Sponsor

Novartis

Generic Drug Name

NIC002 vaccine

Trial Indication(s)

Cigarette smoking

Protocol Number

CNIC002A2201

Protocol Title

A double blind, placebo-controlled, multi-center study to evaluate the efficacy, safety, tolerability and immunogenicity of repeated s.c. Administrations of 100 µg NIC002 vaccine in cigarette smokers who are motivated to quit smoking

Clinical Trial Phase

Phase IIa

Study Start/End Dates

04-Aug-2008 to 01-Nov-2009

Reason for Termination (If applicable)

Not Applicable

Study Design/Methodology

This study was a multi-center, randomized, double blind, placebo-controlled study.

Centers

Germany (2)

Objectives:

Primary objective:

- To test the hypothesis that treatment with NIC002 increases the 4-week rate of continuous abstinence from smoking between weeks 8 and 12 inclusive compared with placebo.

Secondary objectives

- To further evaluate clinical efficacy of NIC002 in smokers willing to quit, as determined by:

the rate of continuous abstinence from smoking for Weeks 8 through 26, Weeks 26 though 52 and Weeks 8 through 52.

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Test Product (s), Dose(s), and Mode(s) of Administration

Investigational treatment: NIC002 vaccine 100 µg delivered subcutaneous (s.c.).

Statistical Methods

The primary efficacy measure was the 4-week rate of continuous abstinence from smoking between weeks 8 and 12 inclusive. This was based on self-report of no smoking or use of any nicotine-containing products during the specified time period and confirmed by an exhaled CO measurement below 10 ppm. Assessments from Visits 11 through 14 inclusive (effectively covering the time period between Weeks 8 and 12) were used for this purpose. Continuous abstinence rates for Weeks 8 through 26, Weeks 26 through 52 and Weeks 8 through 52 will be defined similarly, based on assessments from visits covering the specified time period. The primary objective of the study was to test the hypothesis that the 4-week continuous abstinence rate between Weeks 8 and 12 was significantly greater with NIC002 than with placebo. This test was conducted at the two-sided 0.05 significance level on the Full

Analysis Set (FAS) comprising all randomized subjects who receive a least one injection of study drug. Subjects in the FAS were analyzed according to treatment assigned. The sample size (100 active / 100 placebo) provided approximately 90% power to detect a difference of 22% in the continuous abstinence rate for Weeks 8 through 12 between NIC002 and placebo, assuming abstinence in the active group was 48% and 26% in the placebo group. The primary efficacy analysis was conducted using a chi-square test. The odds ratio and absolute risk difference for NIC002 vs placebo was provided with 95% confidence intervals. Continuous abstinence for Weeks 8 through 26, Weeks 8 through 52 and Weeks 26 through 52, as well as point prevalence of abstinence, were analyzed similarly.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

- Healthy male and female smoking subjects age 18 to 65 years of age.
- Subjects must be smoking 10 or more cigarettes per day during the past 12 months prior to Week 0, with no period of abstinence longer than 7 days in the previous 3 months.
- The exhaled breath carbon monoxide (CO) concentration must be 10 ppm or more at screening. Urine cotinine at screening must be positive.
- The Fagerstrom Test for Nicotine Dependence (FTND) score of 5 or above at screening.

Exclusion Criteria:

- Attempted to quit smoking in the three (3) months.
- Prior use of smoking cessation aid.
- Females of child bearing potential.

Participant Flow Table

Subject disposition – n (%) of subjects (Randomized set)

	NIC002 100µg N=100 n (%)	Placebo N=100 n (%)	Total N=200 n (%)
Subjects			
Randomized	100	100	200
Completed	60 (60.0)	67 (67.0)	127 (63.5)
Discontinued	40 (40.0)	33 (33.0)	73 (36.5)
Main cause of discontinuation			
Adverse event(s)	12 (12.0)	8 (8.0)	20 (10.0)
Subject withdrew consent	20 (20.0)	17 (17.0)	37 (18.5)
Lost to follow-up	8 (8.0)	8 (8.0)	16 (8.0)

Baseline Characteristics

Demographic summary by treatment group (Randomized set)

		NIC002 100µg N=100 n (%)	Placebo N=100 n (%)
Age (years)			
	n	100	100
	Mean	46.4	47.6
	SD	9.08	8.99
	Median	46.0	48.0
	Minimum	23	24
	Maximum	64	64
Gender – n (%)			
	Male	69 (69.0)	63 (63.0)
	Female	31 (31.0)	37 (37.0)
Race – n (%)			
	Caucasian	100 (100.0)	100 (100.0)
Ethnicity – n (%)			
	[1]Other	100 (100.0)	100 (100.0)
Weight (kg)			
	n	100	100
	Mean	79.2	80.3
	SD	12.95	15.65
	Median	78.9	77.8
	Minimum	54	48
	Maximum	118	117

	NIC002 100µg N=100 n (%)	Placebo N=100 n (%)

Height (cm)			
	n	100	100
	Mean	173.9	174.0
	SD	8.57	9.52
	Median	175.0	174.0
	Minimum	152	157
	Maximum	191	198
BMI (kg/m^2)			
	n	100	100
	Mean	26.1	26.5
	SD	3.57	4.40
	Median	25.5	25.8
	Minimum	18.8	18.2
	Maximum	35.0	35.4

***** Subjects reported as other ethnicity were neither Hispanic/Latino, Chinese, Indian (subcontinent), Japanese, nor mixed ethnicity

Summary of Efficacy

Primary and Secondary Outcome Result(s)

Self-Reported Smoking Status: Continuous Abstinence

Weeks	NIC002 100µg n/N [%]	Placebo n/N [%]	Absolute risk difference 80% CI	Odds ratio 80% CI	p-value*
Primary Endpoint					
8-12	13/100 [13]	18/100 [18]	-0.05 (-0.12, 0.02)	0.68 (0.41, 1.13)	0.329
Primary Endpoint (sensitivity analysis[1])					
8-12	13/100 [13]	17/100 [17]	-0.04 (-0.10, 0.02)	0.73 (0.44, 1.22)	0.428
Secondary Endpoints					
8-26	9/100 [9]	15/100 [15]	-0.06 (-0.12, 0.00)	0.56 (0.32, 0.99)	0.192
26-52	10/100 [10]	15/100 [15]	-0.05 (-0.11, 0.01)	0.63 (0.36, 1.10)	0.285
8-52	7/100 [7]	14/100 [14]	-0.07 (-0.13, -0.01)	0.46 (0.25, 0.86)	0.106

n = number of abstainers
N = total number of subjects in treatment group
[1]subject assumed to be smoking for any missing visits between Weeks 8 and 12
Subjects that withdrew prematurely were assumed to be smokers
*p-value from a chi-square test

Summary of Safety

Safety Results

Number (%) of subjects with AEs by primary system organ class and treatment group (Safety set)

	NIC002 100µg N=100 n (%)	Placebo N=100 n (%)	Total N=200 n (%)
Any primary system organ class	87 (87.0)	86 (86.0)	173 (86.5)
Cardiac disorders	2 (2.0)	1 (1.0)	3 (1.5)
Ear and labyrinth disorders	2 (2.0)	2 (2.0)	4 (2.0)
Endocrine disorders	0	2 (2.0)	2 (1.0)
Eye disorders	1 (1.0)	5 (5.0)	6 (3.0)
Gastrointestinal disorders	18 (18.0)	23 (23.0)	41 (20.5)
General disorders and administration site conditions	50 (50.0)	17 (17.0)	67 (33.5)
Hepatobiliary disorders	1 (1.0)	0	1 (0.5)
Immune system disorders	1 (1.0)	1 (1.0)	2 (1.0)
Infections and infestations	49 (49.0)	49 (49.0)	98 (49.0)
Injury, poisoning and procedural complications	6 (6.0)	6 (6.0)	12 (6.0)
Investigations	4 (4.0)	2 (2.0)	6 (3.0)
Metabolism and nutrition disorders	1 (1.0)	2 (2.0)	3 (1.5)
Musculoskeletal and connective tissue disorders	19 (19.0)	29 (29.0)	48 (24.0)
Nervous system disorders	30 (30.0)	24 (24.0)	54 (27.0)
Psychiatric disorders	5 (5.0)	5 (5.0)	10 (5.0)
Renal and urinary disorders	3 (3.0)	1 (1.0)	4 (2.0)
Reproductive system and breast disorders	2 (2.0)	0	2 (1.0)
Respiratory, thoracic and mediastinal disorders	7 (7.0)	9 (9.0)	16 (8.0)
Skin and subcutaneous tissue disorders	11 (11.0)	6 (6.0)	17 (8.5)
Vascular disorders	6 (6.0)	4 (4.0)	10 (5.0)

Primary system organ classes are sorted in alphabetical order
A subject with multiple primary system organ class is counted only once in any system organ class row

Number (%) of subjects with AEs (at least 5% in any group) by preferred term and treatment group (Safety set)

	NIC002 100µg N=100 n (%)	Placebo N=100 n (%)	Total N=200 n (%)
Subjects with any AEs	87 (87.0)	86 (86.0)	173 (86.5)
Nasopharyngitis	35 (35.0)	36 (36.0)	71 (35.5)
Headache	24 (24.0)	17 (17.0)	41 (20.5)
Chills	24 (24.0)	2 (2.0)	26 (13.0)
Pyrexia	16 (16.0)	5 (5.0)	21 (10.5)
Influenza like illness	12 (12.0)	4 (4.0)	16 (8.0)
Bronchitis	10 (10.0)	8 (8.0)	18 (9.0)
Fatigue	8 (8.0)	5 (5.0)	13 (6.5)
Diarrhoea	7 (7.0)	6 (6.0)	13 (6.5)
Rhinitis	7 (7.0)	6 (6.0)	13 (6.5)
Feeling cold	6 (6.0)	1 (1.0)	7 (3.5)
Hyperhidrosis	6 (6.0)	1 (1.0)	7 (3.5)
Malaise	6 (6.0)	0	6 (3.0)
Arthralgia	5 (5.0)	7 (7.0)	12 (6.0)
Pain	5 (5.0)	1 (1.0)	6 (3.0)
Back pain	4 (4.0)	10 (10.0)	14 (7.0)
Nausea	4 (4.0)	7 (7.0)	11 (5.5)
Dizziness	2 (2.0)	5 (5.0)	7 (3.5)
Pulpitis dental	1 (1.0)	5 (5.0)	6 (3.0)
Vomiting	1 (1.0)	5 (5.0)	6 (3.0)
Arthritis	0	6 (6.0)	6 (3.0)

Preferred terms are sorted in descending frequency as reported in the active treatment column
A subject with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment

Serious Adverse Events

	NIC002 100µg N=100	Placebo N=100	Total N=200
Angioedema	1	0	1
Bursitis	1	0	1
Cholelithiasis	1	0	1
Hemorrhoids	1	0	1
Osteoarthritis	0	1	1
Rib fracture	1	0	1
Rotator cuff syndrome	1	0	1
Syncope	1	0	1
Tenosynovitis	0	1	1
Tonsillitis	1	0	1

All SAEs were reported at an incidence of 1 subject each.

No death occurred in this study.

Other Relevant Findings

None

Date of Clinical Trial Report

23-Nov-2010