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To compare the exposure levels of selected smoke constituents as determined by biomarkers of exposure, filter analysis, sensory perception and other parameters when smokers using commercial cigarettes are switched to novel cigarettes

Submission date	Recruitment status	[ ] Prospectively registered
06/03/2009	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
10/03/2009	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
11/01/2013	Injury, Occupational Diseases, Poisoning	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
RTP Study Protocol 3865

Study information

Scientific Title
A single-blinded, controlled study to evaluate the effects of a novel cigarette on biomarkers of exposure, filter analysis and sensory tests, when used by healthy smokers

Study objectives
When smokers switch from conventional cigarettes to novel cigarettes of equivalent International Organization for Standardization (ISO) tar yield but with lower levels of selected smoke toxicants as determined by smoking machines, there is a measurable change in level of exposure to those same toxicants, as determined by biomarkers of exposure and filter analysis methods.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of Arztekramer Hamburg, approved on 11/12/2008.

Study design
Interventional non-randomised single-centre single-blinded switching study

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

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
Exposure to cigarette toxicants

Interventions
The 6 weeks clinical trial will be conducted as per the principles of good clinical practice. The safety of the subjects participating in the study will be evaluated prior to and post study.

The study will be performed in two parts, commencing with the smokers of the 6 mg ISO tar yield cigarettes and the non-smokers in parallel (part 1), followed by the smokers of the 1 mg ISO tar yield cigarettes (part 2). During the first 2 weeks of their involvement in the study, smokers will smoke a supplied commercial brand with ISO tar yield equivalent to the novel cigarette. On day 15 of each study period, the 6 mg ISO tar yield smokers will be split into two cohorts and the 1 mg ISO tar yield smokers will be split into three cohorts. The allocation of the participants in the two groups into smaller cohorts will be done consecutively (non-randomised allocation). One cohort in each group will continue to smoke the supplied commercial brand while the other cohorts will be switched to smoke the novel cigarettes for subsequent 4 weeks. Participants will be instructed to smoke as per their normal smoking behaviour (no minimum or maximum limits on amount smoked) throughout the interventions.

Company identifiers of the novel cigarettes: German Reduced Toxicant Products F752, H671 and T562

During the 6 weeks study period the following procedures will be performed:
1. Urine collection for biomarkers of exposure, exhaled CO at 2, 4 and 6 weeks
2. Saliva collection for cotinine assay on all ambulatory visits and each day resident in the clinic.
3. Blood sample collection prior to switching for genotyping and gene expression, and at the end of 6th week for gene expression only
4. Cigarette filter tips collection every 7 days and on each day of stay in the clinic to assess mouth level exposure of whole smoke
5. Regular collection of all smoked cigarette butts for accountability
6. Sensory perception assessment prior to switching, immediately at the end of first day after switching, end 6th week
7. SF-36® health survey questionnaire prior to switching and at the end of 6th week
8. Smoking Behaviour assessment by means of Smoking Analyser (SA7) and life shirt jacket at 2 and 4 weeks
9. Medical history, physical examination, pulmonary function test, vital signs, ECG at screening, end of 2nd, 4th and 6th week
10. Alcohol breath test and urine drug screen at screening and every 2 weeks
11. Routine safety assessment at screening and at the end of study period
12. Adverse event recording will be done at regular intervals

Principal Investigator:
Dr. Ingo Meyer
Medical Director
Momentum Pharma Services GmbH

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure

To estimate and compare cigarette smoke exposure in healthy adult smokers using both biomarkers of exposure and filter analysis and to quantify any changes in these exposure estimates following a switch from commercial to novel cigarettes. Data collection will be carried out as follows:
1. Urine collection for biomarkers of exposure, exhaled CO at 2, 4 and 6 weeks
2. Cigarette filter tips collection every 7 days and on each day of stay in the clinic to assess mouth level exposure of whole smoke

Secondary outcome measures
1. To determine changes in the following measures during consumption of novel cigarettes and commercial cigarettes:
1.1. Sensory perception questionnaire prior to switching, immediately at the end of first day after switching, end of 6th week
1.2. Smoking behaviour including puffing and inhalation behaviour, assessed by Smoking Analyser (SA7) and life shirt jacket at 2 and 4 weeks
1.3. Quality of life using SF-36® Health Survey prior to switching and at the end of 6th week
1.4. Basic physiological measures: medical history, physical examination, pulmonary function test, vital signs, ECG at screening, end of 2nd, 4th and 6th week

2. To analyse genotype and gene expression to support the interpretation of the biomarkers of exposure:
2.1. Blood sample collection prior to switching for genotyping and gene expression, and at the end of 6th week for gene expression only

Overall study start date
01/02/2009

Completion date
31/08/2009

Eligibility

Key inclusion criteria
The study would enrol 250 healthy adult habitual smokers of 6-7 mg (N = 100) and 1-2 mg (N = 150) ISO tar yield cigarettes and 50 healthy adult non-smokers to take part in the study.

Inclusion criteria for all participants:
1. Subjects of either sex, of any ethnic origin, 21 years of age or older
2. No clinically significant abnormal findings, as judged by the Principal Investigator, on the physical examination, electrocardiogram (ECG), clinical laboratory test results, lung function tests or medical history during screening
3. Voluntarily provide written Informed Consent and demonstrate ability to comprehend the Informed Consent Form
4. Refrain from consuming methylxanthine-containing products (e.g. caffeine) within 24 hours of the first day of each confinement visit
5. Refrain from consuming alcohol from 72 hours prior to the first day of each confinement visit.
6. Female subjects must have negative urine pregnancy test at screening. Other acceptable criteria for including women would be sexual abstinence (provided it is the preferred and usual lifestyle of the subject); women not of child bearing potential (tubal occlusion, hysterectomy, bilateral salpingectomy)

Additional inclusion criteria for smoking groups:
7. Regular smokers whose chosen brand is both within one of the required ISO tar bands and have blend style/mechanics that are typical of the German market
8. Smokers smoking their chosen brand for a minimum of 6 months and have smoked for at least 3 years prior to screening
9. Typically smoke between 6 and 30 cigarettes per day
10. Subjects willing to switch to a novel cigarette

Additional inclusion criteria for non-smoking groups:
11. Individuals who have not smoked for at least five years and have a urinary continine level of <10 ng/ml

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
300 (250 smokers and 50 non-smokers)

Key exclusion criteria
1. Clinically relevant gastrointestinal, renal, hepatic, neurologic, haematologic, endocrine, oncologic, urologic, pulmonary, immunologic, psychiatric, or cardiovascular disease or any other health condition
2. Clinically relevant abnormal findings on the physical examination, medical history, or clinical laboratory results unless deemed not clinically significant by the Principal Investigator
3. History of participation in clinical trial within 90 days prior to screening
4. History of 400 mL or more blood loss within 90 days prior to screening
5. Acute illness (e.g., upper respiratory tract infection, viral infection, etc.) requiring treatment within 4 weeks prior to enrolment
6. History of drug or alcohol abuse
7. Positive alcohol breath test and urine screen for drugs of abuse (amphetamines, barbiturates, benzodiazepines, cocaine, ecstasy, methamphetine, morphine, methadone, tricyclic antidepressants [TCA] and marijuana [THC]).
8. Positive HIV or hepatitis screen (checked only at screening)
9. History of use of bronchodilator medication (e.g., inhaled or oral beta-agonists) within the 12 months prior to study enrolment
10. History of chronic medication which interferes with the cyclooxygenase pathway (anti-inflammatory drugs such as aspirin or ibuprofen)
11. Any prescribed chronic systemic medication within 14 days of enrolment (except for hormonal contraceptive and hormone replacement therapy)
12. History of intake of drugs or substances known to be inducers of cytochrome P450 enzymes within 28 days prior to screening
13. Women of child bearing potential who fail to use any reliable contraception.
14. Pregnant or lactating women
15. Smokers of cigarettes that are not within the required ISO tar bands or smoke cigarettes that have been identified as atypical of the German Market with respect to blend style and mechanics

16. Smokers who smoke less than 6 and more than 30 cigarettes per day
17. Smokers consuming any nicotine or tobacco products other than filter cigarettes
18. Smokers who are known to only take puffs of smoke without inhaling or observed with similar smoking pattern during the study
19. Non-smokers with levels of cotinine >10 ng/ml in their urine test
20. Employees of the tobacco industry, journalism, TV and radio reporting, public relations, market research and advertising

Date of first enrolment
01/02/2009

Date of final enrolment
31/08/2009

Locations

Countries of recruitment
England

Germany

United Kingdom

Study participating centre
Chief Scientific Officer
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Sponsor information

Organisation
British American Tobacco (Investments) Ltd (UK)

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Funder(s)

Funder type
Industry

Funder Name
British American Tobacco (Investments) Ltd (UK)

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