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An open observational study investigating the effect on oral health when using tobacco free nicotine pods

Submission date
22/11/2017

Recruitment status
No longer recruiting

Registration date
28/11/2017

Overall study status
Completed

Last Edited
12/02/2024

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
Snus is a moist form of smokeless tobacco which is usually placed under the upper lip. It is sometimes used as a last resort for people who have failed stopping smoking with the available pharmaceutical smoking cessation aids. Clinical experience does not show that habitual use of regular, tobacco based snus affects biofilm acidogenicity (the acid levels of the cells that line a surface in the mouth). Contributing factors may be that snus includes food approved pH regulating substances (such as sodium carbonate) which maintains a relatively high pH in the snus pinch/pouch (c. pH 8-8.5), nicotine itself does not seem to affect biofilm acidogenicity, Nicotine itself does not seem to affect biofilm acidogenicity, and that the tobacco does not function as a substrate for the oral microflora. These circumstances may help to explain why caries does not seem to be more prevalent among snus users than among non-tobacco users. The non-tobacco based nicotine pouch (ZYN®) is an alternative form of orally delivered nicotine. The physical properties of ZYN® in terms of pH (aciditiy levels) is the same as with regular, tobacco-based snus and the product is used the same way, that is, it is placed in the upper sulcus for 30-60 minutes. However, the matrix for the nicotine in ZYN® is different from that in regular snus: microcrystals of maltitol and cellulose instead of ground tobacco leaves. In food stuffs, maltitol and cellulose have not been associated with changes in biofilm acidogenicity. However, the prolonged exposure (c. 30-60 minutes) associated with use in a product like ZYN® constitutes a somewhat different type of exposure. The aim of this study is to assess if the use of ZYN® will adversely affect biofilm acidogenicity.

Who can participate?
Adults aged 19 and older who are Snus users.

What does the study involve?
This study contains two parts. In the first part, participants are randomly allocated as to what order they receive the following: ZYN® Smooth 3 mg, ZYN® Peppermint 3 mg, 10% sucrose and 10% xylitol. These are single doses and are put between the upper lip and the gum for 60

minutes. In the second part of the study, participants can choose from 3 or 6 mg pouches of ZYN® Smooth, ZYN® Peppermint or ZYN® Cinnamon. Participants use these for six weeks and report to the clinic every other week for oral assessments.

What are the possible benefits and risks of participating?
There are no possible benefits of participating. The tested products are commercially available and only participants who are well acquainted with and used to the effects of nicotine will participate. The only side effects are the effects likely to be related to nicotine exposure (such as salivation, nausea, and dyspepsia).

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

When is the study starting and how long is it expected to run for?
September 2017 to March 2019

Who is funding the study?
Swedish Match North Europe (Sweden)

Who is the main contact?
Camilla Pramfalk
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
SM 17-02

Study information

Scientific Title
Oral Safety Study: Open observational study of oral health associated with use of a non-tobacco based nicotine pouch (ZYN®) among current daily snus users

Acronym
OSS

Study objectives
Clinical experience does not indicate that habitual use of regular, tobacco based snus affects biofilm acidogenicity. Although there are no priori reasons to believe that use of a non-tobacco based nicotine pouch will adversely affect biofilm acidogenicity, it is reasonable to rigorously assess this possibility in the context of a controlled clinical trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
EPN Gothenburg, 24/10/2017, ref: Dnr 778-17

Study design
Part 1: Single-centre open randomized four-way crossover single administration trial including 20 subjects
Part 2: Single-centre open observational follow-up study during 6 weeks including 60 subjects

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
ICD-10 code Z72: ”Tobacco use not otherwise specified (NOS)”

Interventions
This study contains two parts. The first part of the study assessed the dental plaque acidogenicity after short-term exposure to study protocols.

Part 1:
Participants are randomly allocated in four ways in this cross over trial:
1. ZYN® Smooth 3 mg
2. ZYN® Peppermint 3 mg
3. 10% sucrose
4. 10% xylitol
The treatments are administered as single doses in a pre-determined computer-generated randomized order according to a four sequence list. The subject keeps the pouch still between the upper lip and the gum for 60 minutes. The duration of the treatments and follow-up takes approximately 30 days.

Part 2: Ad libitum use of a ZYN® nicotine pouch, participants can choose from 3 or 6 mg pouches of ZYN® Smooth, ZYN® Peppermint or ZYN® Cinnamon.
The treatments are administered as ad libitum use during 6 weeks. Subjects will report to the clinic every second week for oral assessments. Each visit takes approximately 75 minutes.

Intervention Type

Other

Primary outcome(s)
Assessment of dental plaque acidogenicity, using the pH microtouch method, during exposure of nicotine pouch at baseline, one, two, 5, 10, 20, 30, 40, 50 and 60 minutes.

Key secondary outcome(s))
1. Adverse events are measured using patient interviews at screening, 0, 7, 14, 21 and 28 days (Part 1) or screening, baseline, 14, 28, 42 and 49 days (Part 2)
2. Oral microflora is measured using plaque sampling with a sterile toothpick from the buccal areas of respective quadrants at screening, 14, 28 and 42 days (Part 2)
3. Oral mucosa and pathological changes are recorded using the four-grade clinical scale measured using at screening, 14, 28 and 42 days (Part 2)

Completion date
21/03/2019

Eligibility

Key inclusion criteria
1. Snus user, with a minimum weekly consumption of three or more snus cans (brands with nicotine content <1%) or two or more cans (brands with nicotine content >1%) since ≥1 year
2. Consent to participate voluntarily and sign Informed Consent Form prior to any study procedure
3. Healthy male/female, age ≥19. Female subjects should have a negative pregnancy test
4. Willing and able to comply with study procedures
5. Normal stimulated salivary secretion rate (>0.7 ml/min)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
79

Key exclusion criteria
1. A history or presence of diagnosed hypertension or any cardiovascular disease
2. Surgery within 6 months of the screening visit that, in the opinion of the investigator, could negatively impact on the subject’s participation in the clinical study
3. Any surgical or medical condition, which, in the judgment of the clinical investigator, might interfere with the absorption, distribution, metabolism or excretion of nicotine
4. Subjects who are pregnant

5. Allergy towards composite materials
6. Antibiotic use during or within the last 4 weeks prior to the study period

Date of first enrolment
06/11/2017

Date of final enrolment
05/06/2018

Locations

Countries of recruitment
Sweden

Study participating centre
CTC Clinical Trial Consultants AB
Sweden
SE-752 37

Sponsor information

Organisation
Swedish Match North Europe

Funder(s)

Funder type
Industry

Funder Name
Swedish Match North Europe

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Interim results article	Effects on mucosal lesions and cytokine levels	19/07/2022	25/07/2022	Yes	No
Other unpublished results	clinical study report	21/03/2019	12/02/2024	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 1.0	14/09/2017	01/12/2022	No	No