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A study to assess the processing of nicotine by the body and subjective effects of oral nicotine products in healthy adult users of cigarettes and smokeless pouch products

Submission date
06/04/2022

Recruitment status
No longer recruiting

Registration date
19/04/2022

Overall study status
Completed

Last Edited
04/09/2023

Condition category
Other

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

Plain English summary of protocol

Background and study aims
This is a clinical study to assess the nicotine uptake of nicotine pouches versus nicotine replacement therapies. The aims are to encourage smokers to switch to Velo nicotine pouches that are potentially reduced risk products, and to prove that the Velo pouches do not have an abuse liability higher than a conventional cigarette and trend more towards nicotine gum.

Who can participate?
Healthy adults who are daily users of snus or nicotine pouch.

What does the study involve?
Participants will be confined to the clinic for 10 days for product use and biological sample collection. They will be randomly allocated to use CTS usual brand cigarettes, Velo pouch 11 mg, Velo pouch 15 mg, Velo pouch 20 mg or Nicorette gum. They will use the cigarette for up to 10 minutes, the Velo pouch for 20 minutes and the gum for up to 30 minutes. They will have samples taken during and after product use. They will also be asked to complete a range of questionnaires and undertake a physiological assessment (pulse rate).

What are the possible benefits and risks of participating?
Participants may benefit from switching to a product that has less harmful constituents. The risk of participating is deemed low.

Where is the study run from?
Clinical Trial Consultants (CTC) AB (Sweden)

When is the study starting and how long is it expected to run for?
February 2022 to September 2022

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

Who is the main contact?
Elaine Brown, elaine_brown@bat.com

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
BAT51121036

Study information

Scientific Title
A single dose, randomised, crossover study to assess the nicotine pharmacokinetics and product subjective effects of oral nicotine products in healthy adult users of cigarettes and smokeless pouch products

Acronym
Velo

Study objectives
To evaluate subjective effects on product liking (PL) during and after product use.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Approved 21/03/2022, Etikprovningsmyndigheten (Box 2110, 750 02, Uppsala, Sweden; +46 (0) 10-475 08 00; registrator@etikprovning.se), ref: 2022-00830-01-250273

Study design
Randomised five-way cross-over pharmacokinetic study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Nicotine uptake and subjective measures

Interventions
Screening (Visit 1) will take place from Day -28 to Day 1 and will include an eligibility check, a review of the subject's health status and a product familiarisation session. At the end of the screening visit, the subjects will complete a product familiarisation session in which they will be given one of the pouch products (20 mg nicotine), to ensure acceptability of the products. The subjects will use the product in the same way they would normally use a smokeless snus product or nicotine pouch (i.e., under the upper lip). There will be a minimum of 20 minutes duration of use of the product (from the time the subject places the product in his/her mouth until the time the subject removes the product from his/her mouth). Subjects who successfully complete this familiarisation session, i.e., they tolerate the use of the product without any adverse effects different from what is expected from typical smokeless pouch use, will be allowed to continue in the study.

At Visit 2, subjects will be admitted to the clinic on Day -1 and will remain at the clinic until the afternoon of Day 5 for once daily single IP use, assessments of subjective effects, and PK and safety assessments.

In the morning of Day 1, the subjects will be randomly assigned to one of five sequences and then undertake each study arm once, in accordance with the assigned sequence. There will be 9 subjects per randomisation sequence. The products tested are CTS usual brand cigarettes, Velo pouch 11 mg, Velo pouch 15 mg, Velo pouch 20 mg and NRT Nicorette gum.

On Days -1 to 5, subjects will be required to refrain from using nicotine products for a period of at least 12 hours before each IP use. The subjects are allowed to use their own choice of nicotine

products (except smoking products) between the last PK sample (4 hours post IP use) until 12 hours prior to the next IP use. Subjects must bring a sufficient supply of their usual nicotine products for the own product use periods of Visit 2.

IP will be administered by study personnel according to the randomisation list. Subjects will use the cigarette for up to 10 minutes, the Velo pouch for 20 minutes and up to 30 minutes for the gum. Subjects will have PK samples taken during IP use and post IP use. They will also be asked to complete a range of questionnaires and undertake a physiological assessment (pulse rate). The subjects will be instructed not to eat, drink, chew chewing gum or brush their teeth from 30 minutes before the use of any of the IP, during use of the IP and up to 30 minutes after IP use. After 20 minutes use, the used nicotine pouches will be collected and frozen (-20°C) pending analysis of residual nicotine content.

End-of-use assessments will be performed on Day 5 (Visit 2) after use of the IP or upon early withdrawal.

A final end-of-study telephone call (Follow-up) will take place on Day 12 (±1 day) to assess AEs and concomitant medications.

Intervention Type
Supplement

Primary outcome measure
Product liking (PL) measured using a visual analogue scale (VAS) score from 5 minutes to 240 minutes after the start of investigation product (IP) use

Secondary outcome measures
1. Area under the positive Product Effect(s) VAS score versus time curve from 5 minutes to 240 minutes after the start of IP use (AUECPEpos 5-240)
2. Area under the negative PE VAS score versus time curve from 5 minutes to 240 minutes after the start of IP use (AUECPEneg 5-240)
3. Maximum positive PE VAS score after the start of IP use (Emax PEpos)
4. Maximum negative PE VAS score after the start of IP use (Emax PEneg)
5. Area under the UTS VAS score-versus-time curve from time zero to 15 minutes after the start of IP use (AUECUTS 0-15)
6. Area under the UTS VAS score-versus-time curve from time zero to 240 minutes after the start of IP use (AUECUTS 0-240)
7. Minimum UTS VAS score after the start of IP use (Emin UTS)
8. Overall PL, measured at 240 minutes after the start of IP use (Eoverall PL)
9. Overall IUA, measured at 240 minutes after the start of IP use (Eoverall IUA)
10. Plasma nicotine maximum plasma concentration (Cmax), time to Cmax (Tmax) and area under the plasma concentration time curve 0 to 4 hours (AUC0-240).
11. Maximum increase in physiological measures (Emax) and time to first instance of Emax [TEmax].
12. Comparison Cmax, Tmax and AUC0-240 between products.
13. In vivo extracted amount (mg/unit) and extracted fraction (%) of nicotine, for each product.
14. Frequency, intensity and seriousness of adverse events (AEs)
15. Clinically significant changes in electrocardiograms (ECG), clinical laboratory parameters and physical examinations.

Overall study start date

01/02/2022

Completion date
30/09/2022

Eligibility

Key inclusion criteria
1. Willing and able to give written informed consent for participation in the study.
2. Healthy male or female subject aged 19-55 years inclusive.
3. Body Mass Index (BMI) ≥18.5 and ≤30.0 kg/m² and a minimum weight of ≥45 kg (females) or ≥52 kg (males).
4. Clinically normal medical history, physical findings, vital signs, electrocardiogram (ECG) and laboratory values at the time of screening, as judged by the Investigator. No abnormal results judged by the Investigator as clinically significant are allowed.
5. Daily snus and/or nicotine pouch user who must have used pouched products for at least 12 months and who use these pouch products under their upper lip. Subjects who use pouched snus and/or nicotine pouches should typically use at least 5 pouches per day, with pouch weights of 0.6 g or above. Subjects should be willing and able to use products with a nicotine content ≥15 mg/g.
6. Smoker of commercially available, factory made cigarettes, smoking 5 cigarettes or more on average per week and who has smoked for at least 1 year prior to the first IP use.
7. Stated willingness to abstain from nicotine and tobacco products (except for the IPs provided) from 12 hours prior to each study product administration until the end of each PK sampling.
8. Successful completion of the product familiarisation session for study product use prior to the first study product administration (subject is able to follow the instructions, can tolerate the product and does not experience any adverse effects different from what is expected from typical smokeless pouch use during the training session).
9. Positive urine cotinine test (≥200 ng/mL) at screening and at Day -1.
10. Women of child bearing potential (WOCBP) must be willing to use a sufficient contraceptive method for the duration of the study, this includes mechanical barrier (e.g., a male condom or a female diaphragm), combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal), progestogen-only hormonal anticonception associated with inhibition of ovulation (oral, injectable, implantable), intrauterine device (IUD) or intrauterine system (IUS). Sexual abstinence is allowed when this is the preferred and usual lifestyle of the subject.
Women of non-childbearing potential are defined as pre-menopausal females who are sterilised (tubal ligation or permanent bilateral occlusion of fallopian tubes); or females who have undergone hysterectomy or bilateral oophorectomy; or post-menopausal defined as 12 months of amenorrhea (in questionable cases a blood sample with detection of follicle stimulating hormone [FSH] 25-140 IE/L is confirmatory).

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
68

Total final enrolment
40

Key exclusion criteria
1. History of any clinically significant disease or disorder which, in the opinion of the Investigator, may either put the subject at risk because of participation in the study, or influence the results or the subject's ability to participate in the study.
2. Any clinically significant illness, medical/surgical procedure or trauma within 2 weeks of the first administration of IP.
3. Malignancy within the past 5 years with the exception of in situ removal of basal cell carcinoma.
4. Any planned major surgery within the duration of the study.
5. Any positive result on screening for serum hepatitis B surface antigen, hepatitis C antibody and Human Immunodeficiency Virus (HIV).
6. After 10 minutes supine rest at the time of screening, any vital signs values outside the following ranges:
• Systolic blood pressure <90 or >140 mmHg, or
• Diastolic blood pressure <50 or >90 mmHg, or
• Pulse <40 or >90 bpm
7. Prolonged QTcF interval (>450 ms), cardiac arrhythmias or any clinically significant abnormalities in the resting ECG at the time of screening, as judged by the Investigator.
8. Presence of braces, partials, dentures or any dental work that could, in the opinion of an Investigator, affect the conduct of the study (including missing molars).
9. Presence or history of significant form of oral and/or pharyngeal inflammation, oral lesions and/or gum disease or temporomandibular joint dysfunction.
10. Existing signs of skin irritation or skin damage at the sites where the Equivital LifeMonitor device is to be located, as judged by the Investigator.
11. Subjects with implanted defibrillators or pacemakers.
12. Female subject who is pregnant or lactating.
13. History of severe allergy/hypersensitivity or ongoing allergy/hypersensitivity, as judged by the Investigator, or history of hypersensitivity to drugs with a similar chemical structure or class to nicotine.
14. Subjects who are self-reported non-inhalers. (Smokers who draw smoke from the cigarette into the mouth and throat but who do not inhale.)
15. Plan to quit using tobacco- or nicotine-containing products within 3 months of the end of the current study or previously attempted to quit using tobacco- or nicotine-containing products in the 28 days prior to the first IP use.
16. Planned treatment or treatment with an investigational medicinal product or another IP within 3 months prior to Day -1. Subjects consented and screened but not dosed in previous phase I studies are not excluded.
17. Positive screening result for drugs of abuse or alcohol at the time of screening or on admission to the unit prior to first use of IP. Positive results that are expected given the subject' s medical history and prescribed medications can be disregarded as judged by the Investigator.
18. History of alcohol abuse or excessive intake of alcohol, as judged by the Investigator.
19. Presence or history of drug abuse, as judged by the Investigator

20. History of, or current use of, anabolic steroids.
21. Plasma or platelet donation within one month of the first IP use or blood donation (or corresponding blood loss, ≥450 mL) during the three months prior to the first IP use.
22. Employees or immediate relatives of the tobacco industry or the clinical site.
23. Investigator considers the subject unlikely to comply with study procedures, restrictions and requirements.

Date of first enrolment
01/04/2022

Date of final enrolment
30/04/2022

Locations

Countries of recruitment
Sweden

United Kingdom

Study participating centre
Clinical Trial Consultants (CTC) AB
Dag Hammarskjölds väg 10B
Uppsala
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SE-752 37

Sponsor information

Organisation
British American Tobacco (United Kingdom)

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Sponsor type
Industry

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ROR
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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

Publication and dissemination plan
A manuscript will be published on the study results on completion of the clinic phase.

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
Results available on approved request from elaine_brown@bat.com

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	10/02/2022	14/04/2022	No	Yes