Design of a Clinical Trial to Compare Smoking Cessation Rates with Camel SNUS and a Nicotine Lozenge

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Presentation Outline

- Study Design
  - Objectives
  - Conduct
  - Subject Characteristics
- Study Results
  - Covered in Second Presentation

Study Design

Study Objectives:

Develop clinical data to address the following questions:

- Will smokers use SNUS to stop smoking?
- Does risk communication facilitate cessation?
- Does product use reduce smoke exposure for dual users?

Study Overview

- Followed recommended standard cessation study design.
- Conducted at six clinical sites in accordance with Good Clinical Practices (GCP)
  - International Conference on Harmonization (ICH)
  - Applicable parts of 25 CFR parts 11, 50, 56, and 312

Cessation Criteria

R1-R4 are specified by the protocol and are commonly used criteria for assessing cessation.

- R1 – Continuous smoking abstinence (narrow)
- R2 – Continuous smoking abstinence (broad)
- R3 – Prolonged smoking abstinence
- R4 – Repeated point prevalence smoking

Cessation Criteria

R1-R4 are specified by the protocol and are commonly used criteria for assessing cessation.

- R1 – Continuous smoking abstinence (narrow)
  - The subject has not smoked following the quit date (day after Visit 1)
- R2 – Continuous smoking abstinence (broad)
- R3 – Prolonged smoking abstinence
- R4 – Repeated point prevalence smoking abstinence

Cessation Criteria

R1-R4 are specified by the protocol and are commonly used criteria for assessing cessation.

- R1 – Continuous smoking abstinence (narrow)
- R2 – Continuous smoking abstinence (broad)
  - The subject has no periods of two-consecutive weeks following the quit date during which the subject has smoked
- R3 – Prolonged smoking abstinence
- R4 – Repeated point prevalence smoking abstinence

Cessation Criteria

R1-R4 are specified by the protocol and are commonly used criteria for assessing cessation.

- R1 – Continuous smoking abstinence (narrow)
- R2 – Continuous smoking abstinence (broad)
- R3 – Prolonged smoking abstinence
  - There are no periods of two-consecutive weeks following a two week grace period from the quit date during which the subject has smoked
- R4 – Repeated point prevalence smoking abstinence

Cessation Criteria

R1-R4 are specified by the protocol and are commonly used criteria for assessing cessation.

- R1 – Continuous smoking abstinence (narrow)
- R2 – Continuous smoking abstinence (broad)
- R3 – Prolonged smoking abstinence
- R4 – Repeated point prevalence smoking abstinence
  - The subject has not smoked within the past seven days following a two-week grace period from the quit date

Study Overview

- Followed recommended standard cessation study design.
- Conducted at six clinical sites in accordance with Good Clinical Practices (GCP)
- Included three study cohorts
  - Camel SNUS *with* smokeless risk reduction information
  - Camel SNUS *without* smokeless risk reduction information
  - Nicotine Replacement Therapy (NRT) (4 mg lozenge)

Study Products

- SNUS
  - Frost (600 mg pouch)
  - Mellow (600 mg pouch)
- Nicorette® Lozenge
  - Mint (4 mg nicotine)
  - Original (4 mg nicotine)

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  - Nicotine Replacement Therapy (NRT) (4 mg lozenge)
- Enrolled ~200 subjects / cohort

Study Powering

- Summary: Study was powered to determine whether SNUS was ~twice as effective as NRT at expected NRT cessation rates
- Detail:
  - Small scale study (n=63) by Tilashalski *et al.* suggests that smokeless tobacco is highly successful as a cessation aid
  - Based upon the powering calculation, with 200 subjects per cohort there is a 80% chance at $\alpha=0.05$ of seeing a difference between NRT at a cessation rate of 6%, and SNUS at a 15% cessation rate (0.389 odds ratio) (The NRT rate is consistent with the literature and the SNUS rate is lower than observed for smokeless tobacco in the Tilashalski *et al.* study)

Inclusion Criteria (summarized)

Inclusion:

- Male or female between 21 and 65 years of age
- Generally healthy
- Self-report smoking ≥ 10 cigarettes per day for at least the past year
- ECO level ≥ 8 parts per million (ppm) at Screening and at Visit 1
- Willing to quit smoking with the aid of Camel SNUS or Nicorette® Lozenge
- Agree not to use drugs of abuse over the course of the study
- Able to read, understand, and complete questionnaires in English
- Able to comprehend and willing to sign an informed consent form

Exclusion Criteria (summarized)

Exclusion:

- Use of prohibited medication including:
  - NRT
  - Prescription or herbal cessation products
  - Medical marijuana
- Recent use of smokeless tobacco products
- Recent participation in a cessation study
- Health related exclusions (multiple criteria)
- Positive test for drugs / alcohol
- Bias-related restrictions
- Deemed by the Investigator to be inappropriate for this study

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  - Camel SNUS *without* smokeless risk reduction information
  - Nicotine Replacement Therapy (NRT) (4 mg lozenge)
- Enrolled ~200 subjects / cohort
- Provided study product for 12 weeks.
- Followed-up (biomarker, questionnaires) at 3, 6, 9, and 12 months.

Study Endpoints

Safety

- Screening
  - Medical History
  - Brief Physical Exam
  - Oral Assessment
  - Height, Weight, Vital Signs
  - Electrocardiogram
  - Drug, Pregnancy, Alcohol Screen
  - HbA1C
  - Chemistry, Hematology, Urinalysis, Serology
- All visits
  - Adverse Event Assessment
  - Concomitant Medication Review
  - Vital Signs
- 6-Month Visit
  - Oral Assessment
  - Height, Weight
- 12-Month Visit
  - Height, Weight

Study Endpoints

Questionnaire

- Cessation Criteria
- Produce Usage
- Fagerström Test of Nicotine Dependence
- Minnesota Nicotine Withdrawal Scale
- Brief Questionnaire of Smoking Urges

Biomarkers

- Exhaled CO
- Nicotine
- Cotinine
- Thiocyanate

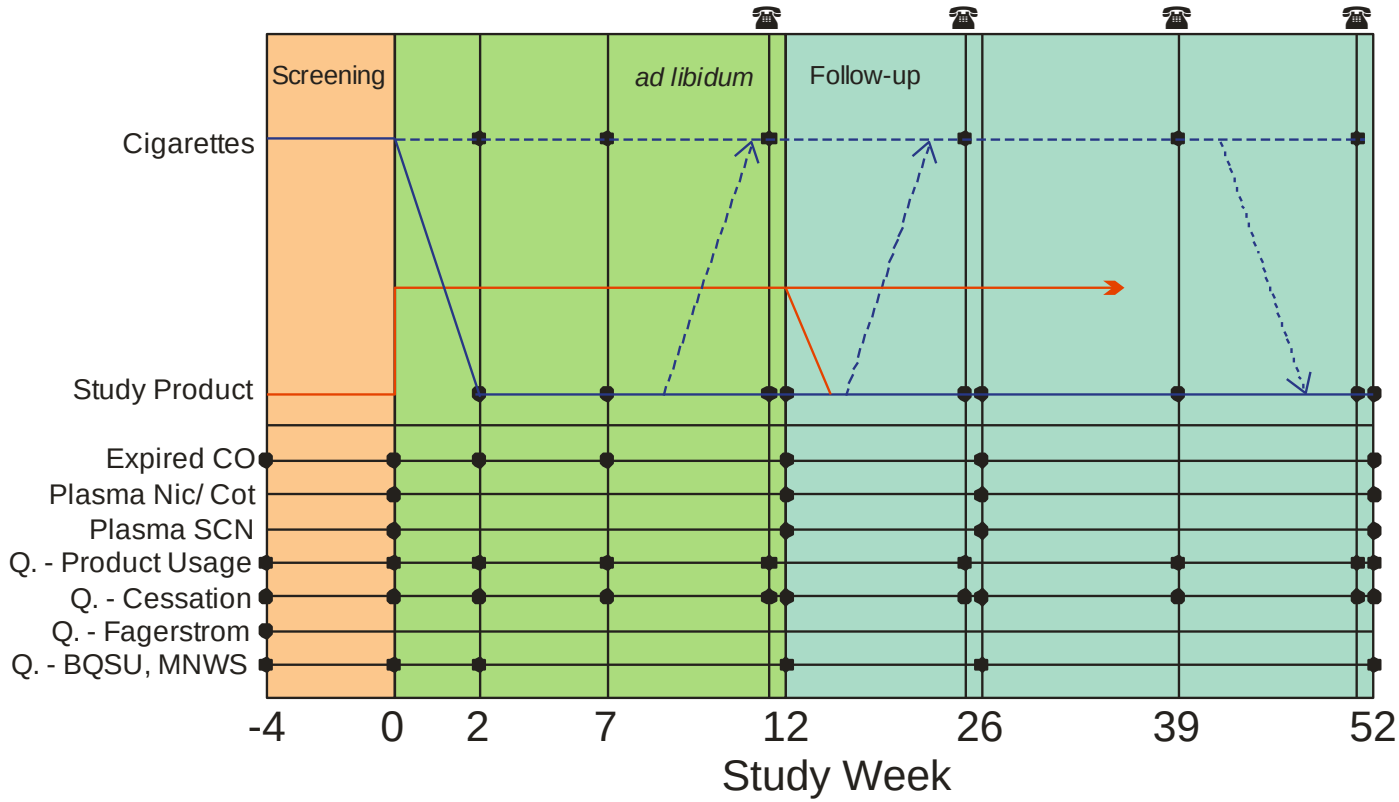
Biomarker Confirmation of Cessation Status

Per published recommendations, cessation status was confirmed at the Month 3, 6, and 12 visits by:

- Exhaled CO < 8 ppm
  - Measured at clinical site
  - Subject dismissed from study if failed Exhaled CO measure
- Plasma Cotinine < 15 ng/ml (if *not* reporting SNUS or Nicorette® use)
  - Sample drawn at clinical site
  - Subject was considered a treatment failure in analysis as of collection date
  - This analysis was applied at the end of the study, so the subject may have continued through additional visits

Study Design

Summary of study endpoints measured at each visit. Quitters followed Study Product visits, non-quitters followed Cigarettes procedures.



Subject Characteristics

Subject Demographics

Demographics were similar among cohorts.

	Cohort 1	Cohort 2	Cohort 3
Age (std. dev)	41.5 (12.0)	43.3 (11.6)	41.4 (12.0)
Sex			
Male	109	112	110
Female	109	106	103
Ethnicity			
Hispanic	6.4%	6.9%	6.6%
Non-Hispanic	93.6%	93.1%	93.4%

Cohort 1 = SNUS w/ smokeless risk information
Cohort 2 = SNUS w/o smokeless risk information
Cohort 3 = Nicorette® Lozenge

Subject Demographics

Demographics were similar among cohorts.

	Cohort 1	Cohort 2	Cohort 3
Race			
White	73.4%	73.9%	72.8%
Black or African American	24.3%	24.8%	23.9%
Asian	1.4%	1.8%	1.9%
Native Hawaiian or other Pacific Islander	0.0%	0.5%	0.9%
American Indian or Alaska Native	3.2%	0.9%	0.9%

Cohort 1 = SNUS w/ smokeless risk information
Cohort 2 = SNUS w/o smokeless risk information
Cohort 3 = Nicorette® Lozenge

Subject Characteristics

Characteristics were similar among cohorts.

	Cohort 1	Cohort 2	Cohort 3
Height (cm) (Std. Dev.)	171.4 (9.7)	170.9 (9.0)	171.4 (9.9)
Weight (kg) (Std. Dev.)	83.2 (19.4)	82.5 (18.0)	83.5 (19.2)
Body Mass Index (kg/m^2) (Std. Dev.)	28.2 (5.4)	28.2 (5.4)	28.2 (5.2)
FTND Score (Std. Dev.)	5.7 (1.9)	5.9 (2.0)	5.8 (2.0)

Subject Characteristics

Characteristics were similar among cohorts.

Education	Cohort 1	Cohort 2	Cohort 3
Grade School (grades 1-8)	0.0%	0.9%	0.9%
High School (grades 9-11)	10.6%	10.1%	8.9%
High School Graduate	27.5%	26.6%	33.8%
Technical School	6.9%	6.0%	4.7%
Some College	33.5%	35.3%	34.3%
College Graduate	16.5%	17.4%	14.6%
Graduate School	5.0%	3.7%	2.8%

Subject Characteristics

Characteristics were similar among cohorts.

Household Income	Cohort 1	Cohort 2	Cohort 3
< $20,000	36.2%	39.9%	44.1%
$20,000 - $39,999	30.3%	27.1%	27.7%
$40,000 - $59,999	12.4%	10.6%	12.7%
$60,000 - $79,999	5.5%	7.3%	2.8%
$80,000 - $99,999	2.8%	3.2%	1.4%
$100,000 - $119,999	0.9%	2.3%	1.4%
> $120,000	0.0%	1.8%	0.5%

Summary

- Study was conducted in accordance with GCP
- Primary focus of study was cessation
- Secondary focus included product use
- Cohorts had similar demographics and characteristics