Clinical trial results:
A Double-Blind, Placebo Controlled Study of Pharmacodynamic Effects Of 4 Mg Nicotine Gum. A Study in Healthy Smokers Willing to Quit

Summary

EudraCT number	2018-004229-10
Trial protocol	PL
Global end of trial date	26 September 2019

Results information

Result version number	v1 (current)
This version publication date	28 May 2020
First version publication date	28 May 2020

Trial information

Trial identification

Sponsor protocol code	CCSSMC000766

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	McNeil AB
Sponsor organisation address	Norrbroplatsen 2, Helsingborg, Sweden, 25109
Public contact	McNeil AB, Global Regulatory Affairs, 0046 42288000,
Scientific contact	McNeil AB, Global Regulatory Affairs, 0046 42288000,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 September 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of study was to evaluate the effect of 4 milligrams (mg) nicotine chewing gum on subjects' perceived relief of overall withdrawal symptoms including urges to smoke, compared to placebo over the first 2 treatment days.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices (GCP) and applicable regulatory requirements. Safety was evaluated by examining the incidence and type of adverse events, changes in clinical laboratory tests and vital signs.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 August 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 220
Worldwide total number of subjects	220
EEA total number of subjects	220

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	220
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall, 220 subjects were randomized: 110 subjects received placebo and 110 subjects received active treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received matching placebo Freshfruit E104 gum (maximum 15 gums per day) from Days 1 to 14 or until day before end of study visit.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicated chewing-gum
Routes of administration	Oromucosal use

Dosage and administration details:

Subjects received matching placebo Freshfruit E104 gum from Days 1 to 14 or until day before end of study visit.

Arm title	Nicorette Freshfruit Gum 4 mg

Arm description:

Subjects received Nicorette Freshfruit gum 4 milligrams (mg) maximum 15 gums per day orally from Days 1 to 14 or until day before end of study visit.

Arm type	Experimental
Investigational medicinal product name	Nicorette Freshfruit Gum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicated chewing-gum
Routes of administration	Oromucosal use

Dosage and administration details:

Subjects received Nicorette Freshfruit gum 4 mg from Days 1 to 14 or until day before end of study visit.

Number of subjects in period 1	Placebo	Nicorette Freshfruit Gum 4 mg
Started	110	110
Completed	108	108
Not completed	2	2
Consent withdrawn by subject	-	2
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo Freshfruit E104 gum (maximum 15 gums per day) from Days 1 to 14 or until day before end of study visit.	
Reporting group title	Nicorette Freshfruit Gum 4 mg
Reporting group description:	
Subjects received Nicorette Freshfruit gum 4 milligrams (mg) maximum 15 gums per day orally from Days 1 to 14 or until day before end of study visit.	

Reporting group values	Placebo	Nicorette Freshfruit Gum 4 mg	Total
Number of subjects	110	110	220
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	110	110	220
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	37.4	36.6	
standard deviation	± 10.95	± 11.54	-
Title for Gender Units: subjects			
Female	60	66	126
Male	50	44	94

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo Freshfruit E104 gum (maximum 15 gums per day) from Days 1 to 14 or until day before end of study visit.	
Reporting group title	Nicorette Freshfruit Gum 4 mg
Reporting group description:	
Subjects received Nicorette Freshfruit gum 4 milligrams (mg) maximum 15 gums per day orally from Days 1 to 14 or until day before end of study visit.	

Primary: Mean of Daily Self-assessed Visual Analog Scale (VAS) Ratings of Relief of Overall Withdrawal Symptoms Over Days 1 and 2

End point title	Mean of Daily Self-assessed Visual Analog Scale (VAS) Ratings of Relief of Overall Withdrawal Symptoms Over Days 1 and 2
End point description:	
VAS is self-assessed tool to record the treatment effects on overall relief of withdrawal symptoms. VAS scale ranges from 0 to 100 millimetre (mm). 0 indicated no relief of withdrawal symptoms and 100 indicated complete relief of withdrawal symptoms. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
Days 1 and 2	

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	109		
Units: unit on scale				
least squares mean (standard error)	26.64 (± 1.971)	32.53 (± 1.980)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	5.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	11.39

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Overall Withdrawal Symptoms Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Overall Withdrawal Symptoms Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects on overall relief of withdrawal symptoms. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of withdrawal symptoms and 100 indicated complete relief of withdrawal symptoms. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	110		
Units: unit on scale				
least squares mean (standard error)	33.08 (± 2.107)	38.91 (± 2.078)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	5.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	11.66

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Overall Withdrawal Symptoms Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Overall Withdrawal Symptoms Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects on overall relief of withdrawal symptoms. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of withdrawal symptoms and 100 indicated complete relief of withdrawal symptoms. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14.

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	106		
Units: unit on scale				
least squares mean (standard error)	37.38 (± 2.483)	46.71 (± 2.506)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	214
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	9.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.37
upper limit	16.28

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Urge to Smoke Over Days 1 and 2

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Urge to

	Smoke Over Days 1 and 2

End point description:

VAS is self-assessed tool to record the treatment effects on relief of urge to smoke. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of urge to smoke and 100 indicated complete relief of urge to smoke. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 1 and 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	108		
Units: unit on scale				
least squares mean (standard error)	25.93 (± 1.965)	33.06 (± 1.983)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	7.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	12.6

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Urge to Smoke Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Urge to Smoke Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects on relief of urge to smoke. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of urge to smoke and 100 indicated complete relief of urge to smoke. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Day 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	108		
Units: unit on scale				
least squares mean (standard error)	31.88 (± 2.097)	39.73 (± 2.048)		

Statistical analyses

Statistical analysis title	statistical analysis 1
Statistical analysis description:	
Database auto-calculates total number of subjects erroneously, analyzed number of subjects were 103.	
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.008
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	7.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.07
upper limit	13.6

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Urge to Smoke Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Urge to Smoke Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects on relief of urge to smoke. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of urge to smoke and 100 indicated complete relief of urge to smoke. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	92		
Units: unit on scale				
least squares mean (standard error)	35.79 (± 2.511)	43.13 (± 2.565)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	7.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	14.43

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of depressed mood Over Days 1 and 2

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of depressed mood Over Days 1 and 2

End point description:

VAS is self-assessed tool to record the treatment effects on relief of depressed mood. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of depressed mood and 100 indicated complete relief of depressed mood. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 1 and 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	33		
Units: unit on scale				
least squares mean (standard error)	23.90 (± 3.286)	19.24 (± 3.185)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.312
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	-4.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.81
upper limit	4.49

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of depressed mood Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of depressed mood Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects on relief of depressed mood. VAS scale ranges from Zero to 100 mm. Zero indicated no relief of depressed mood and 100 indicated complete relief of depressed mood. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	10		
Units: unit on scale				
least squares mean (standard error)	21.86 (± 7.288)	30.97 (± 5.646)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	9.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.66
upper limit	28.89

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of depressed mood Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of depressed mood Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects on relief of depressed mood. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of depressed mood and 100 indicated complete relief of depressed mood. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	6		
Units: unit on scale				
least squares mean (standard error)	29.85 (± 13.165)	37.83 (± 9.309)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.636
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	7.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.15
upper limit	46.11

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of irritability Over Days 1 and 2

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of irritability Over Days 1 and 2

End point description:

VAS is self-assessed tool to record the treatment effects on relief of irritability. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of irritability and 100 indicated complete relief of irritability. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 1 and 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	59		
Units: unit on scale				
least squares mean (standard error)	24.79 (± 3.026)	27.01 (± 2.730)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.588
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	0.588
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.86
upper limit	10.3

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of irritability Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of irritability Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects on relief of irritability. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of irritability and 100 indicated complete relief of irritability. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	21		
Units: unit on scale				
least squares mean (standard error)	28.90 (± 5.058)	32.88 (± 4.415)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.558
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	3.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.66
upper limit	17.61

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of irritability Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of irritability Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects on relief of irritability. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of irritability and 100 indicated complete relief of irritability. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	11		
Units: unit on scale				
least squares mean (standard error)	51.56 (± 6.678)	40.66 (± 5.695)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.231
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	-10.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.42
upper limit	7.62

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Frustration Over Days 1 and 2

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Frustration Over Days 1 and 2

End point description:

VAS is self-assessed tool to record the treatment effects on relief of frustration. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of frustration and 100 indicated complete relief of frustration. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 1 and 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	47		
Units: unit on scale				
least squares mean (standard error)	19.79 (± 3.761)	26.48 (± 3.054)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.171
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	6.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.96
upper limit	16.34

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Frustration Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Frustration Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects on relief of frustration. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of frustration and 100 indicated complete relief of frustration. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N'

signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	12		
Units: unit on scale				
least squares mean (standard error)	27.13 (± 7.033)	37.52 (± 5.742)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.268
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	0.268
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.69
upper limit	29.46

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Frustration Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Frustration Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects on relief of frustration. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of frustration and 100 indicated complete relief of frustration. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	8		
Units: unit on scale				
least squares mean (standard error)	35.79 (± 9.552)	46.07 (± 7.551)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.416
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	0.416
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.52
upper limit	37.08

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Restlessness Over Days 1 to 2

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Restlessness Over Days 1 to 2

End point description:

VAS is self-assessed tool to record the treatment effects on relief of restlessness. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of restlessness and 100 indicated complete relief of restlessness. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 1 and 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	56		
Units: unit on scale				
least squares mean (standard error)	23.25 (± 2.807)	26.22 (± 2.731)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	2.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	10.73

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Restlessness Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Restlessness Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects on relief of restlessness. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of restlessness and 100 indicated complete relief of restlessness. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	27		
Units: unit on scale				
least squares mean (standard error)	35.05 (± 4.426)	35.12 (± 3.995)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.992
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.93
upper limit	12.06

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Restlessness Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Restlessness Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects on relief of restlessness. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of restlessness and 100 indicated complete relief of restlessness. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	18		
Units: unit on scale				
least squares mean (standard error)	49.53 (± 5.312)	40.65 (± 4.849)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.226
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	0.226
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.55
upper limit	5.79

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Increased Appetite Over Days 1 to 2

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Increased Appetite Over Days 1 to 2

End point description:

VAS is self-assessed tool to record the treatment effects on relief of increased appetite. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of increased appetite and 100 indicated complete relief of increased appetite. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 1 and 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	46		
Units: unit on scale				
least squares mean (standard error)	20.13 (± 3.557)	27.22 (± 3.103)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.137
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	7.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.31
upper limit	16.48

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief Increased Appetite Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief Increased Appetite Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects on relief increased appetite. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of increased appetite and 100 indicated complete relief of increased appetite. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: unit on scale				
least squares mean (standard error)	35.06 (± 5.784)	35.86 (± 5.784)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.923
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.96
upper limit	17.56

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief Increased Appetite Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief Increased Appetite Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects on relief increased appetite. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of increased appetite and 100 indicated complete relief of increased appetite. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	11		
Units: unit on scale				
least squares mean (standard error)	41.02 (± 8.215)	40.02 (± 6.553)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.926
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	-0.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.27
upper limit	21.28

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Stress Over Days 1 to 2

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Stress Over Days 1 to 2

End point description:

VAS is self-assessed tool to record the treatment effects of relief of stress. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of stress and 100 indicated complete relief of stress. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 1 and 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	50		
Units: unit on scale				
least squares mean (standard error)	23.17 (± 2.656)	20.48 (± 2.630)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.473
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	-2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.11
upper limit	4.72

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Stress Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Stress Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects of relief of stress. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of stress and 100 indicated complete relief of stress. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	22		
Units: unit on scale				
least squares mean (standard error)	38.47 (± 6.625)	31.83 (± 4.467)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.413
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	-6.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.95
upper limit	9.69

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Stress Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Stress Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects of relief of stress. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of stress and 100 indicated complete relief of stress. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	11		
Units: unit on scale				
least squares mean (standard error)	38.99 (± 9.275)	45.87 (± 7.910)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	6.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.84
upper limit	32.6

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Difficulty Concentrating Over Days 1 to 2

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Difficulty Concentrating Over Days 1 to 2

End point description:

VAS is self-assessed tool to record the treatment effects on relief of difficulty concentrating. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of difficulty concentrating and 100 indicated complete relief of difficulty concentrating. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 1 and 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	33		
Units: unit on scale				
least squares mean (standard error)	23.25 (± 3.509)	22.74 (± 3.114)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.914
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.9
upper limit	8.89

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Difficulty Concentrating Over Days 3 to 7

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Difficulty Concentrating Over Days 3 to 7

End point description:

VAS is self-assessed tool to record the treatment effects on relief of difficulty concentrating. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of difficulty concentrating and 100 indicated complete relief of difficulty concentrating. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 3 to 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	10		
Units: unit on scale				
least squares mean (standard error)	31.95 (± 9.275)	33.87 (± 5.866)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.864
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22
upper limit	25.83

Secondary: Mean of Daily Self-assessed VAS Ratings of Relief of Difficulty Concentrating Over Days 8 to 14

End point title	Mean of Daily Self-assessed VAS Ratings of Relief of Difficulty Concentrating Over Days 8 to 14

End point description:

VAS is self-assessed tool to record the treatment effects on relief of difficulty concentrating. VAS scale ranges from 0 to 100 mm. 0 indicated no relief of difficulty concentrating and 100 indicated complete relief of difficulty concentrating. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Days 8 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: unit on scale				
least squares mean (standard error)	49.76 (± 9.333)	41.86 (± 8.348)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.548
Method	ANOVA
Parameter estimate	Estimated mean difference
Point estimate	-7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.51
upper limit	21.71

Secondary: Perceived Change in Self-efficacy in Quitting Smoking at Week 1 Visit

End point title	Perceived Change in Self-efficacy in Quitting Smoking at Week 1 Visit

End point description:

Subjects' perceived change in self-efficacy in quitting smoking was recorded. Self-efficacy in quitting smoking was recorded on a 7-grade scale, where 1 indicated much less confident; 7 indicated much more confident. Missing data were imputed with 'Less confident (2)' on a 7-grade scale. Full analysis set included all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 1

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: unit on scale				
arithmetic mean (standard deviation)	4.7 (± 1.15)	5.0 (± 1.20)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051
Method	Wilcoxon (Mann-Whitney)

Secondary: Self- assessed Ratings of Change in Willpower to Quit Smoking After 2 Days

End point title	Self- assessed Ratings of Change in Willpower to Quit Smoking After 2 Days

End point description:

Subjects' self- assessed ratings of change in willpower to quit smoking was recorded. Self- assessed ratings in quitting smoking was recorded on a 7-grade scale, where 1 indicated much weaker willpower; 7 indicated much stronger willpower. Missing data were imputed with 'Weaker (2)' on 7-grade categorical scale for subjects who discontinued study prematurely or imputed using last observation carried forward for subjects who completed the study. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Day 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	107		
Units: unit on scale				
arithmetic mean (standard deviation)	4.4 (± 1.14)	4.5 (± 1.14)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.452
Method	Wilcoxon (Mann-Whitney)

Secondary: Self- assessed Ratings of Change in Willpower to Quit Smoking After 7 Days

End point title	Self- assessed Ratings of Change in Willpower to Quit Smoking After 7 Days

End point description:

Subjects' self- assessed ratings of change in willpower to quit smoking was recorded. Self- assessed ratings in quitting smoking was recorded on a 7-grade scale, where 1 indicated much weaker willpower; 7 indicated much stronger willpower. Missing data were imputed with 'Weaker (2)' on 7-grade categorical scale for subjects who discontinued study prematurely or imputed using last observation carried forward for subjects who completed the study. Full analysis set included all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Day 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: unit on scale				
arithmetic mean (standard deviation)	4.8 (± 1.11)	5.1 (± 1.05)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Self- assessed Ratings of Change in Willpower to Quit Smoking After 14 Days

End point title	Self- assessed Ratings of Change in Willpower to Quit Smoking After 14 Days

End point description:

Subjects' self- assessed ratings of change in willpower to quit smoking was recorded. Self- assessed ratings in quitting smoking was recorded on a 7-grade scale, where 1 indicated much weaker willpower; 7 indicated much stronger willpower. Missing data were imputed with 'Weaker (2)' on 7-grade categorical scale for subjects who discontinued study prematurely or imputed using last observation carried forward for subjects who completed the study. Full analysis set included all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Day 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: unit on scale				
arithmetic mean (standard deviation)	4.8 (± 1.32)	5.3 (± 1.29)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Nicorette Freshfruit Gum 4 mg
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Wilcoxon (Mann-Whitney)

Secondary: Self- assessed Ratings of Change in Willpower to Resist a Cigarette After 2 Days

End point title	Self- assessed Ratings of Change in Willpower to Resist a Cigarette After 2 Days

End point description:

Subjects' self- assessed ratings of change in willpower to resist a cigarette was recorded. Self- assessed ratings in quitting smoking was recorded on a 7-grade scale, where 1 indicated much weaker willpower; 7 indicated much stronger willpower. Missing data were imputed with 'Weaker (2)' on 7-grade categorical scale for subjects who discontinued study prematurely or imputed using last observation carried forward for subjects who completed the study. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'N' signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Day 2

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	107		
Units: unit on scale				
arithmetic mean (standard deviation)	4.4 (± 1.18)	4.6 (± 1.24)		

Statistical analyses

Statistical analysis title	statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.213
Method	Wilcoxon (Mann-Whitney)

Secondary: Self- assessed Ratings of Change in Willpower to Resist a Cigarette After 7 Days

End point title	Self- assessed Ratings of Change in Willpower to Resist a Cigarette After 7 Days

End point description:

Subjects' self- assessed ratings of change in willpower to resist a cigarette was recorded. Self- assessed ratings in quitting smoking was recorded on a 7-grade scale, where 1 indicated much weaker willpower; 7 indicated much stronger willpower. Full analysis set included all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Day 7

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: unit on scale				
arithmetic mean (standard deviation)	4.7 (± 1.11)	5.0 (± 1.21)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo

Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.045
Method	Wilcoxon (Mann-Whitney)

Secondary: Self- assessed Ratings of Change in Willpower to Resist a Cigarette After 14 Days

End point title	Self- assessed Ratings of Change in Willpower to Resist a Cigarette After 14 Days

End point description:

Subjects' self- assessed ratings of change in willpower to resist a cigarette was recorded. Self- assessed ratings in quitting smoking was recorded on a 7-grade scale, where 1 indicated much weaker willpower; 7 indicated much stronger willpower. Missing data were imputed with 'Weaker (2)' on 7-grade categorical scale for subjects who discontinued study prematurely or imputed using last observation carried forward for subjects who completed the study. Full analysis set included all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Day 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: unit on scale				
arithmetic mean (standard deviation)	4.7 (± 1.29)	5.2 (± 1.25)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of Subjects with Self-reported and CO-verified Smoking Abstinence at Week 1 and at the End of Study

End point title	Number of Subjects with Self-reported and CO-verified Smoking Abstinence at Week 1 and at the End of Study

End point description:

Number of subjects with self-reported and CO-verified smoking abstinence at Week 1 and at the end of study visits was reported. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects analyzed for specific arm.

End point type	Secondary

End point timeframe:

Week 1 and Week 2 (end of study)

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: Subjects				
Week 1 (n=109, 108)	1	1		
End of study (n=108, 108)	3	2		

Statistical analyses

Statistical analysis title	Statistical analysis week 1
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.369
Method	ANOVA
Parameter estimate	Estimated Rate mean difference
Point estimate	-1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.44
upper limit	1.72

Statistical analysis title	Statistical analysis (end of study)
Comparison groups	Nicorette Freshfruit Gum 4 mg v Placebo
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	ANOVA
Parameter estimate	Estimated Rate mean difference
Point estimate	-0.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.04
upper limit	2.19

Secondary: Mean Daily Number of Gums Used by study Subjects on Days 1 to 14

End point title	Mean Daily Number of Gums Used by study Subjects on Days 1 to 14

End point description:

Mean daily number of gums used by study subjects on Days 1 to 14 were reported. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects analyzed for specific arm.

End point type	Secondary

End point timeframe:

Days 1 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: number of gums				
arithmetic mean (standard error)				
Day 1 (n=110, 109)	8.5 (± 3.50)	7.2 (± 3.10)		
Day 2 (n=110, 107)	9.3 (± 3.43)	8.3 (± 3.61)		
Day 3 (n=109, 108)	9.1 (± 3.16)	8.6 (± 3.61)		
Day 4 (n=108, 106)	9.3 (± 3.63)	8.6 (± 3.62)		
Day 5 (n=110, 105)	9.3 (± 3.74)	8.2 (± 3.74)		
Day 6 (n=109, 109)	9.3 (± 3.68)	8.7 (± 3.76)		
Day 7 (n=109, 109)	9.0 (± 3.67)	8.5 (± 3.41)		
Day 8 (n=104, 107)	9.9 (± 3.69)	8.9 (± 3.70)		
Day 9 (n=105, 105)	9.7 (± 3.55)	9.1 (± 3.74)		
Day 10 (n=107, 106)	9.7 (± 3.65)	8.8 (± 3.78)		
Day 11 (n=106, 106)	9.4 (± 3.98)	8.7 (± 3.84)		
Day 12 (n=107, 106)	9.7 (± 3.70)	8.3 (± 3.84)		
Day 13 (n=108, 108)	10.0 (± 3.59)	8.5 (± 3.67)		
Day 14 (n=108, 107)	9.5 (± 3.92)	8.5 (± 3.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Daily Number of Cigarettes Smoked by Study Subjects on Days 1

to 14

End point title	Mean Daily Number of Cigarettes Smoked by Study Subjects on Days 1 to 14

End point description:

Mean daily number of cigarettes smoked by study subjects on Days 1 to 14 were reported. Full analysis set included all randomized subjects who received at least 1 dose of study drug. Here 'n' signifies number of subjects analyzed for specific arm.

End point type	Secondary

End point timeframe:

Days 1 to 14

End point values	Placebo	Nicorette Freshfruit Gum 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: number of cigarettes				
arithmetic mean (standard error)				
Day 1 (n=110, 109)	14.7 (± 7.22)	13.0 (± 8.45)		
Day 2 (n=110, 107)	13.7 (± 7.79)	11.2 (± 7.93)		
Day 3 (n=109, 108)	12.9 (± 7.46)	10.5 (± 7.21)		
Day 4 (n=108, 106)	12.3 (± 7.90)	10.1 (± 7.56)		
Day 5 (n=110, 105)	11.8 (± 7.11)	10.2 (± 7.59)		
Day 6 (n=109, 109)	11.3 (± 7.39)	9.7 (± 7.39)		
Day 7 (n=109, 109)	11.4 (± 7.62)	8.7 (± 6.57)		
Day 8 (n=104, 107)	11.2 (± 7.79)	9.1 (± 7.25)		
Day 9 (n=105, 105)	10.8 (± 7.44)	8.5 (± 7.07)		
Day 10 (n=107, 106)	10.6 (± 7.25)	8.0 (± 7.37)		
Day 11 (n=106, 106)	10.7 (± 8.12)	7.9 (± 6.98)		
Day 12 (n=107, 106)	10.3 (± 7.63)	8.2 (± 7.02)		
Day 13 (n=108, 108)	10.4 (± 7.50)	7.9 (± 7.33)		
Day 14 (n=108, 107)	10.4 (± 7.83)	7.8 (± 7.17)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 5 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo Freshfruit E104 gum maximum 15 gums per day from Days 1 to 14 or until day before end of study visit.	
Reporting group title	Nicorette Freshfruit Gum 4 mg
Reporting group description:	
Subjects received Nicorette Freshfruit gum 4 milligram (mg) maximum 15 gums per day orally from Days 1 to 14 or until day before end of study visit.	

Serious adverse events	Placebo	Nicorette Freshfruit Gum 4 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 110 (0.00%)	0 / 110 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Nicorette Freshfruit Gum 4 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 110 (9.09%)	42 / 110 (38.18%)	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 110 (1.82%)	9 / 110 (8.18%)	
occurrences (all)	2	9	
Headache			
subjects affected / exposed	4 / 110 (3.64%)	6 / 110 (5.45%)	
occurrences (all)	5	6	
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	0 / 110 (0.00%)	18 / 110 (16.36%)	
occurrences (all)	0	18	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	0 / 110 (0.00%)	6 / 110 (5.45%)	
occurrences (all)	0	6	
Throat Irritation			
subjects affected / exposed	5 / 110 (4.55%)	16 / 110 (14.55%)	
occurrences (all)	5	16	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported