ClinicalTrials.gov ID: NCT00560313

Study Identification

Unique Protocol ID:	V72P4
Brief Title:	Safety, Tolerability and Immunogenicity of Three Doses of Novartis Meningococcal B Vaccine When Administered to Healthy At-risk Adults
Official Title:	A Phase 2, Multi-Center, Open-label Study of the Safety, Tolerability and Immunogenicity of Novartis Meningococcal B Recombinant Vaccine When Administered at a 0, 2, 6-Month Schedule and of a Single Dose of Novartis Meningococcal ACWY Conjugate Vaccine in Healthy At-risk Adults 18-50 Years of Age
Secondary IDs:	2007-001563-29

Study Status

Record Verification:	December 2011
Overall Status:	Completed
Study Start:	July 2007
Primary Completion:	November 2009 [Actual]
Study Completion:	November 2009 [Actual]

Sponsor/Collaborators

Sponsor:	Novartis Vaccines
Responsible Party:	Sponsor
Collaborators:	Novartis Vaccines

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 341/07 Board Name: Comitato Etico Locale per la Sperimentazione Clinica dei Medicinali Board Affiliation: Azienda Ospedaliera Universitaria Senese Phone: 0577 233204 Email:
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	Germany: Paul-Ehrlich-Institut

Study Description

Brief Summary:	This study is aimed to evaluate safety, tolerability and immunogenicity of three doses of Novartis 4CMenB and of one dose of Novartis Meningococcal ACWY vaccine when administered to healthy at-risk adults.
Detailed Description:	

Conditions

Conditions:	Meningococcal Disease
Keywords:	Meningococcal disease prevention vaccination

Study Design

Study Type:	Interventional
Primary Purpose:	Prevention
Study Phase:	Phase 2
Intervention Model:	Crossover Assignment
Number of Arms:	2
Masking:	Open Label

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 54 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 4CMenB	Biological/Vaccine: 4CMenB All subjects received the study vaccine following a 0,2,6 vaccination schedule. Pre-filled syringe, administered by intramuscular injection into the deltoid area of the non dominant arm.
Experimental: MenACWY CRM	Biological/Vaccine: Men ACWY CRM A single dose of a 0.5 mL injectable solution

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 50 Years

Gender: Both

Accepts Healthy Volunteers?: Yes

Criteria: Inclusion Criteria:

- Healthy adults,18 through 50 years of age, who were or might be routinely exposed to N. meningitidis cultures

Exclusion Criteria:

- Previous ascertained or suspected disease caused by N. meningitidis;
- Pregnancy or breastfeeding;
- History of any anaphylactic shock, asthma, urticaria or other allergic reaction after previous vaccinations or known hypersensitivity to any vaccine component;
- Any present or suspected serious acute or chronic disease
- Known or suspected autoimmune disease or impairment /alteration of immune function

Contacts/Locations

Study Officials: Novartis Vaccines

Study Director
Novartis Vaccines and Diagnostics

Locations: Italy
Azienda USL 7 of Siena
Siena, Italy, 53100

References

Citations: [Study Results] Kimura A, Toneatto D, Kleinschmidt A, Wang H, Dull P. Immunogenicity and safety of a multicomponent meningococcal serogroup B vaccine and a quadrivalent meningococcal CRM197 conjugate vaccine against serogroups A, C, W-135, and Y in adults who are at increased risk for occupational exposure to meningococcal isolates. Clin Vaccine Immunol. 2011 Mar;18(3):483-6. doi: 10.1128/CVI.00304-10. Epub 2010 Dec 22. PubMed 21177912

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	Participants were enrolled at one site in Italy and one site in Germany.
Pre-Assignment Details	Approximately 250 adults were planned to be enrolled in this study but only a total of 54 subjects were enrolled after the screening for the inclusion and exclusion criteria.

Reporting Groups

	Description
4CMenB	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB

Overall Study

	4CMenB
Started	54
Completed	48
Not Completed	6

	4CMenB
Adverse Events or Death	2
Withdrawal by Subject	2
Lost to Follow-up	1
Protocol Violation	1

Baseline Characteristics

Reporting Groups

	Description
4CMenB	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB

Baseline Measures

	4CMenB
Number of Participants	54
Age, Continuous [units: years] Mean (Standard Deviation)	31.8 (6.1)
Gender, Male/Female [units: participants]	
Female	27
Male	27

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Geometric Mean Titer of the Meningococcal B Vaccine Against the Different Strains at One Month After First, Second and Third Vaccination.
Measure Description	Geometric mean titers(GMT) and the respective confidence intervals measured after each vaccination against the three different meningococcal strains.
Time Frame	One month after vaccinations
Safety Issue?	No

Analysis Population Description

The analysis was done on the per protocol population.

Reporting Groups

	Description
4CMenB (44/76-SL)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Response was measured against (44/76-SL) strain
4CMenB (5/99)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Response was measured against the (5/99)strain
4CMen B (NZ98/254)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Response was measured against the (NZ98/254)strain.

Measured Values

	4CMenB (44/76-SL)	4CMenB (5/99)	4CMen B (NZ98/254)
Number of Participants Analyzed	46	46	46
Geometric Mean Titer of the Meningococcal B Vaccine Against the Different Strains at One Month After First, Second and Third Vaccination. [units: titer] Geometric Mean (95% Confidence Interval)			
Baseline titer	2.5 (1.7 to 3.5)	2.3 (1.6 to 3.2)	1.8 (1.3 to 2.6)
Post dose 1 titer (N=25)	33 (15 to 72)	29 (14 to 60)	23 (11 to 49)
Post dose 2 titer	93 (71 to 121)	144 (108 to 193)	32 (21 to 48)
Before dose 3 titer(N=24)	26 (15 to 47)	37 (26 to 53)	9.4 (4.1 to 21)
Post dose 3 titer (N=39)	95 (68 to 131)	269 (205 to 354)	30 (18 to 50)

2. Primary Outcome Measure:

Measure Title	Percentages of Participants With Serum Bactericidal Activity of the Meningococcal B Vaccine Against Different Strains at One Month After First, Second and Third Vaccination.

Measure Description	Percentage of participants with serum bactericidal activity (SBA) of the Meningococcal ACWY vaccine at one month after vaccination against A, C, W-135 and Y strains. Bactericidal activity (% ≥ 1:4, i.e., percentage of subjects with BCA titer ≥ 1:4; % ≥ 1:8, i.e. percentage of subjects with BCA titer ≥ 1:8) against a panel of genetically distinct meningococcal B strains: • prior to the first vaccination • 30 days following the first, second, prior to the third and 30 days after the third vaccination
Time Frame	One month after vaccinations
Safety Issue?	No

Analysis Population Description

The analysis was done on the per protocol population.

Reporting Groups

	Description
4CMenB (44/76-SL)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Response was measured against (44/76-SL) strain
4CMenB (5/99)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Response was measured against the (5/99) strain
4CMen B (NZ98/254)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Response was measured against the (NZ98/254) strain.

Measured Values

	4CMenB (44/76-SL)	4CMenB (5/99)	4CMen B (NZ98/254)
Number of Participants Analyzed	46	46	46
Percentages of Participants With Serum Bactericidal Activity of the Meningococcal B Vaccine Against Different Strains at One Month After First, Second and Third Vaccination. [units: percentage] Number (95% Confidence Interval)			
titer ≥4 (Baseline)	37 (23 to 52)	37 (23 to 52)	22 (11 to 36)
titer ≥4 (Post dose 1) N=25	84 (64 to 95)	88 (69 to 97)	80 (59 to 93)
titer ≥4 (Post dose 2)	100 (92 to 100)	100 (92 to 100)	91 (79 to 98)
titer ≥4 (Before dose 3) N=24	96 (79 to 100)	100 (86 to 100)	67 (45 to 84)

	4CMenB (44/76-SL)	4CMenB (5/99)	4CMen B (NZ98/254)
titer ≥4 (Post dose 3) N=39	97 (87 to 100)	100 (91 to 100)	92 (79 to 98)
titer ≥8 (Baseline)	26 (14 to 41)	15 (6 to 29)	15 (6 to 29)
titer ≥8 (Post dose 1) N=25	80 (59 to 93)	76 (55 to 91)	72 (51 to 88)
titer ≥8 (Post dose 2)	100 (92 to 100)	100 (92 to 100)	83 (69 to 92)
titer ≥8 (Before dose 3) N=24	75 (53 to 90)	100 (86 to 100)	54 (33 to 74)
titer ≥8 (Post dose 3) N=39	97 (87 to 100)	100 (91 to 100)	77 (61 to 89)
≥4 fold increase (Post dose 1) N=25	80 (59 to 93)	64 (43 to 82)	68 (46 to 85)
≥4 fold increase (Post dose 2)	100 (92 to 100)	100 (92 to 100)	78 (64 to 89)
≥4 fold increase (Before dose 3) N=24	71 (49 to 87)	75 (53 to 90)	46 (26 to 67)
≥4 fold increase (Post dose 3) N=39	92 (79 to 98)	100 (91 to 100)	69 (52 to 83)

3. Primary Outcome Measure:

Measure Title	Geometric Mean Titer (GMT) of the Meningococcal ACWY Vaccine at One Month After Vaccination.
Measure Description	Geometric mean titer (GMT) of the Meningococcal ACWY Vaccine at One Month After the Immunization against the A, C, W-135 and Y strains.
Time Frame	One month after vaccinations
Safety Issue?	No

Analysis Population Description

The analysis was done on the per protocol population.

Reporting Groups

	Description
MenACWY-CRM (A)	1 month postvaccination with quadrivalent meningococcal conjugate vaccine (MenACWY-CRM)
MenACWY-CRM (C)	1 month postvaccination with quadrivalent meningococcal conjugate vaccine (MenACWY-CRM)
MenACWY-CRM (W-135)	1 month postvaccination with quadrivalent meningococcal conjugate vaccine (MenACWY-CRM)
MenACWY-CRM (Y)	1 month postvaccination with quadrivalent meningococcal conjugate vaccine (MenACWY-CRM)

Measured Values

	MenACWY-CRM (A)	MenACWY-CRM (C)	MenACWY-CRM (W-135)	MenACWY-CRM (Y)
Number of Participants Analyzed	23	23	23	23
Geometric Mean Titer (GMT) of the Meningococcal ACWY Vaccine at One Month After Vaccination. [units: titer] Geometric Mean (95% Confidence Interval)	54 (34 to 85)	42 (27 to 66)	90 (58 to 139)	36 (16 to 81)

4. Primary Outcome Measure:

Measure Title	Percentage of Participants With Serum Bactericidal Activity of the Meningococcal ACWY Vaccine at One Month After Vaccination
Measure Description	Percentage of participants with serum bactericidal activity (SBA) of the Meningococcal ACWY vaccine at one month after vaccination against A, C, W-135 and Y strains. Bactericidal activity (% ≥ 1:4, i.e., percentage of subjects with BCA titer ≥ 1:4; % ≥ 1:8, i.e. percentage of subjects with BCA titer ≥ 1:8) against a panel of genetically distinct meningococcal B strains: • prior to the first vaccination • 30 days following the first, second, prior to the third and 30 days after the third vaccination
Time Frame	One month after vaccinations
Safety Issue?	No

Analysis Population Description

The analysis was done on the per protocol population.

Reporting Groups

	Description
MenACWY-CRM (A)	1 month postvaccination with quadrivalent meningococcal conjugate vaccine (MenACWY-CRM)
MenACWY-CRM (C)	1 month postvaccination with quadrivalent meningococcal conjugate vaccine (MenACWY-CRM)
MenACWY-CRM (W-135)	1 month postvaccination with quadrivalent meningococcal conjugate vaccine (MenACWY-CRM)
MenACWY-CRM (Y)	1 month postvaccination with quadrivalent meningococcal conjugate vaccine (MenACWY-CRM)

Measured Values

	MenACWY-CRM (A)	MenACWY-CRM (C)	MenACWY-CRM (W-135)	MenACWY-CRM (Y)
Number of Participants Analyzed	23	23	23	23
Percentage of Participants With Serum Bactericidal Activity of the Meningococcal ACWY Vaccine at One Month After Vaccination [units: percentage] Number (95% Confidence Interval)				
titers ≥ 4	96 (78 to 100)	100 (85 to 100)	100 (85 to 100)	83 (61 to 95)
titers ≥8	96 (78 to 100)	96 (78 to 100)	100 (85 to 100)	83 (61 to 95)

5. Primary Outcome Measure:

Measure Title	Number of Subjects Who Reported Solicited Local and Systemic Reactions Post Vaccination.
Measure Description	The number of subjects who reported solicited reactions after the administration of the Meningococcal B vaccine at a 0, 2, 6-month schedule and the administration of the Meningococcal A, C, W, and Y vaccine at month 7.
Time Frame	One month after vaccinations
Safety Issue?	Yes

Analysis Population Description

The analysis was done on the per protocol population.

Reporting Groups

	Description
4CMenB (Post Dose 1)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. We report Numbers (%) of Subjects with Local and Systemic Reactions as indicators of Reactogenicity, by Vaccination post dose 1
4CMenB (Post Dose 2)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. We report Numbers (%) of Subjects with Local and Systemic Reactions as indicators of Reactogenicity, by Vaccination post dose 2.
4CMenB (Post Dose 3)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. We report Numbers (%) of Subjects with Local and Systemic Reactions as indicators of Reactogenicity, by Vaccination post dose 3.

	Description
Men ACWY-CRM (One Dose)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. We report Numbers (%) of Subjects with Local and Systemic Reactions as indicators of Reactogenicity, by Vaccination post one dose of Men ACWY vaccine.

Measured Values

	4CMenB (Post Dose 1)	4CMenB (Post Dose 2)	4CMenB (Post Dose 3)	Men ACWY-CRM (One Dose)
Number of Participants Analyzed	53	52	50	41
Number of Subjects Who Reported Solicited Local and Systemic Reactions Post Vaccination. [units: participants]				
Injection pain (any)	52	50	50	10
Injection pain (severe)	8	7	9	0
Erythema (any)	22	23	28	9
Erythema (severe)	0	0	0	0
Induration (any)	23	24	29	5
Induration (severe)	0	0	0	0
Nausea (any)	7	5	9	4
Nausea (severe)	2	0	0	0
Malaise (any)	16	17	26	11
Malaise (severe)	3	1	2	1
Myalgia (any)	15	19	24	5
Myalgia (severe)	3	3	7	1
Arthralgia (any)	10	12	20	6
Arthralgia (severe)	0	0	3	0
Headache (any)	15	13	21	9
Headache (severe)	2	0	0	1
Fever (≥ 38°C)	2	1	0	2
Stayed home	5	4	5	2

	4CMenB (Post Dose 1)	4CMenB (Post Dose 2)	4CMenB (Post Dose 3)	Men ACWY-CRM (One Dose)
Analgesic, antipyretic medicine used	10	7	5	4

Reported Adverse Events

Time Frame	Adverse events were collected throughout the duration of the study (8 months).
Additional Description	Adverse events categorized as systematic assessment is defined as solicited adverse events.

Reporting Groups

	Description
4CMenB (1st Vaccination)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Post dose 1.
4CMenB (2nd Vaccination)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Post dose 2.
4CMenB (3rd Vaccination)	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Post dose 3.
Men ACWY-CRM	All participants were administered three doses of 4CMenB (0,2,6 months) and all were administered a single dose of MenACWY-CRM 1 month after the third dose of 4CMenB. Post dose 1 MenACWY.

Serious Adverse Events

	4CMenB (1st Vaccination)	4CMenB (2nd Vaccination)	4CMenB (3rd Vaccination)	Men ACWY-CRM
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/53 (0%)	0/52 (0%)	0/50 (0%)	0/41 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	4CMenB (1st Vaccination)	4CMenB (2nd Vaccination)	4CMenB (3rd Vaccination)	Men ACWY-CRM
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	52/53 (98.11%)	51/52 (98.08%)	50/50 (100%)	19/41 (46.34%)
Gastrointestinal disorders				
Nausea [A] *	7/53 (13.21%)	5/52 (9.62%)	9/50 (18%)	4/41 (9.76%)
General disorders				
Injection site erythema [A] †	22/53 (41.51%)	23/52 (44.23%)	28/50 (56%)	9/41 (21.95%)
Injection site induration [A] †	23/53 (43.4%)	24/52 (46.15%)	29/50 (58%)	5/41 (12.2%)
Injection site pain [A] [1] †	52/53 (98.11%)	50/52 (96.15%)	50/50 (100%)	10/41 (24.39%)
Malaise [A] †	16/53 (30.19%)	17/52 (32.69%)	26/50 (52%)	11/41 (26.83%)
Pyrexia [A] †	3/53 (5.66%)	1/52 (1.92%)	0/50 (0%)	2/41 (4.88%)
Infections and infestations				
Nasopharyngitis [A] *	0/53 (0%)	3/52 (5.77%)	3/50 (6%)	1/41 (2.44%)
Musculoskeletal and connective tissue disorders				
Arthralgia [A] †	10/53 (18.87%)	12/52 (23.08%)	20/50 (40%)	6/41 (14.63%)
Myalgia [A] †	15/53 (28.3%)	19/52 (36.54%)	24/50 (48%)	5/41 (12.2%)
Nervous system disorders				
Headache [A] †	16/53 (30.19%)	13/52 (25%)	21/50 (42%)	9/41 (21.95%)

† Indicates events were collected by systematic assessment.

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA

[1] After first vaccination

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

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