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The effects of reduced toxicant prototype (RTP) cigarettes on biomarkers of exposure and of biological effect versus commercial cigarettes when smoked by healthy adult smokers.

Submission date
06/02/2012

Recruitment status
No longer recruiting

Registration date
19/03/2012

Overall study status
Completed

Last Edited
20/05/2016

Condition category
Signs and Symptoms

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

Plain English summary of protocol

Background and study aims
The Sponsor, British American Tobacco (Investments) Limited, has developed an RTP cigarette, the use of which may reduce the exposure of smokers to certain toxicants compared with the use of conventional cigarettes. This prototype cigarette is made using novel technologies and when smoked on a machine, yields lower levels of certain toxicants than conventional cigarettes of equal ISO tar yield (the amount of tar in the smoke produced by the cigarette when machine-smoked under standardised laboratory conditions). The aim of this study is to establish whether the use of the RTP cigarettes results in lower exposure of the smoker to certain smoke toxicants (determined by biomarkers of exposure) and changes in certain of the bodys responses to smoke toxicants (determined by biomarkers of biological effect) compared with the use of conventional cigarettes.

This study investigates the RTP cigarettes and compares them with conventional cigarettes. In this study, the RTP and conventional cigarettes are of an ISO tar yield of 7 mg.

Who can participate?
The study will enrol smokers between 23 and 55 years of age and either sex. A group of healthy non-smokers (never-smokers and ex-smokers) between 28 and 55 years of age will also participate.

What does the study involve?
During the course of the study smokers will start smoking the supplied conventional cigarette for two weeks, then 50% of them will switch to smoking the RTP cigarette, and the other 50% will continue to smoke the conventional cigarette. The smokers may continue using the supplied cigarettes as per their normal smoking behaviour for a period of 6 months. Participants are free to withdraw from the study at any time, without giving any reasons. During this period smokers, ex-smokers and never smokers will visit the clinic several times over the 6 months period to give blood, saliva and urine samples and undergo some clinical investigations in order to measure

toxicant levels and explore their potential health effects. Smokers will collect their cigarette filters on occasions and fill in questionnaires for smoking behaviour assessments.

What are the possible benefits and risks of participating?
Smoking cigarettes is addictive and represents a serious health risk. All study participants will be required to participate in a smoking cessation workshop either during or at the end of the study.

Where is the study run from?
The study is conducted in Germany.

When is the study starting and how long is it expected to run for?
Participant recruitment will begin in February 2012. Eligible participants will start the study in March 2012.

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

Who is the main contact?
Momentum Pharma Services (Germany)
BD@MPS-Hamburg.com

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Study Protocol BAT1110001

Study information

Scientific Title
A single-blinded, single-centre, controlled study in healthy adult smokers to identify the effects of reduced toxicant prototype (RTP) cigarettes on biomarkers of exposure and of biological effect versus commercial cigarettes.

Study objectives
If smokers switch from conventional cigarettes to novel cigarettes of equivalent ISO tar yield, but with lower levels of smoke toxicants (as measured by smoking machine), then it is expected that a measurable reduction in levels of Biomarkers of Exposure (BoE) in urine, saliva and smoke filters will be observed over a prolonged duration of 6 months, with a corresponding change in levels of Biomarkers of Biological Effect (BoBE).

This study involves healthy adult smokers, never smokers and ex-smokers to obtain information on:
1. BoE in urine and saliva
2. BoBE determined in blood and urine
3. Mouth level exposure (MLE) of smoke constituents by analysis of smoked cigarette filters (Filter Analysis)

In addition smoking behaviour will be monitored, and sensory perceptions, quality of life and diet and lifestyle recorded using questionnaires. Finally gene expression analysis will be performed by the Sponsor. The study is conducted in clinical confinement periods and ambulatory visits.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of Ärztekammer Hamburg, Germany, 29/11/2011, ref: PV3824

Study design
Single-blinded single-centre controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a subject information sheet

Health condition(s) or problem(s) studied
Smoking

Interventions
The 6 months clinical study will be conducted in compliance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice (GCP). Participants will be required to read the Subject Information prior to providing their written consent by signing the informed consent form. The safety of the study participants is a primary focus throughout the study. This is achieved by recording the medical history of the study participants, the results of a general physical examination, vital signs, electrocardiogram (ECG), clinical laboratory results and adverse events.

A smoking cessation workshop will be available throughout the study and, if smoking participants have not already attended, will be mandatory at the end of the study..

All participants will be screened and enrolled if determined eligible for the study by the Principal Investigator. Enrolled smokers (n-140) will smoke a supplied commercial control cigarette with ISO tar yield equivalent to the RTP. On day 15, fifty per cent of smokers (n=70) will switch to the RTP whilst the other 70 smokers will continue to smoke the commercial control.

Following screening of volunteers for their eligibility to participate, during the 6 months study period the following events/assessments will be performed:
1. Medical history, physical examination, pregnancy tests, urine drug screen, alcohol breath tests at 2, 11, 16 and 26 weeks
2. Collection of urine (24 hours sample), blood and saliva, urine and serum for creatinine, and assessment of exhaled CO at 2, 7, 11, 16 and 26 weeks
3. Urine cotinine assay on all visits both ambulatory and in-clinic
4. Blood for gene expression at second week (prior to switching) and at the end of 26th week
5. Cigarette filter collection at 2, 7, 11, 16 and 26 weeks to measure mouth level exposure to smoke
6. Cigarette butt collection at 0, 5, 9, 14, 18, 21, 24 weeks
7. Sensory questionnaire assessment prior to switching, immediately at the end of first day after switching (i.e. week 2) and weeks 7,11, 16 and at study end
8. Quality of Life questionnaire, diet and lifestyle questionnaire at 2, 16 and 26 weeks
9. Spirometry, ECG will be recorded at 26 weeks
10. Smoking behaviour will be recorded at 2 weeks and 26 weeks
11. Adverse events to be recorded throughout the study

Principal Investigator:
Dr Ingo Meyer
Momentum Pharma Services GmbH

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure

To descriptively assess within-participant and between-group changes in the identified primary endpoints [BoE and BoBE] following a forced switch from a commercial control cigarette to a combustible RTP cigarette of equivalent ISO tar yield.

Secondary outcome measures
1. To descriptively assess within-participant and between-group changes in the secondary endpoints [BoE and BoBE, QoL, smoking behaviours, physiological measures, MLE and sensory perception] following a forced switch from a commercial control cigarette to a combustible RTP cigarette of equivalent ISO tar yield.
2. To descriptively assess changes in the primary and secondary endpoints following a forced switch from a commercial control cigarette to a combustible RTP cigarette of equivalent ISO tar yield in comparison to the ex-smokers and never-smokers.

Overall study start date
13/02/2012

Completion date
13/10/2012

Eligibility

Key inclusion criteria
Universal Inclusion Criteria
1. Participants may be of either sex and of any ethnic origin
2. Male and female participants must weigh at least 52 kg and 45 kg, respectively, and fall within the normal range according to accepted normal values of Body Mass Index (BMI) 18.5-30.0 kg /m2 (inclusive)
3. Participants must have no clinically significant abnormal findings, as judged by the project investigator (PI) or his appropriately qualified designee, on the physical examination, ECG, clinical laboratory test results, lung function tests or medical history during screening.
4. Participants must give voluntary written informed consent to participate in this study
5. Participants must be willing to refrain from consuming alcohol within 72 hours prior to the first day of each in-clinic evaluation visit
6. Participants must be willing to refrain from consuming grilled, fried or barbequed food and avoid being in the presence of the cooking of grilled, fried or barbequed food for 48 hours prior to the first day of each in-clinic evaluation visit
7. Female participants must not be pregnant or breastfeeding at screening and at check-in of each in-clinic evaluation period and be using a reliable method of contraception as per definition of Note 3 of ICH M3 Guideline

Inclusion Criteria for Smoking Groups:
1. Participants must be aged 23 to 55 years of age (inclusive)
2. Participants must be regular smokers whose chosen brand is both within one of the required ISO tar bands and has blend style/mechanics similar to those found in brands sold in Germany
3. Participants must have smoked their chosen brand for a minimum of 6 months and have smoked for at least 5 years prior to screening
4. Participants must typically smoke between 10 and 30 cigarettes per day (CPD)
5. Participants must be willing to switch to an RTP cigarette and smoke only the products provided to them during the study
6. Have a urinary cotinine level of >100 ng/mL

Inclusion Criteria for Ex-Smoking Group:
1. Participants must be aged 28 to 55 years of age (inclusive)
2. Participants must not have smoked for at least five years but must have been regular cigarette smokers, smoking 10 to 30 CPD, for at least five years prior to quitting
3. Participants must have a urinary cotinine level of <10 ng/mL

Inclusion Criteria for Never-Smoking Group:
1. Participants must be aged 28 to 55 years of age (inclusive)
2. Participants must not have smoked > 100 cigarettes in their lifetime, and none during the previous 5 years
3. Participants must have a urinary cotinine level of <10 ng/mL

Documented exceptions to the inclusion criteria may be permitted at the discretion of the PI or sub investigator in agreement with the Sponsor providing there would be no additional risk involved for the participant and there would be no impact on the realisation of the scientific objectives of the study.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
The study would enrol 260 healthy adult volunteers of which 140 will be regular smokers of 6-8 mg ISO tar yield cigarettes, 60 ex-smokers and 60 never smokers.

Key exclusion criteria
Universal Exclusion Criteria
1. Participants may be excluded from the study if there is evidence of any of the following criteria at Screening, or at any time during the study as appropriate
2. Participants who have clinically relevant gastrointestinal, renal, hepatic, neurologic, haematologic, endocrine, oncologic, urologic, pulmonary, immunologic, psychiatric, or cardiovascular disease or any other condition that, in the opinion of the PI or his appropriately qualified designee, would jeopardize the safety of the participant or impact the validity of the study results.
3. Participants who have clinically relevant abnormal findings on the physical examination, medical history, or clinical laboratory results unless deemed not clinically significant by the PI or his appropriately qualified designee
4. Participants who have participated in a previous clinical trial within 30 days prior to Day 1
5. Participants who have donated or lost 400 mL of blood or more within 90 days prior to Day 1
6. Participants who have donated plasma within 7 days prior to Day 1
7. Participants who have an acute illness (e.g. upper respiratory tract infection, viral infection, etc.) requiring treatment within 4 weeks prior to Day 1

8. Participants who regularly use any nicotine or tobacco products other than commercially manufactured filter cigarettes
9. Participants who are self-reported non-inhalers (smokers who draw smoke from the cigarette into the mouth and throat but do not inhale). Participants who are observed as non-inhalers on Day 12 by the clinic staff will be excluded
10. Participants who have a history of drug or alcohol abuse within 24 months prior to screening
11. Participants who have a positive alcohol breath test and urine screen for drugs of abuse at Screening or Day 1
12. Participants who have a positive HIV or hepatitis screen at Screening
13. Participants who have used prescription or over the counter (OTC) bronchodilator medication (e.g. inhaled or oral â-agonists) to treat a chronic condition within the 12 months prior to Day 1
14. Participants who have used any medication which interferes with the cyclo-oxygenase pathway (anti-inflammatory drugs such as aspirin or ibuprofen) within 14 days of Day 1
15. Participants who have used any prescribed systemic medication within 14 days of Day 1 (except for hormonal contraceptive and hormone replacement therapy)
16. Participants who have used any drugs or substances (except tobacco) known to be strong inducers or inhibitors of CYP enzymes (formerly known as cytochrome P450 enzymes) within 28 days prior to Day 1
17. Participants who performed strenuous physical activity (exceeding the participants normal activity levels) within 7 days prior to screening or prior to each in-clinic evaluation visit throughout the study
18. Any female participant who becomes pregnant during the course of the study will be withdrawn
19. Employees and immediate relatives of the tobacco industry, journalism, TV and radio reporting, public relations, market research, advertising and the clinic

Exclusion Criteria for Smoking Groups:
Smoking participants who, prior to enrolment, are planning to quit smoking in the next 12 months. However, participants will be informed that they are free to quit smoking and withdraw from the study at any time.

Exclusion Criteria for Non Smoking Groups:
1. Participants who smoke at any time during the study
2. Participants who are regularly exposed to second-hand smoke, such as those who live in a household with smokers or work in an environment where smoking is common.

Date of first enrolment
13/02/2012

Date of final enrolment
13/10/2012

Locations

Countries of recruitment
England

Germany

United Kingdom

Study participating centre
British American Tobacco (Investments) Ltd
Southampton
United Kingdom
SO15 8TL

Sponsor information

Organisation
British American Tobacco (Investments) Ltd (UK)

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Sponsor type
Industry

Website
http://www.bat-science.com/

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Protocol article	protocol	29/07/2013		Yes	No
Results article	results	01/07/2015		Yes	No