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A study to assess markers of exposure and potential harm in users of Lyft nicotine pouch products

Submission date 03/03/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 17/03/2021	**Overall study status** Completed	
Last Edited 12/12/2022	**Condition category** Other	

Plain English summary of protocol

Background and study aims
The aim of this study is to assess markers of exposure and potential harm in people who use only nicotine pouches compared to smokers, former smokers, and people who have never smoked. This is part of British American Tobacco's harm reduction process in demonstrating that switching from cigarettes to nicotine products is a less risky option for consumers.

Who can participate?
Nicotine pouch users, smokers, former smokers and people who have never smoked, aged 19 – 55

What does the study involve?
The study involves an overnight stay in the clinics based in Sweden and Denmark. Participants use their own products in their usual way and provide urine and blood samples.

What are the possible benefits and risks of participating?
The study may demonstrate that nicotine pouches have a health benefit compared to cigarettes. No risks are foreseen.

Where is the study run from?
1. CTC Clinical Trial Consultants (Sweden)
2. Sanos (Denmark)

When is the study starting and how long is it expected to run for?
March 2021 to January 2022

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

Who is the main contact?
David Azzopardi
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

Protocol serial number
BAT2120027

Study information

Scientific Title
A cross-sectional study to assess biomarkers of exposure and biomarkers of potential harm in solus users of Lyft nicotine pouch products

Study objectives
To quantitatively assess differences in primary study endpoints between subjects who are solus users of Lyft nicotine pouch products and conventional cigarette smokers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Primary study design
Observational

Study design
Multi-centre cross-sectional study

Study type(s)
Other

Health condition(s) or problem(s) studied
Pharmcokinetic uptake of investigational products

Interventions
Four separate populations of subjects will be recruited as follows:
1. Solus Lyft users must be daily users of Lyft for at least 6 months prior to Screening and have not used any other form of tobacco or nicotine-containing product within this period.
2. Solus cigarette smokers must have smoked >10 cigarettes/day daily for at least the 12 consecutive months prior to Screening.
3. Former cigarette smokers must have quit smoking at least 6-months prior to Screening and have not used any form of tobacco or nicotine-containing product within this period.
4. Never smokers must have smoked <100 cigarettes in their lifetime and have not used any form of tobacco or nicotine-containing product within the 6 months prior to Screening.

Screening
1. Subjects will undergo Screening up to 7 days prior to admission on to the study
2. All subjects will be in clinic 2 days, 1 overnight stay
3. A telephone call follow-up will be performed within 7 days after subjects are discharged from the study

7 days prior to clinic entry subjects will be screened, if they pass screening they will be invited to the site. Once enrolled subjects will start their 24-hour urine collection, used pouch collection, and also provide safety blood samples. They will stay overnight using their own products in their usual way. On Day 2 they will use their own products in their usual way, a single blood sample is collected (less than 100ml in total), and urine collection is completed after 24 hour period.

Intervention Type
Other

Primary outcome(s)
1. Biomarker of Exposure (BoE):
1.1. Total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (Total NNAL) measured using liquid chromatography with tandem mass spectrometry (LC-MS/MS) of 24-hour urine void on days 1-2
2. Biomarkers of Potential Harm (BoPH):
2.1. Nitric oxide in exhaled breath (FeNO) measured using NIOX VEROTM device on days 1-2
In 24-hour urine void:
2.2. 8-epi-prostaglandin F2α Type III (8-Epi-PGF2α Type III) measured using LC-MS/MS of 24 hour urine void on days 1-2
In blood:
2.3. Carboxyhaemoglobin (COHb) measured using gas chromatography–mass spectrometry (GC-MS) of 24-hour urine void on days 1-2
2.4. Total white blood cell count (WBC) measured using automated haematology sampling procedure of 24-hour urine void on days 1-2
2.5. Soluble intercellular adhesion molecule-1 (s-ICAM1) measured using enzyme-linked immunosorbent assay (ELISA) of 24-hour urine void on days 1-2
2.6. High-density lipoprotein (HDL) measured using homogenous enzymatic colorimetry of 24-hour urine void on days 1-2

Key secondary outcome(s)
1. BoPH:
1.2. 11-dehydrothromboxane B2 (11-dTX B2) measured using LC-MS/MS of 24-hour urine void on days 1-2
2. BoE:
Measured from 24-hour urine void on days 1-2:
2.1. Total nicotine equivalents (nicotine, cotinine, 3-hydroxycotinine and their glucuronide conjugates) (TNeq) measured using LC-MS/MS
2.2. Monohydroxybutenylmercapturic acid (MHBMA) measured using LC-MS/MS
2.3. 3-hydroxy-1-methylpropylmercapuric acid (HMPMA) measured using LC-MS/MS
2.4. 3-hydroxypropylmercapturic acid (3-HPMA) measured using LC-MS/MS
2.5. Total N-nitrosonornicotine (Total NNN) measured using LC-MS/MS
2.6. 3-hydroxybenzo[a]pyrene (3-OH-B[a]P) measured using LC-MS/MS

Physiological measures:
1. Forced Expiratory Volume in 1 second as % of predicted (FEV1) measured using spirometer on days 1-2
2. Carotid intima-media thickness (CIMT) measured using ultrasound on days1-2
3. Health-related quality of life measured using RAND-36 on days 1-2
4. Oral health measured using Oral Health Assessment Tool (OHAT) on days 1-2

Completion date
23/01/2022

Eligibility

Key inclusion criteria
Subjects will be required to satisfy all of the following criteria at Screening, unless otherwise stated:
All subjects:
1. Subjects will be:
1.1. Healthy adult males or females
1.2. 19 to 55 years of age, inclusive, demonstrated by appropriate proof of identification
2. Subjects will have a:
2.1. Body mass index (BMI) of 18.5 to 30.0 kg/m^2, inclusive
2.2. Body weight exceeding 52 kg (males) or 45 kg (females)
3. Subjects will be in good health, as judged by the Investigator or the appropriately qualified designee based on:
3.1. Medical history (confirmed by volunteer)
3.2. Physical examination
3.3. Vital signs assessment: Supine systolic and diastolic blood pressure, supine pulse rate, respiratory rate and tympanic body temperature
3.4. 12-lead ECG
3.5. Clinical laboratory evaluations
3.6. Lung function tests/spirometry
4. Subjects will have given their written informed consent to participate in the study and will have agreed to abide by the study restrictions
5. Subjects must demonstrate the ability to comprehend the ICF, be able to communicate well with the Investigator or the appropriately qualified designee, understand and comply with the requirements of the study, and be judged suitable for the study in the opinion of the Investigator or the appropriately qualified designee.

6. Subjects will refrain from consuming alcohol within 24 hours prior to Screening and Admission.
7. Subjects will refrain from consuming cruciferous vegetables, and grilled, fried or barbequed food, and avoid being in the presence of the cooking of cruciferous vegetables, and grilled, fried or barbequed food for 48 hours prior to Screening and Admission.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
Subjects will be excluded from participation in the study if they satisfy any of the following criteria at Screening, unless otherwise stated:

All subjects:
1. Female subjects who are pregnant or breastfeeding. This will be confirmed at Screening.
2. Subjects who have donated:
2.1. ≥400 mL of blood within 90 days prior to screening
2.2. Plasma in the 7 days prior to screening
2.3. Platelets in the 6 weeks prior to screening
3. Subjects who have had an acute illness (e.g. upper respiratory tract infection, viral infection, etc.) requiring treatment or medical investigation within 4 weeks prior to screening as judged by the Investigator.
4. Subjects who have a significant history of alcoholism or drug/chemical abuse (apart from known smoking/vaping history) within 24 months prior to Screening, as determined by the Investigator or the appropriately qualified designee.
5. Subjects who have a positive urine drugs of abuse or breath alcohol screen (confirmed by repeat) at Screening or Admission.
6. Subjects who:
6.1. Have serum hepatitis/are carriers of the hepatitis B surface antigen (HBsAg)
6.2. Are carriers of the hepatitis C antibody
6.3. Have a positive result for the test for human immunodeficiency virus (HIV) antibodies
6.4. Have a positive result in the COVID-19 test at Screening or Admission indicating current, active infection , or not providing proof of a negative COVID-19 test taken within 248 hours of Screening (Denmark only).
7. Subjects who have 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.
8. Subjects who have received any medications or substances (other than nicotine) which:
8.1. Interfere with the cyclooxygenase pathway (e.g. anti-inflammatory drugs including aspirin and ibuprofen) within 14 days prior to Screening

8.2. 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
9. Subjects who would need to take prescription medication not approved by the Investigator during the period beginning with screening and ending with discharge (for female subjects, hormonal contraceptives are acceptable, and for all subjects, painkillers [paracetamol] are permitted).
10. Subjects who are unwilling or unable to comply with the study requirements.
11. Employees and immediate relatives of the tobacco industry or the clinical site.
12. Subjects who have 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 Investigator or the appropriately qualified designee.
13. Subjects who have been diagnosed with a significant history of urticaria or asthma (childhood asthma is acceptable).
14. Subjects who 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 Investigator or the appropriately qualified designee, would jeopardise the safety of the subject or impact on the validity of the study results.
15. Subjects who have previously been diagnosed with any form of malignancy or carcinoma in situ.
16. Subjects who are currently participating in another clinical trial (including follow-up).
17. Subjects who, in the opinion of the Investigator or the appropriately qualified designee, should not participate in this study.
11.2.1. Arm specific exclusion criteria

Arm A:
18. Subjects who have used any form of tobacco or nicotine-containing product, other than the Lyft pouch products, within the six months prior to Screening.

Arm B:
19. Subjects who are self-reported non-inhalers (smokers who draw smoke from the cigarette into the mouth and throat but who do not inhale).

Arms C and D:
20. Subjects who have used any form of tobacco or nicotine-containing product within 6 months prior to Screening

Date of first enrolment
01/04/2021

Date of final enrolment
31/07/2021

Locations

Countries of recruitment
Denmark

Sweden

Study participating centre
CTC Clinical Trial Consultants
Dag Hammarskjöldsväg 10B
752 37 Uppsala
Sweden
752 37

Study participating centre
Sanos
Herlev Hovedgade 82
Herlev
Denmark
2730

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

The datasets generated during and/or analysed during the current study are/will be available upon request from David Azzopardi (David_azzopardi@bat.com). These data won't be available until January/February 2022.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		09/12/2022	12/12/2022	Yes	No
Protocol article		06/10/2022	25/11/2022	Yes	No