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Uptake of nicotine following a single use of "Heat Not Burn" (HNB) 1.2 and a cigarette

Submission date
22/09/2015

Recruitment status
No longer recruiting

Registration date
06/10/2015

Overall study status
Completed

Last Edited
30/04/2018

Condition category
Respiratory

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Cigarette smoking is one of the biggest causes of illness and death in the UK. Nicotine is a chemical which is found in all tobacco products. Nicotine is extremely addictive, as it works quickly on the brain to activate neural pathways (connections in the brain) causing feelings of pleasure. Research highlighting the risks of smoking has already helped many people to quit, and there are many products on the market designed to help. Most of these products are designed to provide nicotine, without the other harmful substances contained in standard cigarettes (nicotine delivery system). A recently developed product is the “heat-not-burn” (HNB) cigarette. These HNB products heat tobacco to produce a vapor containing nicotine which is then inhaled. As tobacco is not actually lit on fire, smoke produced has a significantly reduced level of harmful toxins as compared to a conventional cigarette. The aim of this study is to find out whether a HNB 1.2 product (a HNB cigarette containing approximately 1.2 mg of nicotine) is an effective nicotine delivery system.

Who can participate?
Adults aged between 21 and 50 years in good general health, who have smoked at least 10 cigarettes a day for at least one year.

What does the study involve?
All participants “check-in” to the study centre for a total period of four days. On the first day, they are allowed to continue their usual smoking habits until 11pm. They are then asked not to smoke so that all of the nicotine leaves their system for the second day. On the third and fourth days, participants are given a HNB 1.2 product and a normal cigarette to smoke in a random order. Before and after the participants have used each product, a number of blood samples are taken so that the amount of nicotine in their body can be measured. The amount of each product that they have smoked is then recorded.

What are the possible benefits and risks of participating?
A potential benefit of participating is that participants may find a potential alternative to conventional cigarettes and be able to cut down the amount they smoke. There are not expected to be any major risks of participating, however health risks of the HNB device are expected to be similar to those of other tobacco products.

Where is the study run from?
Celerion (UK)

When is the study starting and how long is it expected to run for?
January 2015 to October 2015

Who is funding the study?
Japan Tobacco International (Geneva)

Who is the main contact?
Mrs Kirsten Gill

Contact information

Type(s)
Public

Contact name
Mrs Kirsten Gill

Contact details
Celerion
22-24 Lisburn Road
Belfast
United Kingdom
BT9 6AD

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
JTGP-001

Study information

Scientific Title
An assessment of the biological uptake of nicotine among healthy adult smokers following a single controlled use of "Heat Not Burn" (HNB) 1.2 and a combustible cigarette

Study objectives
To characterise the nicotine uptake profiles (Cmax, tmax and AUClast) of the HNB 1.2 product and a conventional tobacco cigarette in healthy volunteers who smoke.

Ethics approval required

Old ethics approval format

Ethics approval(s)
South East Scotland REC 02, 24/8/2015, ref: 15/SS/00133

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

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet

Health condition(s) or problem(s) studied
Nicotine uptake

Interventions
Potential subjects will undergo screening procedures to ensure they satisfy the inclusion and exclusion criteria of the study. During Screening, potential subjects will practice with the HNB 1.2 product under the supervision of the clinic staff to ensure that they would be willing and able to use it as required during study conduct.
Subjects will check-in to the clinic and will be allowed to smoke their usual brand cigarette products ad libitum until 23:00. Following check-in procedures, a sample will be collected for trans-3'-hydroxycotinine cotinine ratio determination. Participants will then abstain from nicotine and tobacco product use for 24 hours (wash-out period). Days 1 and 2 will be product administration days.

Each product administration day will include a controlled administration of either the HNB 1.2 product or the reference cigarette according to the randomisation schedule. The administration of the HNB 1.2 product will consist of 10 puffs for 3 minutes, at approximately 20-second intervals, or smoking one reference cigarette, 10 puffs for 3 minutes, at approximately 20-second intervals. The number of puffs from the HNB 1.2 and the reference cigarette will be documented by the clinical staff. The MLE from the HNB 1.2 will be assessed from the change in product weight from before to after use. Used cigarette butts will be collected and saved to assess MLE nicotine from the filter tips.

Subject health status will be evaluated on Day 2 prior to discharge. Serial blood samples will be collected at approximately 10 minutes prior to and at 2, 3, 4, 5, 6, 7, 8, 10, 15, 20, 25, 30, 45, 60, 90, and 120 minutes following the start of the controlled product administration to determine plasma nicotine concentrations. Nicotine PK parameters will be determined using a non-compartmental approach. Parameters will include Cmax, tmax, AUClast, AUC0-∞, t1/2, F(AUC0 ∞), tlast, Clast, λz, number of points, λz_lower, λz_upper, R2adj, and AUCext%. Baseline adjustments

may be performed to correct for pre-administration nicotine concentration if deemed appropriate. Nicotine concentrations and PK parameters will be listed by subject and summarized by study product using descriptive statistics.

Intervention Type
Device

Primary outcome measure
Uptake of nicotine from the HNB 2.1 product as measured using plasma nicotine concentrations obtained from blood samples taken at 2, 3 ,4, 5, 6, 7, 8, 10, 15, 20, 25, 30, 45, 60 and 90 minutes following use of the HNB 1.2 product.

Secondary outcome measures
1. Nicotine pharmacokinetic parameters (e.g. maximum nicotine concentration (Cmax) and time to Cmax (tmax)) measured using plasma nicotine concentrations obtained from blood samples taken at 2, 3 ,4, 5, 6, 7, 8, 10, 15, 20, 25, 30, 45, 60 and 90 minutes following use of the HNB 1.2 product
2. Volunteer mouth level exposure (MLE) to nicotine during use of the HNB 2.1 product, as measured by the difference in weight of HNB 2.1 product + its associated pod insert before and after product use
3. Volunteer mouth level exposure (MLE) to nicotine during use of the CC1 product, as measured by assessing the amount of nicotine present in the product filter after product use
4. Volunteer inhalation to non-inhalation ratios during use of the HNB 2.1 product as measured by vidual analogue scare (VAS) questionnaire following use of the HNB 1.2 product

Overall study start date
06/01/2015

Completion date
10/10/2015

Eligibility

Key inclusion criteria
1. Aged between 21 to 50 years of age
2. Good general health
3. Smoker for at least 12 months prior to check-in and currently smokes an average of 10 or more manufactured cigarettes per day (no restriction on brand-style, king size [~83 – 85 mm] and 100s [~98 – 100 mm] only)
4. Positive urine cotinine at screening (> 200 ng/mL) at screening
5. Female subjects must be non-pregnant and non-lactating
5. Pre-menopausal female subjects must be surgically sterile, use an investigator-approved method of birth control, or agree to be sexually abstinent from 14 days prior to check-in through the end of the study

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
Up to 24 participants

Key exclusion criteria
1. History or presence of clinically significant gastrointestinal, renal, hepatic, neurologic, hematologic, endocrine, oncologic, urologic, pulmonary (especially bronchospastic diseases), immunologic, psychiatric, or cardiovascular disease, or any other condition that, in the opinion of the Investigator, would jeopardize the safety of the subject or impact the validity of the study results
2. Clinically significant abnormal findings on the physical examination, medical history, ECG, or clinical laboratory results at Screening or Check-in, in the opinion of the Investigator
3. Positive test for HIV, HBsAg, or HCV
4. An acute illness (e.g., upper respiratory infection, viral infection) requiring treatment within 2 weeks prior to Check-in
5. Fever (>38C) at Screening or at Check-in
6. Systolic blood pressure <90 mmHg or >150 mmHg, diastolic blood pressure <40 mmHg or >95 mmHg, or pulse rate <40 bpm or >99 bpm at screening
7. BMI <18 kg/m2 or >35 kg/m2 at screening
8. Use of prescription anti-diabetic medication and/or insulin therapy within 12 months of day 1 product administration.
9. Use of medications known to interact with CYP2A6 (including, but not limited to, amiodarone, desipramine, isoniazid, ketoconazole, miconazole, phenobarbital, rifampin, tranylcypromine, methoxsalen) within 3 months prior to day 1 product administration
10. Use of inhalers to treat any medical condition within 3 months prior to day 1 product administration and throughout the study
11. Positive urine screen for alcohol or drugs of abuse at screening or at check-in
12. History or presence of alcoholism or drug abuse within the past 2 years prior to screening
13. Drink alcohol in excess of 21 glasses/units per week for males or 14 glasses/units per week for females, with one unit = 150 ml of wine or 360 mL of beer or 45 mL of 45% alcohol
14. Males who have donated blood within 12 weeks or females who have donated blood within 16 weeks prior to day 1 product administration.
15. Donation of bone marrow within the last 6 months prior to day 1 product administration
16. Participation in a previous clinical study for an investigational drug, biologic, medical device, or tobacco product within 90 days prior to day 1 product administration
17. Planning to quit smoking during the study period or postponing a quit attempt in order to participate in the study
18. Use of any prescription smoking cessation treatments, including, but not limited to, varenicline (Champix®) or buproprion (Zyban®) within 3 months prior to day 1 product administration and throughout the study
19. Known hypersensitivity to glycerol or propylene glycol
20. Subject or a first-degree relative is a current or former employee of the tobacco industry or a named party or class representative in litigation with the tobacco industry

Date of first enrolment
01/09/2015

Date of final enrolment
03/10/2015

Locations

Countries of recruitment
Northern Ireland

United Kingdom

Study participating centre
Celerion
22-24 Lisburn Road
Belfast
United Kingdom
BT9 6AD

Sponsor information

Organisation
Japan Tobacco International

Sponsor details
JT International S.A.
1 Rue de la Gabelle
Geneva
Switzerland
1211 Geneva 26

Sponsor type
Industry

ROR
https://ror.org/04f5ks076

Funder(s)

Funder type
Industry

Funder Name
Japan Tobacco International

Results and Publications

Publication and dissemination plan

Publication in a peer reviewed journal on completion of the study. Additionally study results will be dissemmination at tobacco related conferences and workshops such as CORESTA (Cooperation Centre for Scientific Research Relative to Tobacco) and TSRC (Tobacco Science Research Conference).

30/04/2018: Results presented at CORESTA 2016 (abstract: https://www.coresta.org/abstracts/pharmacokinetics-nicotine-following-single-controlled-use-new-type-tobacco-heated-tobacco , slides: https://www.jt-science.com/sites/default/files/2017-08/2016-O2.pdf)

Intention to publish date

01/11/2016

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No