. Glo THP1.0(RT)
2. Glo THP1.1(RT)

3. Nicorette® Inhalator (15mg)
4. Standard own-brand cigarette
Products 1 and 2 consist of a tobacco heating device with a tobacco stick consumable. Product 3 consists of a mouthpiece and a cartridge consumable. Product 4 is the subject's usual brand cigarette.
During each of their 4 investigational clinic visits, following a minimum of 12 hours' abstinence from tobacco and nicotine use, participants will be asked to use one of the investigational products ad libitum, during a single-use session with maximum 5 minutes' duration (no more than one single consumable/cartridge/cigarette may be used in each session). It is intended that each participant will use all 4 products during the trial. The order of use will be assigned by a pre-defined computer-generated randomisation schedule according to a 4 sequence list, with an equal number of participants in each sequence. Blood samples (13 per session) will be taken for nicotine analysis and a number of questionnaires will be administered before, during and for up to 4 hours after each single-use session. The total duration of treatment will be approximately 4 weeks (from randomisation to the last treatment session) with follow-up 5-7 days after the last treatment.

Intervention Type
Other

Primary outcome(s)
1. Plasma nicotine pharmacokinetic parameters, assessed 240 minutes after the first puff:
1.1. Cmax
1.2. Tmax
1.3. AUC0
2. Product liking assessment, assessed using the Product Liking Questionnaire (PLQ), at 5 minutes prior to and at 3, 5, 9, 30, 60, 120 and 240 minutes after first puff during the PK session
3. Intent to use product again, assessed using the Overall Intent to Use Again (OIUA) questionnaire at 240 minutes after first puff during the PK session
4. Urge to smoke a cigarette, as measured using the Urge To Smoke (UTS) questionnaire at 5 minutes prior to and at 3, 5, 9, 15, 30, 45, 60, 90, 180 and 240 minutes after first puff during the PK session
5. Urge to use the investigational product assessed using the Urge For Product (UFP) questionnaire at 5 minutes prior to and at 15 and 120 minutes after first puff during the PK session

Key secondary outcome(s)
1. Puff count during 5 minute investigational product use session
2. Product evaluation using the Product Evaluation Scale (PES) at 5 minutes prior to and at 15 and 240 minutes after first puff during the PK session

Completion date
30/09/2018

Eligibility

Key inclusion criteria
1. Signed informed consent form (ICF)
2. Aged 19-60 years old
3. Body mass index (BMI) of 18.5 to 30.0 kg/m², inclusive, and a body weight of at least 52 kg for males and 45 kg for females

4. Current smokers:
4.1. At least 10 cigarettes per day
4.2. Smoke conventional factory-made cigarettes
4.3. eCO ≥ 10 ppm
4.4. Urinary cotinine ≥ 200 ng/ml at screening
5. Current smokers of non-menthol cigarettes
6. Smoked their chosen brand for a minimum of 6 months and must have smoked for at least one year prior to screening
7. Normal (or abnormal and not clinically significant) laboratory values (biochemistry, haematology, urinalysis) at screening
8. Normal (or abnormal and not clinically significant) 12-lead ECG at screening
9. Normal (or abnormal and not clinically significant) findings at the screening physical examination
10. Willing to refrain from performing vigorous exercise for 2 days outside of their normal routine before screening and for the total study duration
11. Willing to abstain from alcohol for 24 hours before screening and the in-clinic evaluation;
12. Willing to avoid eating foods containing poppy seeds for 72 hours prior to screening and the in-clinic evaluation;
13. No childbearing potential at the time of the study for female participants (female participants of childbearing potential (i.e. not in menopausal status from at least one year or permanently sterilised) must have a negative serum pregnancy test at screening (to be confirmed by urine pregnancy test at each of the four study visits))
14. Ability to understand the requirements of the investigation
15. Willing to comply with all investigation procedures.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
32

Key exclusion criteria
1. Acute illness (e.g. upper respiratory tract infection, viral infection, etc) requiring treatment within 4 weeks prior to screening
2. Used any nicotine or tobacco product other than commercially-manufactured cigarettes within 14 days prior to screening
3. Self-reported non-inhalers (smokers who draw smoke from the cigarette into the mouth and throat but who do not inhale)
4. Medical history of asthma or chronic obstructive pulmonary disease (COPD)

5. Used prescription or over-the-counter (OTC) bronchodilator medication (e.g. inhaled or oral β-adrenergic agonists or anticholinergic agents) to treat a chronic condition within the 12 months prior to screening
6. Received any medications or substances 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
7. Donated any of the following:
7.1. ≥ 450 ml of blood within 90 days prior to screening
7.2. Plasma in the 7 days prior to screening
7.3. Platelets in the 6 weeks prior to screening
8. Perform strenuous physical activity (exceeding the subject's normal activity levels) within 2 days prior to screening and the in-clinic evaluation
9. Medical history of any surgical or medical condition which, in the opinion of the investigator may interfere with participation in the investigation, or may jeopardize the safety of the subject or their compliance with the protocol, or may otherwise affect the outcome of the investigation
10. Any relevant surgical treatment during the previous 3 months or planned during the investigation
11. Medical history of serious psychiatric disorders
12. Serum hepatitis, carriers of the hepatitis B surface antigen (HBsAg), carriers of the hepatitis C antibody or a positive result for the test for human immunodeficiency virus (HIV) antibodies
13. Pulmonary function tests showing a forced expiratory volume after 1 second [FEV1]/forced vital capacity [FVC] < 0.7, FEV1 < 80% predicted value, and FVC < 80% predicted value
14. Abnormal QTcB interval value in the 12-lead ECG at screening (i.e. > 470 msec in both males or females)
15. Intake of illicit drugs within 6 months prior to screening, as determined by the investigator, or positive urine drug screen at screening
16. History of alcohol abuse within 6 months prior to screening, as determined by the investigator, or positive alcohol screen at screening (alcohol screen may be performed via a breath test)
17. Pregnant or lactating women at screening
18. Women physiologically capable of becoming pregnant during the overall investigation duration, unless willing to use a highly effective method of contraception. Highly effective birth control methods include:
18.1. Combined hormonal contraception (containing oestrogen and progestogen) associated with the inhibition of ovulation (oral, intravaginal, transdermal)
18.2. Progestogen-only hormonal contraception associated with the inhibition of ovulation (oral, injectable, implantable)
18.3. Intrauterine device (IUD)
18.4. Intrauterine hormone-releasing system (IUS)
18.5. Double-barrier method - condom and occlusive cap (diaphragm or cervical/vault caps) plus spermicidal agent (foam/gel/film/cream/suppository)
18.6. Bilateral tubal occlusion performed at least 90 days prior to screening
18.7. Vasectomised partner
18.8. Sexual abstinence (periodic abstinence e.g. calendar, ovulation, symptothermal, post-ovulation methods and withdrawal are not acceptable methods of contraception)
19. Previous participation in this investigation
20. Anticipated poor compliance by the participant
21. Employees, and immediate relatives, of the tobacco industry and members of the clinical staff at the investigational site
22. Administration of an investigational drug or implantation of an investigational device, or participation in another trial, within 6 months prior to screening

Date of first enrolment
05/07/2018

Date of final enrolment
31/07/2018

Locations

Countries of recruitment
Italy

Study participating centre
Centro Ricerche Cliniche di Verona
c/o Azienda Ospedaliera Universitaria Integrata di Verona
Policlinico G. B. Rossi
P.le L. A. Scuro 10
Verona
Italy
37134

Sponsor information

Organisation
British American Tobacco (Investments) Ltd

ROR
https://ror.org/01znsh139

Funder(s)

Funder type
Not defined

Funder Name
Britich American Tobacco (UK)

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		29/08/2022	01/09/2022	Yes	No